Volume 2; No. 1-2; 2025

Medicina Academica Integrativa

Journal for General Integrative Medicine

ISSN (Print): 3029-3308; ISSN (Online): 3029-3316

Volume 2; No. 1-2; 2025

Medicina Academica Integrativa

Journal for General Integrative Medicine

ISSN (Print): 3029-3308; ISSN (Online): 3029-3316

Published by
University of Mostar, Mostar, Bosnia and Herzegovina
University Publishing House PRESSUM
Zibeline International Publishing, Cyberjaya, Malaysia
Pro Mente d. o. o., Zagreb, Croatia
Journal is published biannually.
ISSN: 3029-3308 | eISSN: 3029-3316

MEDICINA ACADEMICA INTEGRATIVA

CONTENTS

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

INTEGRATIVE BIO/GEOMEDICINE AND HEALTH FOR ALL IN THE AI AGE

Miro Jakovljević[1] & Milenko Bevanda[2]

[1]University of Zagreb, School of Medicine, Zagreb, Croatia
[2]University of Mostar, School of Medicine, Mostar, Bosnia and Herzegovina

SUMMARY

Bio/Geomedicine with AI represents a powerful intersection between geography, medicine, and technology to improve medical understanding, prediction, decision-making and therapeutic effectiveness as well as health promotion and diseases prevention. This intersection provides a holistic transdisciplinary understanding of how life, environment, and health affect each other in order to promote health at all levels and predict, prevent, and manage diseases through an eco-geographical model. Human health is significantly influenced by the places where people live and work, including natural, man-made and social environments. Bio/geomedicine involves environmental epidemiology, public health planning and precision medicine and gives a hope for integrative holistic health care.

Key words: *integrative medicine, geohealth, medical geology, bio/geomedicine, health for all, artificial intelligence.*

*****

INTRODUCTION

In the past three decades much interests has been attracted by bio/geomedicine and geohealth concepts around the globe. Geohealth (geography and public/global health) is the discipline that focuses on the natural environment has impacted the health of plants, animals and humans (Finkelman 2025). Bio/Geomedicine (geography and personalized medicine) using artificial intelligence and modern technology may help physicians in more precise clinical understanding of their patients and more successful health care. The concept of bio/geomedicine is not new, it has a long past but a short history. It is well known that there is a strong connection between human and animal health and the state of environment. The ancient Greek Physician Hyppocrates (ca.460-370 BC), known to history as the "Father of Medicine" and the ancient Greek philosopher Aristotle (384-322 BC) recognized connection between the places in people live and their respective influence on individual and collective health. Paracelsus (1493-1541) called the "father of pharmacology" claimed that "all substances are poisons"… and "the right dosage differentiates a poison and a remedy". Medical geology is a field of geomedicine studying the relationship between natural geological factors and their effects on human health.

"Health for all in the 21st century" aims to help realize the vision of "Health for All", launched at the Alma-Ata conference in 1978. Committed action at all levels – global, regional, national and local – will be crucial to transforming the "Health for all and All for Health" vision into a practical and sustainable public and global health reality. This proclamation of the World Health Organization (WHO) is fundamental to achieve that every individual has access to the health services they need, regardless of the geographical position and economic status. Bio/Geomedicine with AI represent as a powerful intersection between geography, medicine, and technology may improve medical understanding, prediction, decision-making and treatment outcome in medical care and diseases prevention and likewise health promotion.

BIO/GEOMEDICINE: AN INTEGRATIVE HOLISTIC APPROACH

Bio/Geomedicine is a more and more important interdisciplinary and integrative field that studies the interaction between the environment and health at all levels, from individual, to public and global level. The air we breathe, the food we eat, the water we drink, and the ecosystems which sustain us are estimated to be responsible for 23 per cent of all death worldwide (Setia et al. 2016). The ultimate goals of health promotion as well as disease prediction, prevention, and person-centered treatment can be achieved with various disciplines to collaborate together and complement each other in additive (multidisciplinary), interactive (interdisciplinary) and holistic (transdisciplinary) way (see Kamel Boulos & Le Blond 2016). The focus of bio/geomedicine is on the impact of various factors such as climate specifics and changes, industrialization, agricultural production, deforestation, water and air pollution, demographic changes, population growth and e/migrations, natural disasters, political and socio-economic transformations, and cultural practices in the health-disease-illness processes. For bio/geomedicine as an interdisciplinary and intersectoriald field according the concept "One health – One medicine" the earth as well as the population and its environment is the patient (see Roa-Castellanos et al. 2016). The environment form

people as the environment are formed by people. Health is strongly influenced by the physical, social, mental, spiritual, cultural, economic, and political environment of the communities in which we live. Good health is both a resource for, and an aim of development at all levels.

The three terms bionomia (law or order of life), biophilia (love of life and nature) and bioempathy (ethical understanding of all life) are cornerstones of better understanding bio/geomedicine and human-nature/environment relationship. Bionomia refers to the principles or laws that govern life and how living beings interact with their environment. It represents the concept of natural order, sustainability, ecological harmony and balance. It is interesting that Erich Fromm coined the term "biophilia" meaning "passionate love of life and of all that is alive" what refers in general to the innate human affinity for nature and living beings. Biophilia represents the concept of connection, attraction, well-being, and nature-inspired design. Bioempathy is the capacity to cognitively understand and emotionally respect life from the perspective of other living beings, animals, plants, and ecosystems. Emphatizing individual, family, community and public commitment to health literacy is the best way towards health promotion.

Artificial intelligence (AI) enhances bio/geomedicine by analyzing vast and complex datasets that traditional statistical methods struggle with detecting patterns, make predestinations, and provide personalized recommendations based on spatial and environmental data. Geographic information system (GIS) is "computerized system that relates and displays data collected from a geographic entity in the form of a map (see Setia et al. 2016). Moulding of AI and the GIS dimension creates geospatial artificial intelligence (GeoAI), a more intelligent, predictive, and automated analysis. The use of GeoAI in medicine has tremendous potential in changing the way we understand, diagnose, and respond to health issues as well as in improving public health and addressing global health challenges (Amponsah et al. 2023). Precision medicine is an effort to tailor prevention and treatment strategies through considering individual variability in genetics, environment and life-style. Bio/geomedicine has the potential to transform the way physicians see patients and to provide a more holistic view of the many hidden factors that often defeat achieving successful long-term health outcomes (Setia et al. 2016). Applications of AI in precision medicine have included using machine learning for prediction of patient diagnosis and outcome (Kamel Boulos et al. 2019).

HEALTH FOR ALL IN THE 21ST CENTURY: IS IT UTOPIAN VISION IN AN ANTIUTOPIAN WORLD?

"Our task must be to free ourselves…by widening our circle of compassion to embrace all living creatures and the whole nature and its beauty."
– Albert Einstein (1879-1955)

"Health for all" is the slogan of an idealistic humanistic project of the World Health Organization (WHO) that has been initiated in the 1970s to promote global health, human dignity, well-being and quality of life to be attained by the year 2000. "Health for All in the 21st century" is aimed to "provision of the highest attainable standard of health as a fundamental right; continued and strengthened application of ethics to health policy, research and service provision; implementation of equity-oriented policies and strategies that emphasize solidarity; and incorporation of a gender perspective into health policies and strategies (https://apps.who.int/gb/ebwha/pdf_files/EB101/pdfangl/ang8.pdf). "Health for all and All for Health" sounds as a utopia but we have still a real hope to make progress through the emphatizing culture of global mind to lay the foundations for the earth sustainability and global health enlightenment (Jakovljevic). It seems bio/geomedicine is moving toward becoming practical in contributing to global health, in other words to health for all. However, can "health for all" be achieved in a fundamentally unequal world and within capitalistic system in which the goals of equity, egalitarianism and inclusion are undervalued by commodification, profit-making, inequality and division (Kehr et al. 2023). The concept "health for all" is related to concepts of human rights for all, social justice, solidarity and culture of empathization. Bio/geomedicine and "health for all" attend to language of ethical universalism, epistemic justice, and global health, collective welfare and social security. Bio/geomedicine may be a great support to "WHO as the world's health conscience to advocate global health and health equity between and within countries; identify policies and practices that benefit or harm health; and protect the health of vulnerable and poor communities (https://apps.who.int/gb/ebwha/pdf_files/EB101/pdfangl/ang8.pdf). Health for all as one of the conceptual foundations for empathic civilizations in the age of the clash of civilizations can be a powerful bridge to peace.

CONCLUSIONS

In this century medical geology and bio/geomedicine have been recognized around the globe. Bio/Geomedicine is important interdisciplinary and integrative field that focuses on geographic location and environment into account when analyzing individual and public health. There is an emerging role for GeoAI in health and healthcare as location is an integral part of

both population and individual health. Health for all in the 21st century tends to ensure that everyone has access to essential health care and the opportunity to achieve appropriate health literacy and a high level of well-being enabling a productive life and self-actualization.

REFERENCES

1. Amponish, A., Latue, P., & Rakusa, H. (2023). *Utilization of GeoIA applications in the health sector: A review. Journal of Health Science and Medical Therapy, 1:49-60.*
2. Finkel, R.B. (2025). *Evolution from Medical Geology to GeoHealth and future development. China Geology, 8:471-474.*
3. Jakovljevic, M. Brave New Psychiatry (2024a): *Culture for empathy and mental health for all. Psychiatria Danubina; 36(suppl 2):S9-S14*
4. Jakovljevic, M. (2024b). *Global Mental Health Enlightenment and culture of empathy: How to navigate a world in existential crisis and wars. Psychiatria Danubina; 36:287-292*
5. Kamel Boulos, MN., Peng, G., VoPham, T. (2019): *An overview of GeoAI applications in health and healthcare. International Journal of Health Geographics 18, article number 7*
6. Kehr, J., Muinde, JVC., & Prince, R.J. (2023). *Health for all? Pasts, presents and futures of aspirations for universal healthcare. Social Science & Medicine 339;115660*
7. Roa-Castellanos, R.A., Anadon Baselga, M.J., & Capo Marti, M.A. (2016). *Biogeomedicine: The earth as the new patient for biomedical sciences under the "one health" concept facing climate change. Medicina Balear 31(3):11-17*
8. Setia, S., Singh, S., Mathur, A., Makkar, D.K. & Aggarwal, W.P. (2016). *Health care and geomedicine: A review. World Journal of Environmental Biosciences 6; 1:1-3*
9. World Health Organization: *Health for All in the 21st Century. https://apps.who.int/gb/ebwha/pdf_files/EB101/pdfangl/ang8.pdf*

Correspondence:
Miro Jakovljević, Professor Emeritus
School of Medicine, University of Zagreb
Šalata 3, 10000 Zagreb, Croatia
jakovljevic.miro@yahoo.com

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

HOW WELL DO WE SLEEP? – REVIEW OF SLEEP QUALITY AND ITS IMPORTANCE IN MENTAL HEALTH DISORDERS

Marijana Gajić & Nuša Kirbiš
Faculty of Health Sciences, University of Maribor, Slovenia
received: 03.02.2025; revised: 04.03.2025; accepted: 15.07.2025

SUMMARY

Introduction: *Sleep quality as a basic physiological need can be challenged in patients diagnosed with serious mental health disorders. Sleep disorders such as nightmares and insomnia can affect individuals greatly and in various ways, in some cases resulting in exacerbation of their primary mental health disorder. We took a closer look into the treatment of sleep disorders, focusing mainly on pharmacological treatment.*

Methods: *This review included three international databases were searched, with appropriate key words (sleep quality, sleep disorder, mental health disorder, pharmacological treatment, medicine). Literature no older than 10 years was consulted, limited to English language.*

Results: *Seven articles matched our search, where we got a closer look into pharmacological approaches in the treatment of sleep disorders. Results show the effects of variety of medicaments. In the treatment of insomnia olanzapine, quetiapine, zolpidem, trazodone and dimdazenil showed to be effective. Gabapentin has shown to be as effective as clonazepam in the treatment of sleep disturbances in depression. For the treatment of nightmares, prazosine and hydroxyzine showed effect in certain trials. However, this type of treatment combined with other, non-pharmacological approaches, such as cognitive behavioral therapy shows to be much more effective.*

Conclusion: *Effective treatment often combines pharmacological and non-pharmacological approaches, with a wide range of medications, including antipsychotics, antidepressants, benzodiazepines, and non-psychopharmacologic drugs, tailored to the specific disorder and sleep issue.*

Key words: *schizophrenia; post traumatic sleep disorder; depression; treatment; sleep quality.*

*****

INTRODUCTION

Representing one of the important basic physiological needs and a complex construct, sleep and sleep quality are a widely researched topic in the literature (Buysee et al. 1989, Fabbri et al. 2021, Irwin, 2015). Sleep represents a physiological, reversible state of rest characterized by reduced consciousness, limited sensory activity, and decreased voluntary muscle activity, during which the body recovers, regenerates with an aim of preparing for the upcoming everyday challenges (Buysse 2014). Taking into consideration the complexity of sleep quality, through concept analyses, sleep quality can be defined as an individual's overall satisfaction with various aspects of their sleep experience, assessed through numerous factors such as sleep efficiency, sleep latency, wake after sleep onset, and objective sleep architecture measures. It plays an essential role in maintaining health and well-being (Nelson et al. 2022). In the modern, busy world, sleep quantity shows a decrease, with an effect on its quality as well. The golden 8 hours of sleep a day seem to vary depending on the lifestyle, environment, physical and mental health status. However, sleep quality plays a more significant role in day to day life of an individual (Crivello et al. 2019, Kohyama 2021).

The well-known sleep structure, consisting of two basic phases: non-rapid eye movement sleep (NREM) and rapid eye movement (REM) sleep, is stimulated by brain's natural regulatory cycles. Naturally, throughout the night, we go through several cycles of these basic cycles which provide various benefits in regeneration of the body and mind. Disruption of this sleep pattern can affect its quality greatly, showing a negative effect on individual's daily functioning (Carley & Farabi 2016, Diagnostic and Statistical Manual of Mental Disorders 1994, Irwin 2015).

When it comes to measuring sleep quality, in practice we have subjective and objective methods (Crivello et al. 2019, Carley & Farabi 2016, Barbato 2021). The golden standard for objective evaluation of sleep quality is polysomnography (PSG), consisting of electroencephalogram (EEG), electrooculography (EOG), and electromyography (EMG).

It measures NREM stages 1 and 2, slow wave sleep (NREM stages 3 and 4) as well as rapid eye movement (REM) stage over the duration of sleep (Crivello et al. 2019, Barbato 2021, Irwin 2015).

On the other hand, subjective sleep quality measures fill in the gaps the objective measures can't reach. Despite the lack of its standard format, the gold standard for subjective sleep evaluation is sleep diary. It provides

insight into various details of one's night's sleep. Self-report questionnaires such as Pittsburgh's Sleep Quality Index (PSQI), with their pre-defined formats, represent great tools for getting information of special interest, focusing on different variables of sleep quality such as total sleep time, sleep onset latency, sleep efficiency, difficulties falling asleep, disturbances, medication use, and various others (Buysse et al. 1984, Crivello et al. 2019).

In this paper, we focus on exploring sleep quality, sleep disorders and the effects they have on mental health, as well as discuss the characteristics of pharmacological approaches in the treatment of sleep disorders among people diagnosed with serious mental health disorders, schizophrenia, depression and posttraumatic stress disorder in particular.

SLEEP DISORDERS AMONG SERIOUS MENTAL HEALTH DISORDERS

Changes in sleep patterns and sleep quality can lead to variety of potentially dangerous sleep disorders and even mental illnesses. Sometimes poor sleep quality is a consequence of other illnesses, but can also be their trigger or an initiator. More and more attention is paid to effects sleep has on mental health. Research recognizes the association of sleep disturbances not only with neurocognitive dysfunctions, attention deficits, struggles with cognitive performances but also with mental health disorders such as depression, anxiety, stress, schizophrenia and various others (Fabbri et al. 2021, Freeman et al. 2020, Mollayeva et al. 2016). In objective screening methods, sleep depth and REM variables are shown to be predictors of existing psychiatric comorbidity processes (Baglioni et al. 2016). Inclusion of various sleep quality treatments in the standard mental health disorders treatment may bring significant improvements in the overall mental health (Scott et al. 2021).

The main problems individuals diagnosed with a serious mental health disorder face are inadequate sleep during the night often resulting in insomnia, followed by impaired daytime functioning, also known as daytime sleepiness; sleep disturbances such as waking up, nightmares, snoring, sleep walking, muscle tension and various others (Fabbri et al. 2021).

Sleep is also shown to be a predictor of good socio-occupational functioning, which in individuals diagnosed with a serious mental illness may be compromised (Stafford et al. 2024) Among mental health disorders nightmares and insomnia are the most frequent sleep disorders to occur (Akkaoui et al. 2020).

1. Schizophrenia

Among people diagnosed with schizophrenia sleep disturbances are greatly present. Sleep disorders are not only prevalent in early psychosis, but also have effects on psychotic episodes, increasing their frequency and intensity (Davies et al. 2017, Freeman et al. 2020). Polysomnographic testing showed lower total sleep time and sleep efficiency, prolonged sleep onset latency and total awake time, as well as increase in stage one NREM, meanwhile the remaining sleep stages, including REM sleep are reduced. REM sleep can vary on the duration of the disorder, where a decrease in REM sleep was recorded in patients with a diagnosis of schizophrenia of over three years (Chan et al. 2017). Rapid eye movement stage in patients diagnosed with schizophrenia is characterized with shortened REM latency and increased REM density, which means that they enter the REM stage quickly but the eye movement activity is increased, which may result in more vivid dreams (Baglioni et al. 2016, Barbato 2023, Chan et al. 2017). Increased REM density could also be a predictor of insomnia (Barbato 2023).

When it comes to sleep disorders, insomnia, nightmares, troubles staying asleep, hypersomnia and irregular sleep patterns are most often recorded (Freeman et al. 2020, Seeman 2018, Waite et al. 2020). Nightmares in people diagnosed with schizophrenia come in more vivid scenarios, leaving a bigger impact than they would on an individual with no comorbidities regarding their mental health. Their importance is significant due to warning signs they give out, upcoming psychotic episode, cognitive decline, increased delusions, as well as risk of suicide. However, in the assessment and further patient's therapy, they're rarely discussed (Akkaoui et al. 2020, Seeman 2018).

2. Depression

Individuals diagnosed with depression commonly report changes in their sleep patterns, ranging from inability to fall asleep to hypersomnia, where they escape into sleep to manage the effect of symptoms the depression carries. When it comes to polysomnographic testing, the changes in REM sleep are noticeable.

The alteration of REM sleep is present in all its variables: latency, density and duration (Baglioni et al. 2016) REM latency is shortened, meanwhile the duration of REM sleep is prolonged and REM sleep intensity is increased (Baglioni et al. 2016, Barbato 2023, Seithikurippu et al. 2020).

In the typical symptomatology of depression, insomnia is the most common sleep disorder, affecting the individual's processes of thoughts, as well as daily functioning. However, in the atypical symptomatology, hypersomnia, defined as excessive sleepiness or prolonged sleep duration, as well as increased daytime sleepiness, can be present. In this subtype of depression are symptoms like mood reactivity, increased appetite, and sensitivity to rejection, also included (Murphy & Peterson 2015, Plante et al 2017).

When it comes to depression as a segment of bipolar disorder, changes in REM correlate to changes in mood of individuals diagnosed with bipolar disorder, exhibiting

in more early awakenings and less rapid eye movements, which can be a predictor of an upcoming depressive phase. In individuals with bipolar disorder, the density of the REM phase has shown to be significantly higher (Barbato 2023).

Frequent nightmares, which in people diagnosed with depression are doubled, compared to the healthy population, especially the vivid ones, can contribute to increased suicidality, or even suicide attempts among people with depression. In comparison to bipolar depression, nightmares are more frequent in individuals with unipolar depression (Akkaoui et al. 2020).

3. Post-traumatic stress disorders

Patients with post-traumatic stress disorder (PTSD) exhibit significant sleep dysfunctions, particularly in REM sleep. Meta-analytic reviews highlight that PTSD patients experience greater REM density, more stage 1 sleep, and reduced slow wave sleep compared to healthy individuals. Increased REM density persists even in chronic PTSD cases spanning decades and is notably higher in these patients compared to those with depressive disorders, though trauma-related nightmares correlate more with REM interruptions than density (Barbato 2023). Additionally, polysomnographic studies reveal decreased total sleep time, slow wave sleep, and sleep efficiency, alongside increased wake time after sleep onset in PTSD patients. Sleep efficiency and slow wave sleep percentage decline with greater PTSD severity, while REM sleep percentage is reduced in younger PTSD patients but not in older age groups. These findings confirm pervasive sleep abnormalities in PTSD (Barbato 2023, Zhang et al. 2019).

Nightmares are an important part of post-traumatic stress disorder, affecting up to 70% of diagnosed patients, which correlates with the severity of the disorder. Severity of the nightmares can sometimes lead to suicidal behavior as well (Akkaoui et al. 2020).

TREATMENT OF SLEEP DISORDERS

1. Pharmacological therapy

The results indicate that sleep disorders, including insomnia and nightmares, can be effectively managed through pharmacological treatments. Notably, a single class of medications is not solely responsible for achieving positive outcomes. Instead, various medication groups, used in combinations and tailored dosages, offer promising solutions for treating these conditions.

We highlighted several pharmacological approaches that align with our aims and are focused on the treatment of sleep disorders among psychiatric disorders, with various outcomes, from which the majority were quite effective (Table 1).

Table 1. Summary of pharmacological therapy for sleep disorders.

Authors	Research type	Interventions	Results
Feng et al. 2024	Meta-analysis	Olanzapine, quetiapine 50-800mg/day	effect in reduction of insomnia in sleep disorders among individuals diagnosed with psychotic disorders
Morin et al. 2023	RCT	1st stage CBT + Zolpidem (5-10mg/d) for 6 weeks 2nd stage = CBT + trazodone (50-150mg/d)	reduced daytime symptoms of insomnia improvement in daytime functions among healthy individuals as well as among those with a psychiatric comorbidity
Huang et al. 2024	Meta-analysis	Prazosine 1-15mg /day for 8 weeks Hydroxyzine 10-100mg /day for 8 weeks	reduced nightmare severity in individuals diagnosed with PTSD
Mowla et al. 2015	RCT	Gabapentin (100–600 mg/day) or Clonazepam (0.5–2 mg/day) / weeks along with current antidepressant therapy (sertraline, fluoxetine, citalopram)	Gabapentin has shown to be as effective as clonazepam in treatment of sleep disturbances in individuals diagnoses with depression
Raskind et al. 2018	RCT	Prazosine 2-15mg / day for 16 weeks	no significant effect on trauma-related nightmares in military veterans with a diagnose of PTSD
Kishi et al. 2024	Systematic review	Dual orexin receptor antagonists (DORAs) – suvorexant and lemborexant	No significant effect on insomnia in individuals diagnosed with psychiatric disorders
Ran et al. 2024	Systematic review	Dimdazenil 1.5 - 5 mg /day up to 2 weeks	Significant effect in reduction of insomnia (presence of psychiatric diagnoses was not specified)

Quetiapine, a medication from antipsychotic group used mainly in the treatment of psychotic disorders, showed positive effects in reduction of insomnia, along with olanzapine which contributed to good regulation of not only insomnia, but mania as well (Feng et al. 2024). These results show the universality of antipsychotic drugs, where, instead of the focus on their antipsychotic effects, their other qualities come into light. Dependable on the dose, these medicaments could potentially show an excellent effect in the treatment of sleep disorders among other psychiatric disorders as well, with calculated doses in the combination with their existing treatment, focusing on the individual needs of the patient.

Morin et al. (2023) report positive effects of a non-benzodiazepine sedative-hypnotic, zolpidem treatment combined with cognitive behavioral therapy for reducing insomnia symptoms in comparison to the control group using only behavioral therapies for insomnia. The second stage of their trial included a serotonin receptor antagonists and reuptake inhibitor medication, trazodone for non-remitters, after a 6 week therapy with zolpidem, with a controlled withdrawal schedule. The shift to trazodone contributed to increased daytime functions of individuals.

Huang et al. (2024) report reduction of nightmare severity in people with post-traumatic stress disorder while on prazosin and hydroxyzine treatment. Prazosin, a medication mainly known as an antihypertensive agent, has a significant effect in the treatment of nightmares as well, along with hydroxyzine, an antihistamine, in this case have shown to be of bigger priority in treatment of nightmares than other approaches. (Huang et al. 2024). However, in the trial including military veterans with posttraumatic stress disorders and trauma induced nightmares, prazosin as a medicine of choice hasn't shown significant effects on reducing the nightmare frequency and intensity (Raskind et al. 2018).

In comparison to clonazepam, which is a benzodiazepine medicament, with addictive side effects, gabapentin, an antiepileptic drug, has shown equal potency in regulating sleep problems in people diagnosed with depression, with lower risk of developing addiction (Mowla et al. 2015).

Dual orexin receptor antagonists (DORAs) work by blocking the both orexin receptors in the brain, which are in charge of regulating wakefulness, arousal and appetite, therefore, they have shown to be a safe and tolerable option in the treatment of sleeping problems in people diagnosed with mental disorders, even though the reviewed medications, suvorexant and lemborexant, haven't shown a very significant effect in the treatment of insomnia in particular (Kishi et al. 2024). The safety of these drugs offers a good path for the future testing, in potential combinations with other medicaments or for the purposes of the achieved treatments' maintenance.

Dimdazenil, as a benzodiazepine derivate with a moderate GABAα receptors activation, has shown significant improvement in certain objective and subjective sleep outcomes in individuals with insomnia, such as reduced sleep latency and increased total sleep time. These benefits stand out because these was no significant excessive daytime sleepiness or impairment of daytime functioning happening. Additionally, it has shown to be a very tolerable medication (Ran et al. 2024). By exploring the findings, with a focus on the cause of the insomnia, whether it be a underlying psychiatric diagnosis or a lifestyle obstacle, these results could be of an even bigger benefit to the future efficacy of dimdanezil as a medicament for sleep disorders' treatment.

The consulted literature emphasizes the presence of non-pharmacological approaches, mainly cognitive behavioral therapy in the treatment of sleep disorders, which is definitely an important segment of the treatment. Various methods of cognitive behavioral therapy can be applied and at the same time be very effective, especially if they're personalized, matching the person's habits, interests and wishes.

2. Non-pharmacological treatment

We can't forget the importance of non-pharmacological approaches in the treatment of sleep disorders in people diagnosed with mental health disorders. To make pharmacological treatment show its best results, another approaches are included such as cognitive behavioral therapy, exercising, or some other alternative approaches.

In many examples, cognitive behavioral therapy is considered a first line treatment, often applied together with medicaments. However, it comes in different forms and shapes, created according to the individual's needs (Hertenstein et al. 2022).

2.1. Cognitive behavioral therapy

Cognitive behavioral therapy in treating sleep disorders consists of sets of steps, aimed to modify one's daily habits related to sleep. In patients with mental health disorders, treatment is based on individual needs and triggers. Basic CBT techniques consist of ensuring adequate enviroment, stimulus control, stabilizing circadian rhythm, getting the bedtime routine in check, relaxation and productive daytime activities. Additionally, specific cognitive techniques can be included, such as imagery rehearsal, grounding techniques and reduction of hypnotic medicaments (Waite et al. 2016). Randomized controlled studies involving cognitive behavioral therapy for sleep disorders in the population of patients diagnosed with serious mental health disorder, report positive results regarding the reduction of sleep disorders, particularly nightmares and insomnia (Sheaves et al. 2019).

Image rehearsal therapy as a component of cognitive behavioral therapy, shows great results in the treatment of nightmares. It is based on rehearsing dreams, where individuals practice reshaping the nightmares they have into less disturbing dreams with a positive ending by imagining it on several occasions during the day (Van Schagen et al. 2016).

Sheaves et al. (2019), in their randomized controlled trial of imagery-focused cognitive therapy approach, report great patient satisfaction and reduction of nightmare severity, comorbid insomnia and persecutory delusions in their follow up assessments.

There is a noticeable positive response to cognitive behavioral therapy treatment for insomnia and nightmares in patients with psychosis, depressive disorders and post-traumatic stress disorders (Huang et al. 2024, Seeman 2018). Cognitive behavioral therapy is characterized with multiple different combinations of approaches, which can be adjusted to the individual's needs. We once again emphasize that the important segment of cognitive behavioral therapy is the collaboration with the patient, valuing and respecting their needs, habits, as well as wishes. Optimizing this kind of approach might not always be easy, but once done, can show great results.

2.2. Controlled sleep deprivation and sleep restriction

Sleep restriction, or restricting the time in bed, is a component of cognitive behavioral therapy for insomnia, which is based on restricting time spent in bed (Falloon et al. 2015, Steinmetz, et al. 2023). Short term effects on insomnia were reported in various samples. However, it shows a promising treatment method for long term effects in treatment of insomnia (Falloon et al. 2015, Kalmbach et al. 2019, Maurer et al. 2021).

Sleep deprivation, on the other hand, focuses on intentional sleep restriction, where an individual remain awake through the night with an aim to reset the circadian rhythm. It can be a complete or partial, depending on the severity of the sleep disturbance. As an addition to standard treatment, its effect is shown in short term alleviation of depressive symptoms in individuals diagnosed with depression or bipolar depression (He et al. 2023, Ioannou et al. 2021, Ramirez-Mahaluf et al. 2020, Xu et al. 2024). In some cases, improved effect of pharmacological therapy in combination with sleep deprivation, was reported (Ramirez-Mahaluf et al. 2020). With little to no side effects, this method is safe to use for depressive disorders, but not recommended for psychosis, due to risk of triggering a psychotic episode (Meyhöfer et al. 2017). As healthcare professionals, instead of primarily focusing on the mental or sleep disorder itself, our duty is to observe the person as a whole with all of their attributes, needs, and wishes, in order to provide the optimal, person centered, holistic care.

2.3. Other approaches

Acupuncture, a complementary medicine based approach, as an addition to the regular treatment of sleep disorders, has shown moderate positive results in treatment of insomnia, with minimal to no side effects to the patients (Bergdahl et al. 2016, Chung et al. 2018, Lee et al. 2020). Lucid dreaming therapy has shown some potential in the reduction of nightmare intensity (Ouchene et al. 2023). Regular exercise, low-impact cardio and resistance in particular, showed a significant improvement in sleep quality as well as quality of life in people diagnosed with schizophrenia (Tous-Espelosin et al. 2024, Xie et al. 2021). In addition to psychotherapeutic and pharmacological treatment, yoga as a form low impact exercise has shown to be helpful in insomnia management, as well as in improvement of everyday quality of life in people with serious mental health disorders (Bhatia et al. 2022, Broderick et al. 2017, Verma et al. 2022, Yin et al. 2024). Offering a variety of options to the individuals with sleep disorders helps them contribute to their own healing journey, improving their motivation and day to day life.

CONCLUSION

Sleep disorders in people diagnosed with serious mental health disorders are inevitable, followed by symptoms which can contribute to the development or exacerbation of the disorders themselves. Most common ones are insomnia and nightmares, which impact the daytime functioning greatly. Treatment of sleep disorders in the population of people with mental health disorders focuses mainly on non-pharmacological and pharmacological approaches, which in combination bring the optimal results. The pharmacological approaches vary depending on the mental health disorder itself and the existing sleep disorder. It's shown that a good variety of effective medicines exist, from antipsychotic and antidepressant drugs, to benzodiazepines, non-benzodiazepines, as well as other, non-psychopharmacologic, drug groups. The combination of adequate doses of medicaments, in combination of approaches for improving life quality can benefit the affected population greatly.

Limitations and suggestions for future research

In this review, the focus was mainly on schizophrenia, depression and posttraumatic stress disorder, whereas sleeping problems persist in other mental health disorders as well. Expansion of sources is a goal for the future, more extensive literature reviews, meta-analyses even.

Acknowledgements: None.

Conflict of interests: None.

Contributors:

Marijana Gajić: conceptualization, methodology, manuscript writing,
Nuša Kirbiš: conceptualization, data collection.

LITERATURE

1. Akkaoui MA, Lejoyeux M, d'Ortho M-P & Geoffroy PA: *Nightmares in patients with major depressive disorder, bipolar disorder, and psychotic disorders: A systematic review. J Clin Med 2020; 9(12):3990.*
2. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-4). 4th ed. Washington DC: American Psychiatric Association, 1994.*
3. Baglioni C, Nanovska S, Regen W, Spiegelhalder K, Feige B, Nissen C, Reynolds CF & Riemann D: *Sleep and mental disorders: A meta-analysis of polysomnographic research. Psychol Bull 2016; 142(9):969-990.*
4. Barbato G: *REM sleep: An unknown indicator of sleep quality. Int J Environ Res Public Health 2021; 18(24):12976.*
5. Barbato G: *Is REM density a measure of arousal during sleep? Brain Sci 2023; 13(3):378.*
6. Bergdahl L, Broman JE, Berman AH, Haglund K, von Knorring L & Markström A: *Auricular acupuncture and cognitive behavioural therapy for insomnia: A randomised controlled study. Sleep Disord 2016; (1):7057282.*
7. Bhatia T, Kumari N, Yadav A, Beniwal RP, Shah G, Joel W, Jones JR, Iyenger S, Nimgaonkar VL & Deshpande SN: *Feasibility, acceptability and evaluation of meditation to augment yoga practice among persons diagnosed with schizophrenia. Acta Neuropsychiatr 2022; 34(6):330-343.*
8. Buysse DJ: *Sleep health: Can we define it? Does it matter? Sleep 2014; 37(1):9-17.*
9. Buysse DJ, Reynolds III CF, Monk TH, Berman SR & Kupfer DJ: *The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989; 28(2):193-213.*
10. Broderick J, Crumlish N, Waugh A & Vancampfort D: *Yoga versus non-standard care for schizophrenia. Cochrane Database Syst Rev 2017; 9(9):CD012052.*
11. Carley DW & Farabi SS: *Physiology of sleep. Diabetes Spectrum 2016; 29(1):5.*
12. Chan MS, Chung KF, Yung KP & Yeung WF: *Sleep in schizophrenia: A systematic review and meta-analysis of polysomnographic findings in case-control studies. Sleep Med Rev 2017; 32:69-84.*
13. Chung KF, Yeung WF, Yu BY-M, et al.: *Acupuncture with or without combined auricular acupuncture for insomnia: A randomised, waitlist-controlled trial. Acupunct Med 2018; 36(1):2-13.*
14. Davies G, Haddock G, Yung AR, Mulligan LD & Kyle SD: *A systematic review of the nature and correlates of sleep disturbance in early psychosis. Sleep Med Rev 2017; 31:25-38.*
15. Fabbri M, Beracci A, Martoni M, Meneo D, Tonetti L & Natale V: *Measuring subjective sleep quality: A review. Int J Environ Res Public Health 2021; 18(3):1082.*
16. Falloon K, Elley CR, Fernando A, Lee AC & Arroll B: *Simplified sleep restriction for insomnia in general practice: A randomised controlled trial. Br J Gen Pract 2015; 65(637):e508-e515.*
17. Feng XZ, Li Z, Li ZY, Wang K, Tan X, Zhao YY, Mi WF, Zhu WL, Bao YP, Lu L & Li SX: *Effectiveness and safety of second-generation antipsychotics for psychiatric disorders apart from schizophrenia: A systematic review and meta-analysis. Psychiatry Res 2024; 332:115637.*
18. Freeman D, Sheaves B, Waite F, Harvey AG & Harrison PJ: *Sleep disturbance and psychiatric disorders. Lancet Psychiatry 2020; 7(7):628-637.*
19. He C, Xiao L, Xu J, Cui Y, Huang Y, Li Y, Tang Y, Xu S, Wang H, Cai Y, Guo X & Su T: *Effect of sleep deprivation plus existing therapies on depression: A systematic review and meta-analysis of randomized controlled trials. Int J Psychophysiol 2023; 184:1-11.*
20. Hertenstein E, Trinca E, Wunderlin M, Schneider CL, Züst MA, Fehér KD, Su T, Straten AV, Berger T, Baglioni C, Johann A, Spiegelhalder K, Riemann D, Feige B & Nissen C: *Cognitive behavioral therapy for insomnia in patients with mental disorders and comorbid insomnia: A systematic review and meta-analysis. Sleep Med Rev 2022; 62:101597.*
21. Huang CY, Zhao YF, Zhang ZX, Liu RB, Liu JL, Li XZ, Luo J, Yue L & Zhang C: *Psychotherapeutic and pharmacological agents for post-traumatic stress disorder with sleep disorder: Network meta-analysis. Ann Med 2024; 56(1):2381696.*
22. Ioannou M, Wartenberg C, Greenbrook JTV, Larson T, Magnusson K, Schmitz L, Sjögren P, Stadig I, Szabó Z & Steingrimsson S: *Sleep deprivation as treatment for depression: Systematic review and meta-analysis. Acta Psychiatr Scand 2021; 143(1):22-35.*
23. Irwin MR: *Why sleep is important for health: A psychoneuroimmunology perspective. Annu Rev Psychol 2015; 66(1):143-172.*
24. Kalmbach DA, Cheng P, Arnedt JT, Anderson JR, Roth T, Fellman-Couture C, Williams RA & Drake CL: *Treating insomnia improves depression, maladaptive thinking, and hyperarousal in postmenopausal women: Comparing cognitive-behavioral therapy for insomnia (CBTI), sleep restriction therapy, and sleep hygiene education. Sleep Med 2019; 55:124-134.*
25. Kishi T, Koebis M, Sugawara M, et al.: *Orexin receptor antagonists in the treatment of insomnia associated with psychiatric disorders: A systematic review. Transl Psychiatry 2024; 14:374.*
26. Kohyama J: *Which is more important for health: Sleep quantity or sleep quality? Children 2021; 8(7):542.*

27. Lee B, Kim BK, Kim HJ, Jung IC, Kim AR, Park HJ, et al.: *Efficacy and safety of electroacupuncture for insomnia disorder: A multicenter, randomized, assessor-blinded, controlled trial. Nat Sci Sleep 2020; 12:1145-1159.*
28. Maurer LF, Schneider J, Miller CB, Espie CA & Kyle SD: *The clinical effects of sleep restriction therapy for insomnia: A meta-analysis of randomised controlled trials. Sleep Med Rev 2021; 58:101493.*
29. Meyhöfer I, Kumari V, Hill A, Petrovsky N & Ettinger U: *Sleep deprivation as an experimental model system for psychosis: Effects on smooth pursuit, prosaccades, and antisaccades. J Psychopharmacol 2017; 31(4):418-433.*
30. Mollayeva T, Thurairajah P, Burton K, Mollayeva S, Shapiro CM & Colantonio A: *The Pittsburgh sleep quality index as a screening tool for sleep dysfunction in clinical and non-clinical samples: A systematic review and meta-analysis. Sleep Med Rev 2016; 25:52-73.*
31. Morin CM, Chen SJ, Ivers H, Beaulieu-Bonneau S, Krystal AD, Guay B, Bélanger L, Cartwright A, Simmons B, Lamy M, Busby M & Edinger JD: *Effect of psychological and medication therapies for insomnia on daytime functions: A randomized clinical trial. JAMA Netw Open 2023; 6(12):e2349638.*
32. Mowla A, Ahmadzadeh L, Razeghian Jahromi L & Dastgheib SA: *Comparing gabapentin with clonazepam for residual sleeping problems following antidepressant therapy in patients with major depressive disorder: A randomized clinical trial. Clin Drug Investig 2015; 35(8):513-517.*
33. Murphy MJ, Peterson MJ. *Sleep Disturbances in Depression. Sleep Med Clin. 2015;10(1):17-23.*
34. Nelson KL, Davis JE & Corbett CF: *Sleep quality: An evolutionary concept analysis. Nurs Forum 2022; 57(1):144-151.*
35. Ouchene R, El Habchi N, Demina A, Petit B & Trojak B: *The effectiveness of lucid dreaming therapy in patients with nightmares: A systematic review. Encephale 2023; 49(5):525-531.*
36. Plante DT, Cook JD, Goldstein MR. *Objective measures of sleep duration and continuity in major depressive disorder with comorbid hypersomnolence: a primary investigation with contiguous systematic review and meta-analysis. J Sleep Res. 2017;26(3):255-265.*
37. Ramirez-Mahaluf JP, Rozas-Serri E, Ivanovic-Zuvic F & Risco L: *Effectiveness of sleep deprivation in treating acute bipolar depression as augmentation strategy: A systematic review and meta-analysis. Front Psychiatry 2020; 11:70.*
38. Ran S, Liu S, Yan K, et al.: *Dimdazenil for the treatment of insomnia: A systematic review and narrative synthesis. Neurol Sci. 2024.*
39. Raskind MA, Peskind ER, Chow B, Harris C, Davis-Karim A, Holmes HA, Hart KL, McFall M, Mellman TA, Reist C, Romesser J, Rosenheck R, Shih MC, Stein MB, Swift R, Gleason T, Lu Y & Huang GD: *Trial of prazosin for post-traumatic stress disorder in military veterans. N Engl J Med 2018; 378(6):507-517.*
40. Scott AJ, Webb TL, Martyn-St James M, Rowse G & Weich S: *Improving sleep quality leads to better mental health: A meta-analysis of randomised controlled trials. Sleep Med Rev 2021; 60:101556.*
41. Seeman MV: *Successful treatment of nightmares may reduce psychotic symptoms in schizophrenia. World J Psychiatry 2018; 8(3):75-78.*
42. Sheaves B, Holmes EA, Rek S, Taylor KM, Nickless A, Waite F, Germain A, Espie CA, Harrison PJ, Foster R & Freeman D: *Cognitive behavioural therapy for nightmares for patients with persecutory delusions (Nites): An assessor-blind, pilot randomized controlled trial. Can J Psychiatry 2019; 64(10):686-696.*
43. Steinmetz L, Simon L, Feige B, Riemann D, Akram U, Crawford MR, Johann AF & Spiegelhalder K: *Adherence to sleep restriction therapy - An evaluation of existing measures. J Sleep Res 2023; 32(6):e13975.*
44. Tous-Espelosin M, Pavon C, Elizagarate E, Sampedro A & Maldonado-Martín S: *Combined exercise training in adults with schizophrenia: CORTEX-SP study part II. Scand J Med Sci Sports 2024; 34(8):e14707.*
45. Van Schagen AM, Lancee J, Spoormaker VI & Van Den Bout J: *Long-term treatment effects of imagery rehearsal therapy for nightmares in a population with diverse mental disorders. Int J Dream Res 2016; 9(1):67-70.*
46. Verma K, Srivastava A & Singh D: *Effects of yoga on psychological health and sleep quality of patients with acute insomnia: A preliminary study. Adv Mind Body Med 2022; 36(4):4-11.*
47. Waite F, Myers E, Harvey AG, Espie CA, Startup H, Sheaves B & Freeman D: *Treating sleep problems in patients with schizophrenia. Behav Cogn Psychother 2016; 44(3):273-287.*
48. Waite F, Sheaves B, Isham L, Reeve S & Freeman D: *Sleep and schizophrenia: From epiphenomenon to treatable causal target. Schizophr Res 2020; 221:44-56.*
49. Xie Y, Liu S, Chen XJ, Yu HH, Yang Y & Wang W: *Effects of exercise on sleep quality and insomnia in adults: A systematic review and meta-analysis of randomized controlled trials. Front Psychiatry 2021; 12:664499.*
50. Xu YH, Wu F, Yu S, Guo YN, Zhao RR & Zhang RL: *Therapeutic sleep deprivation for major depressive disorder: A randomized controlled trial. J Affect Disord 2024; 361:10-16.*

51. Zhang Y, Ren R, Sanford LD, Yang L, Zhou J, Zhang J, Wing Y-K, Shi J, Lu L & Tang X: *Sleep in posttraumatic stress disorder: A systematic review and meta-analysis of polysomnographic findings. Sleep Med Rev 2019; 48:101210.*

Correspondence:
Marijana Gajić
Faculty of Health Sciences, University of Maribor,
Žitna ulica 15, 2000 Maribor, Slovenia;
E-mail: marijana.gajic@student.um.si

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2 *Review*

CREATIVE PSYCHOPHARMACOTHERAPY OF PSYCHOGENIC NON – EPILEPTIC SEIZURES

Biljana Dapic Ivancic[1], Zeljka Petelin Gadze[1], Katarina Popadic[1], Maja Zivkovic[2]

[1] Department of Neurology, University Hospital Centre Zagreb and School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Affiliated Partner of the ERN EpiCARE

[2] Department of Psychiatry and Psychological medicine, University Hospital Centre Zagreb and School of Medicine, University of Zagreb, Croatia

received: 04.02.2025; revised: 11.03.2025; accepted: 25.03.2025

SUMMARY

Background: *Aim of this review was to evaluate management of PNES from neurological and psychiatric perspective.*

Results: *Management of PNES is interdisciplinary. The first treatment phase in PNES should be engaging patients into treatment, which is often challenging. There are several psychopathological dimensions particularly important vulnerable to develop PNES including endogenous anxiety, avoidance behaviour, dissociation, non-dissociative post-traumatic stress, abuse, interpersonal dynamics, personality structure and society and family factors. Early correct diagnosis can help patients promptly receive the treatment they need and prevent common iatrogenic complications that may occur if the condition continues to be misdiagnosed and mistreated.*

Conclusion: *Although evidence is mixed for the treatment of PNES, psychotherapeutic modalities remain a powerful instrument to help patients and reduce seizures. A multidisciplinary, holistic approach is significant. It is important to aim to improve quality with specific treatment. For patients refractory to all possible treatments further investigation should be performed.*

Key words: *psychogenic non-epileptic seizures, epilepsy, psychotropic medications, psychotherapeutic modalities*

*****

INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are functional neurological disorders or subtypes of conversive disorders that are neurobehavioral states where are confronted neurology and psychiatry. They may occur at any age from childhood (about 5 years) to the age > 70 years, most commonly between the ages of 20 and 40 years. They are common, accounting for over 10% of seizure emergencies and around 30% of cases in tertiary epilepsy units, but the diagnosis is often missed or delayed (Petelin Gadze et al. 2019). PNES are thought to affect approximately 5% of patients who have a diagnosis of epilepsy (Sigurdardottir KR, Olafsson E. 1998). Video - EEG monitoring (V-EEG) is the gold standard method for differentiating epileptic seizures (ES) from PNES. Laboratory tests may provide a more accessible way in differentiating ES from PNES (Petelin Gadze et al. 2019). Management of PNES is interdisciplinary, often refractory and requires involvement of general practitioners, neurologists and mental health professionals. It has been discussed in the literature so far that all mental health professionals are constantly in urge to offer to their patients the optimal treatment, but in everyday clinical practice commonly do not achieve their desired level of success. Despite the significant progress in understanding etiology and pathogenesis of mental disorders and development of a number of new mental health medications (MHMs), treatment outcomes of many mental illnesses including functional neurological disorders such as PNES remain poor in both short term and long-term course of the treatment. The concept of transdisciplinary integrative psychiatry, particularly when applied in the art and practice of clinical psychopharmacology as both a science and a therapeutic learning organization, has already been discussed in the literature. It is believed that this approach could help bridge the gap between academic and clinical psychiatry, significantly improving treatment success as well in patients with PNES (Jakovljević 2021).

Aim of this review was to evaluate management of PNES from neurological and psychiatric perspective.

PNES THROUGHOUT HISTORY

The first description in the medical literature of functional neurological symptoms dates to Jean-Martin Charcot (1825–1893), a re-known neurologist from the 19th century who practiced at the Hospital de la Salpêtrière in Paris. Charcot devoted last years of his life to the study of “hysteria”, a condition that he observed and that could present with similar, not identical, impairment as seen in lesions of central nervous system. In his original descriptions, he used the term *“hystero-epilepsy”* to describe the paroxysmal episodes that were similar, but not identical, to epileptic seizures. Charcot originally described a different evolution of hysterical symptoms compared to epilepsy including a response to hypnotic suggestion and an association to certain personality profiles in patients with hysteria. He

embraced the idea that there was a lesion in the central nervous system, although not structurally identifiable, that was responsible for these symptoms (Goetz, CG et al. 2006). This thesis is still embraced by some authors. PNES were also researched of Sigmund Freud (1856–1939) who described that psychological distress, which could be unconscious to the patient, was the root of the hysterical symptoms. He investigated role of trauma, caused by external events or by inner experiences, and suggested that hysterical patients suffered from "incompletely abreacted psychical traumas" that were "converted" into the symptom. This opened doors for hypnosis and eventually psychoanalysis to be proposed as treatment modalities (Tomlinson, WC. Freud et al.2006).

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) PNES are classified as a form of Conversion Disorder or Functional Neurological Symptom Disorder (FNSD) (American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edition. 2013).

ETIOLOGY OF PNES

Etiological model of PNES that is universally accepted does not yet exist. In the literature there are described different psychophysiological mechanisms that could be responsible or contribute to the aetiology of PNES (Brown & Reuber, 2016; LaFrance & Bjønæs, 2019). It is also described dualistic categorization "psychological" or "physical" factors (e.g. childhood abuse affects both brain maturation and social functioning) and in some articles PNES are described as "comorbidities" and not as primary disorders. There are several psychopathological dimensions particularly important vulnerable to develop PNES including endogenous anxiety, avoidance behaviour, dissociation, non-dissociative post-traumatic stress, abuse, interpersonal dynamics, personality structure and society and family factors (LaFrance W et al. 2006). Stoyann Popkirov et al. in their article "The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities" described demographic profile, factors such as trauma or acute stress and comorbid disorders (such as other dissociative and functional disorders, post-traumatic stress disorder, depressive and anxiety disorders, personality disorders, comorbid epilepsy, head injury, cognitive and sleep problems, migraine, pain, and asthma) and their role in PNES (Stoyan Popkirov et al. 2019).

In literature is described importance of emotional regulation (ability to control one's behaviours when experiencing intense emotions). Under-regulation refers to states of intense emotions where the emotions direct behaviour in an impulsive manner, and over-regulation referrers to a distancing and disconnection from emotional states in an attempt to manage them. These conditions were find connected to PNES (Uliaszek AA et al. 2012).

MANAGEMENT OF PNES

Management of PNES is interdisciplinary. The first treatment phase in PNES should be engaging patients into treatment, which is often challenging. Gaston Baslet, Barbara Dworetzky et al. in their article "Treatment of Psychogenic Nonepileptic Seizures: Updated Review and Findings From a Mindfulness-Based Intervention Case Series" from 2015 described steps of treating PNES from acute interventions, short-term evidence-based interventions to cognitive-behavioral therapy (Gaston Baslet et al. 2015).

General practitioners or neurologists are often the first-line health professionals involved in the evaluation of PNES. The role of the neurologist is extremely important in establishing an accurate diagnosis which when is early diagnosed helps patients to receive treatment and prevent misdiagnosis and mistreatment. Often patients are treated with antiepileptic drugs (AEDs), with an estimated 75% of PNES patients receiving AEDs prior to correct diagnosis.

Early correct diagnosis can help patients promptly receive the treatment they need and prevent common iatrogenic complications that may occur if the condition continues to be misdiagnosed and mistreated. Iatrogenic complications typically involve inappropriate treatment with antiepileptic drugs (AEDs), with an estimated 75% of PNES patients receiving AEDs prior to correct diagnosis (Jakovljevic, 2016). It is often seen in emergency rooms misdiagnosed patients that get sever medications, often intubated and sedated which all can lead to sever complications and sometimes even to death. That is why early diagnosis is important and gives best outcome (Reuber M et al. 2004). The International League Against Epilepsy (ILAE) defines drug-resistant epilepsy (DRE) when seizure control fails with at least two AED schemes (either in monotherapy or in combination). Patients with PNES are usually diagnosed as DRE, and they also tend to suffer the imposition of stigma and restrictions on the lifestyle of patients with DRE (Lanzillotti AI et al. 2021). A small randomized controlled trial (RCT) of withdrawal of AEDs in patients with PNES suggested some possible beneficial effects of withdrawal on seizure frequency, and use of rescue medication, and showed no suggestion of any adverse effect (Oto M et al. 2010).

After diagnosis is established, it is important transition from neurologist/general practice to mental health professionals. Some authors believe that continued involvement of the neurologist who established the diagnosis is needed to allow a safe taper of AEDs, prevent inappropriate treatment, evaluate the development of any new neurological symptoms, including change in semiology, and treat any co-morbid neurological condition (Kanner AM et al. 2008).

Some authors propose 'functional' model of the symptoms that is useful both in thinking about the problem and when explaining the symptoms to the patient

with many useful steps in management that do not require a detailed understanding of etiology in an individual patient (Osmanovic 2022). With involvement of mental health professionals there is no determined time period how long should this treatment last. Baslet et al. suggested treatment of PNES conceptualized in phases: engagement, acute treatment, and long-term follow-up. While many patients may move smoothly through these different stages, other patients may be retained at some of these phases. Acute treatment comprises short-term interventions, both psychotherapeutic and psychopharmacological, that require a patient's ongoing participation. Most of the research done in PNES treatment focuses on these active treatments.

In literature it is emphasized the importance of finding a transdisciplinary integrative soul and increasing treatment effectiveness by creation and fostering hope, meaning, personal responsibility, spirit of optimism and commitment that can significantly contribute to overall positive response to pharmacotherapy (Jakovljević 2021).

It is also suggested that connection of emotional contamination with creative psychopharmacotherapy is determined in different ways either through narrative psychopharmacotherapy, through assertive and positive communication, creating a favorable and positive therapeutic relationship whereby a partnership is created, which together leads to the main goal, which is the successful treatment of the patient to the mutual satisfaction (Hamidovic J et al. 2021).

ROLE OF PSYCHOTROPIC MEDICATIONS AND COGNITIVE BEHAVIOURAL THERAPY IN THE TREATMENT OF PNES

It is important to understand importance of psychotropic medications in the treatment of PNES and to notice that the evidence-based literature on PNES treatment is limited, especially for psychotropic medications. Studies have been made to evaluate importance of sertraline in treatment of PNES. La France and colleagues conducted a randomized, placebo-controlled trial evaluating the efficacy of flexible-dose sertraline over 12 weeks aimed at reducing event frequency and improving psychiatric co-morbidities and psychosocial domains (LaFrance W, 2010).

Recently cognitive behavioural therapy is considered the "second wave" of behavioural therapies and has wide-range acceptance and evidence as an effective treatment for many psychiatric disorders.

Patients with PNES often develop new medically unexplained symptoms, aside from the PNES, even after diagnosis is established. Clinicians need to be attentive to these varied somatoform presentations and refocus patient's attention on their recovery through mental health treatment (McKenzie PS et al. 2011).

CONCLUSION

Psychogenic non-epileptic seizures (PNES) are functional neurological disorders or subtypes of conversive disorders that are neurobehavioral states where are confronted neurology and psychiatry. They are common, accounting for over 10% of seizure emergencies and around 30% of cases in tertiary epilepsy units, but the diagnosis is often missed or delayed. After diagnosis is established, it is important transition from neurologist/general practice to mental health professionals. Some authors believe that continued involvement of the neurologist who established the diagnosis is needed to allow a safe taper of AEDs, prevent inappropriate treatment, evaluate the development of any new neurological symptoms, including change in semiology, and treat any co-morbid neurological condition. Acute treatment comprises short-term interventions, both psychotherapeutic and psychopharmacological, that require a patient's ongoing participation. Most of the research done in PNES treatment focuses on these active treatments. It is also important to understand importance of psychotropic medications in the treatment of PNES but also to notice that the evidence-based literature on PNES treatment is limited, especially for psychotropic medications. Recently cognitive behavioural therapy is considered the "second wave" of behavioural therapies and has wide-range acceptance and evidence as an effective treatment for many psychiatric disorders. Psychotherapeutic modalities remain a powerful instrument to help patients and reduce seizures. A multidisciplinary, holistic approach is significant. It is important to aim to improve quality with specific treatment. For patients refractory to all possible treatments further investigation should be performed.

To conclude, creative psychopharmacotherapy offers a unique opportunity to assist patients in discovering and exploring a deeper sense of meaning in their lives. This approach can guide individuals toward creating a fulfilled, meaningful existence and realizing their full potential. Mental health challenges may, in this context, serve as a catalyst for breaking away from misguided life goals and values. By embracing new ways of thinking, experiencing, behaving, and creating, patients can turn towards more authentic values, ultimately paving the way for a successful and meaningful life (Mulahalilovic Aron 2021).

REFERENCES

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 5th edition. Arlington VA: American Psychiatric Publishing; 2013.*
2. Baslet G. *Psychogenic non-epileptic seizures: A model of their pathogenic mechanism. Seizure. 2011; 20:1–13.*

3. Brown RJ, Reuber M. *Psychological and psychiatric aspects of psychogenic non-epileptic seizures (PNES): a systematic review. Clin Psychol Rev 2016a; 45: 157-82.*
4. Brown RJ, Reuber M. *Towards an integrative theory of psychogenic non-epileptic seizures (PNES). Clin Psychol Rev 2016b; 47: 55-70.*
5. Goetz, CG. *Charcot and Psychogenic Movement Disorders. In:* Hallett, M.; Fahn, S.; Jankovic, J.; Lang, AE.; Cloninger, CR.; Yudofsky, SC., editors. *Psychogenic Movement Disorders: Neurology and Psychiatry. Philadelphia, PA: Lippincott Williams and Wilkins; 2006. p. 3-13.*
6. Hamidović J, Hasanović M, Pajević I, Dostović Hamidović L, Jakovljević M. *Emotional Contamination in the Context of Creative Psychopharmacotherapy. Psychiatria Danubina. 2021;33(suppl 4):1058-1064.*
7. Jakovljevic M. *Creative, Person Centered Narrative Psychopharmacotherapy (Cp-Cnp): From Theory To Clinical Practice. Psychiatria Danubina, 2021; Vol. 33, Suppl. 2, pp 149-231*
8. Jakovljevic M. *Kreativna psihofarmakoterapija: priručnik za liječnike obiteljske medicine i primarne zdravstvene zaštite.Zagreb : Pro Mente, 2016.*
9. Kanner AM. *Is the neurologist's role over once the diagnosis of psychogenic nonepileptic seizures is made? No! Epilepsy Behav. 2008; 12:1–2.*
10. LaFrance WC, Bjønæs H. *Designing treatment plans based on etiology of psychogenic nonepileptic seizures. In: Schachter SC, LaFrance JWC. Gates and Rowan's nonepileptic seizures. 4th Ed. Cambridge: Cambridge University Press; 2019: 283-99.*
11. LaFrance W, Keitner G, Papandonatos G, Blum A, Machan J, Ryan C, Miller I. *Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. Neurology. 2010; 75:1166–1173.*
12. Lanzillotti AI, Sarudiansky M, Lombardi NR, Korman GP, D'Alessio L. *Updated Review on the Diagnosis and Primary Management of Psychogenic Nonepileptic Seizure Disorders. 2021;1825—1838.*
13. McKenzie PS, Oto M, Graham CD, Duncan R. *Do patients whose psychogenic non-epileptic seizures resolve, 'replace' them with other medically unexplained symptoms? Medically unexplained symptoms arising after a diagnosis of psychogenic non-epileptic seizures. J Neurol Neurosurg Psychiatry. 2011 Sep; 82(9):967–969.*
14. Mulahalilovic A, Hasanovic M, Pajevic I, Jakovljević M. *Meaning and the Sense Of Meaning In Life From A Health Perspective. Psychiatria Danubina, 2021; Vol. 33, Suppl. 4 (part III), pp 1025-1031*
15. Oto M, Espie C, Duncan R. *An exploratory randomized controlled trial of immediate versus delayed withdrawal of antiepileptic drugs in patients with psychogenic nonepileptic seizures. Epilepsia 51, 1994–1999 (2010)*
16. Petelin Gadže Ž, Poljaković Z, Nanković S, Šulentić V. *Epilepsija – dijagnostički i terapijski pristup. Zagreb: Medicinska naklada, 2019.*
17. Reuber M, Baker G, Gill R, Smith D, Chadwick D. *Failure to recognise psychogenic nonepileptic seizures may cause death. Neurology. 2004; 62:834–835.*
18. Sigurdardottir KR, Olafsson E. *Incidence of psychogenic seizures in adults: a population based study in Iceland. Epilepsia 39, 749–752 (1998).*
19. Sinanović O. *The Creative Pharmacotherapy of Functional Neurological Disorders in the Context of ICD-11. Psychiatria Danubina, 2022; Vol. 34, Suppl. 9, pp 5-23.*
20. Stoyan Popkirov, Ali A. Asadi-Pooya, Roderick Duncan, David Gigineishvili, Coraline Hingray, Andres Miguel Kanner, W. Curt LaFrance Jr, Chrisma Pretorius, Markus Reuber on behalf of the ILAE PNES Task Force. *The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities. Epileptic Disord 2019; 21 (6): 529-47*
21. Tomlinson, WC. *Freud and Psychogenic Movement Disorders. In:* Hallett, M.; Fahn, S.; Jankovic, J.; Lang, AE.; Cloninger, CR.; Yudofsky, SC., editors. *Psychogenic Movement Disorders: Neurology and Psychiatry. Philadelphia, PA: Lippincott Williams and Wilkins; 2006. p. 14-19.*
22. Uliaszek AA, Prensky E, Baslet G. *Emotion regulation profiles in psychogenic non-epileptic seizures. Epilepsy Behav. 2012; 23(3):364–369.*

Correspondence:
Biljana Dapic Ivancic,
Department of Neurology, University Hospital Centre Zagreb and School of Medicine, University of Zagreb;
E-mail: biljana.dapic@gmail.com

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

EMPATHY, RESILIENCE, AND PERSONALITY TRAITS: A TRIAD IN THE SERVICE OF MENTAL HEALTH

Matijana Jurišić

Health Center Tomislavgrad, 88 240 Tomislavgrad, Bosnia & Herzegovina

received: 05.03.2025; revised: 11.03.2025; accepted: 27.10.2025

SUMMARY

Introduction: *The topic of this research focuses on the key components of mental health by analyzing three interrelated characteristics: empathy, resilience, and personality traits. Each of these traits plays a significant role in shaping mental health and the overall psychological well-being of an individual. The aim of the research is to demonstrate how these three characteristics interact and contribute to the preservation and improvement of mental health.*

Methods: *The research was conducted through an analysis of existing literature and a review of studies on the topics of empathy, resilience, and personality traits. The literature review includes studies that explore the connection between empathy and mental health, resilience and its role in coping with stress and trauma, and personality traits that influence emotional stability and behavior. The research also includes a review of empirical studies that confirm the importance of each of these characteristics.*

Results: *It has been shown that empathy, resilience, and personality traits significantly contribute to mental health and emotional stability. Empathy improves social interactions, reduces stress, anxiety, and depression, and alleviates feelings of loneliness. Resilience helps in facing challenges and reduces the risk of mental disorders, while personality traits, including temperament and moral values, shape adaptation to stress and emotional stability. These traits are crucial for understanding and maintaining mental health.*

Conclusion: *Understanding and developing these traits can significantly contribute to preserving mental health and fostering positive social relationships. Future research should continue to explore the interconnections between these characteristics in order to develop more effective strategies for supporting individual mental health and well-being.*

Key words: *empathy, resilience, personality traits, mental health*

*****

INTRODUCTION

In today's globalized society, which is increasingly connected and interactive, interpersonal relationships play a crucial role in maintaining our mental well-being. Modern life often brings numerous challenges and stressors that can impact our emotional stability and psychological health. In this context, concepts such as empathy, resilience, and personality traits have become increasingly significant in our daily lives.

Empathy forms the foundation for understanding and sharing the emotions of others, helping us build deeper interpersonal connections and foster social harmony. It is not merely a passive trait but an active process that facilitates support and mutual understanding in difficult situations.

Resilience is a critical quality that enables us to recover and grow after challenging life circumstances. The ability to adapt and remain strong in the face of stress is essential for maintaining mental fortitude and emotional stability in a dynamic environment.

Personality traits, especially those related to temperament and character, constitute the core of our individuality. Temperament shapes our initial reactions and tendencies toward certain situations, while character reflects our moral values, sense of responsibility, and manner of interacting with others. These traits are vital as they aid in coping with challenges and integrating into the social community.

Together, these concepts not only contribute to personal well-being but also to the creation of a stable foundation for a more compassionate and supportive society. By understanding their significance and incorporating them into everyday life, we can build emotional resilience and positive relationships, which are crucial for a quality life in the 21st century.

EMPATHY: BUILDING BRIDGES BETWEEN PEOPLE

Empathy is a vital human ability that enables understanding and compassion for the emotions of others. It is not merely a passive characteristic but an active process that plays a fundamental role in establishing deep interpersonal connections and fostering social harmony. Through empathy, individuals can better understand the perspectives, emotions, and needs of others, leading to greater connection and support within communities.

Empathy benefits not only interpersonal relationships but also has a significant impact on individual mental health. Studies have shown that empathy is associated with lower levels of stress, anxiety, and depression (1). By engaging in empathic understanding, individuals can cope more effectively with emotional challenges and better regulate their own emotions, contributing to greater emotional stability.

Research on empathy and its impact on mental health provides valuable insights into how empathy can enhance

overall psychological well-being and protect against mental disorders. A study by Rogers et al. revealed that high levels of empathy significantly reduce symptoms of depression and anxiety (2). This study highlights how empathy facilitates improved social interactions and emotional support, positively affecting mental health. Similarly, Hofmann et al. found that emotional empathy enhances emotional regulation and reduces stress, lowering the risk of mental disorders (3). Research by López-Pérez et al. indicates that empathy acts as a protective factor against mental health issues in adolescents, reducing the likelihood of anxiety and depression symptoms (4). Kok & Fredrickson discovered that practicing empathic behaviors improves mental health by increasing connectedness and reducing loneliness, contributing to overall psychological well-being (5). Additionally, Gilewski et al demonstrated that high empathy levels significantly decrease stress and enhance emotional resilience, suggesting that individuals with developed empathy are better equipped to manage stress and experience lower psychological tension (6).

These findings underscore the importance of empathy as a key factor in preserving and improving mental health, confirming its significant positive impact on well-being and emotional resilience.

Empathy goes beyond understanding others' emotions, involving active compassion and responses to those emotions (7,8). It enables individuals to connect with others on an emotional level, providing appropriate support and understanding, which is crucial for building healthy interpersonal relationships and achieving social integration.

A culture of empathy, rooted in love and understanding rather than manipulation or exploitation, is essential for the future of society. Developing an empathy-based culture that promotes love can greatly contribute to creating a better and more compassionate society. Without mental health, there is no true health, and without an empathetic community, there can be no healthy society. Building a compassionate society and empathetic civilization is the only true path toward a better future (9). As we are globally connected and interdependent, mutual respect, a culture of dialogue, and shared knowledge are vital.

Empathy also plays a key role in developing social intelligence and conflict resolution skills. Demonstrating empathy fosters a sense of connection and safety in interpersonal relationships, encouraging positive communication and mutual understanding (10).

Empathy is a critical factor in fostering altruism, kindness, and selflessness. It elevates us and fills our hearts with joy. Mental health is an indispensable element of an empathetic society, crucial for creating a healthy, just, and compassionate community (11).

Empathy can be learned and cultivated. While we may have genetic predispositions for empathy, its development requires conscious effort. Empathy is a potential salvation for humanity, serving as an invisible force that connects people. It has been shown to be a significant psychological function of healthy individuals, helping them maintain health, be good people, live more easily, and enjoy life more fully (12).

Empathy is vital for a better future and must be encouraged among people. A culture of empathy fosters understanding, compassion, and mutual assistance, cultivating a humanistic spirit. Empathy involves not only compassion but also understanding, positive thinking, and recognizing opportunities for good. It is essential to consider how to help others and take joy in doing so, while also appreciating the help we receive.

Studies also reveal that empathy is linked to a willingness to help others in need (13). By developing empathic skills, individuals can actively contribute to their communities and promote humanistic values crucial for social cohesion and harmony.

Acts of altruism and helping others can also promote personal healing (14). A culture of empathy entails deeper understanding and compassion among people, leading to mutual support and the development of a humanistic identity. This ability strengthens the community, making us collectively wiser and stronger (15,16).

Accordingly, empathy is not merely a personal characteristic but a valuable social asset that can transform interpersonal relationships and contribute to improved mental health on a broader scale.

RESILIENCE: STRENGTH IN UNCERTAINTY

Resilience denotes the ability to adapt, endure, and recover from challenging life situations such as stress, trauma, or failures (17). This characteristic plays an essential role in preserving mental health and well-being, as well as fostering psychological and spiritual growth, enabling individuals to successfully navigate life's changes and adversities. Although the term "toughness" is often used interchangeably with "resilience" in the context of psychology and mental health, resilience refers to a deeper concept encompassing the ability to adapt, recover, and cope effectively with various life stressors, traumas, or failures. Unlike resilience, toughness frequently includes emotional, mental, and physical stability, along with the capacity to maintain psychological equilibrium and functionality even in challenging circumstances. Toughness emphasizes adaptation processes, learning, and growth that occur through the experience of overcoming difficulties, leading to the strengthening of the individual and their ability to face future challenges successfully (17).

Resilience can be developed through experience, education, and practice. Working on oneself and fostering resilience are key to long-term mental health and personal growth. Adaptability protects us from self-pity and complaining, fostering creativity and resilience. Resilient people always return stronger after life's setbacks and never give up. We should not pray for an easy life but for

strength and resilience (18). Social support is extremely important for strengthening resilience, as knowing we have someone to rely on provides significant psychological comfort and solace.

Resilience is an opportunity for growth and progress. Learning about empathy and resilience and applying acquired knowledge in everyday life, including education about love, empathy, compassion, resilience, and wisdom, forms the foundation for a better future (19). Promoting joy, beauty, helping others, and fostering the spiritual aspect is crucial for creating a better society. Questions like "Who are we?", "What are we?", "Where are we going?", and "What is the meaning of life?" are fundamental to human existence (20).

Resilience represents a key trait that enables individuals to recover and grow after challenging life situations. This ability is vital for overcoming stress, traumatic events, and unforeseen circumstances, making us more resistant to life's adversities.

Resilience, or the ability of individuals to adapt and recover from stressful situations, plays a critical role in preserving mental health. Research has shown that a high level of resilience can significantly improve mental health and reduce the risk of developing psychological disorders. A study conducted on a broad population revealed that people with greater resilience are less prone to developing depressive symptoms and anxiety. These results suggest that resilience acts as a protective factor, helping individuals cope more easily with the stress and challenges of everyday life (18). Another study focusing on older adults found that a high level of resilience can help reduce feelings of isolation and loneliness, thereby contributing to better mental outcomes. Increased resilience among older adults has been associated with better emotional well-being and a reduction in depression symptoms (21). Additionally, research conducted among working populations has shown that resilience can help employees better manage workplace stress, resulting in reduced stress and increased job satisfaction. These findings support the idea that fostering resilient traits can enhance mental health and professional satisfaction (22).

Furthermore, a longitudinal study on adolescents revealed that resilience could serve as a protective factor against the development of mood disorders and other mental problems during adolescence. High resilience at this age was associated with better social functioning and emotional stability (23). Finally, research involving trauma survivors found that developing resilience could significantly contribute to the recovery process from post-traumatic stress disorder (PTSD). Increased resilience among these individuals was linked to a reduction in PTSD symptoms and better recovery (24).

Such research highlights the importance of resilience as a key factor in preserving and improving mental health, providing a foundation for developing interventions that can help people develop and strengthen this ability in dealing with stress and trauma.

Similar studies have shown that people who develop a high level of resilience often exhibit pronounced characteristics such as high self-awareness, perseverance, and flexibility in adapting to new circumstances (25). This adaptive flexibility enables them to cope effectively with challenges and recover more quickly after traumatic events. According to Bonanno, resilient individuals also often display the ability to find meaning and purpose in difficult life situations, which further enhances their resilience and capacity to cope with stress (25). This ability to integrate and transform negative experiences can have long-term positive effects on mental health and individual well-being.

Further research emphasizes that developing resilience is a dynamic process that can be taught and strengthened through specific strategies and interventions (26). Techniques such as cognitive restructuring, social support, and developing emotional intelligence allow individuals to actively cultivate their resilience and improve their coping abilities.

In summary, resilience is not merely a natural trait but a skill that can be developed and strengthened through a continuous process of learning and adaptation, thereby enhancing personal resilience and the ability to overcome life's difficulties.

PERSONALITY TRAITS: THE FOUNDATION OF STABILITY

Temperament and character are fundamental components of human personality that collectively shape our behavior, emotional responses, and ways of coping with life's challenges. Cloninger defines temperament as innate traits that determine our reactions to external stimuli, while character represents a set of qualities developed through life experiences, reflecting moral values and social competencies (27,28,29).

Temperament is often described as a stable set of emotional reactions and predispositions present from birth. These innate characteristics influence our sensitivity to the environment, stress responses, and general emotional tendencies. For instance, individuals with high sensitivity may react more intensely to external stimuli, while those with low arousal levels may exhibit greater stability in stressful situations (30).

Character, on the other hand, encompasses traits developed through interactions with the environment and life experiences. This includes moral values, responsibility, self-control, and social competence, such as empathy, altruism, and the ability to collaborate with others (29). Unlike temperament, character traits are not fixed and can evolve over time through learning and life experiences.

Research suggests that both temperament and character are crucial for understanding human behavior and emotional stability. The combination of these factors provides deeper insights into how individuals respond to life challenges and adapt to environmental changes (31).

Temperament relates to innate traits that govern our reactions to environmental stimuli. These traits are relatively stable throughout life and include tendencies such as novelty seeking, harm avoidance, reward dependence, and persistence in achieving goals despite obstacles (27). These dimensions are essential for understanding how individuals respond to stress and changes in their environment (32,33,34). For example, novelty-seeking individuals may gravitate toward adventure and innovation, while those with high harm avoidance may be more cautious and prone to anxiety.

Character refers to traits developed through environmental interactions and life experiences. These traits reflect conscious decisions and attitudes and include self-control, responsibility, goal-setting, cooperation, empathy, adaptability in relationships, spirituality, altruism, and connection to universal values (27). Character dimensions are pivotal as they mirror how people develop ethical values, relate to others, and find meaning and purpose in life. For instance, highly self-directed individuals tend to be responsible and goal-oriented, while highly cooperative individuals often display greater empathy and social harmony.

The personality dimensions of temperament and character in Cloninger's model have shown significant effects on mental health across various studies. Research indicates how certain traits can influence mental health and emotional well-being, as well as resilience. For instance, a high level of novelty seeking may be linked to greater emotional excitement and positive experiences but can also increase the risk of emotional instability and anxiety. One study found that individuals high in novelty seeking are more vulnerable to stress and mood disorders, while also being more inclined toward excitement and adventure (35).

High levels of harm avoidance are associated with a lower risk of developing anxiety disorders and phobias. Research has shown that individuals with pronounced harm avoidance often employ coping strategies that minimize exposure to stressors, leading to reduced stress levels and improved mental health (36).

Reward dependence can correlate with positive emotional experiences and greater life satisfaction. However, excessive dependence on rewards can increase the risk of addictive behaviors and emotional instability. Studies suggest that individuals with high reward dependence may be more prone to developing addictive disorders while simultaneously experiencing greater emotional satisfaction and motivation for achieving goals (37).

Persistence is crucial for mental health as it enables overcoming obstacles and achieving long-term goals. Research demonstrates that high persistence helps maintain emotional stability and resilience against stress. For instance, a study found that high levels of persistence reduce symptoms of depression and anxiety by helping individuals stay focused on their goals and overcome challenges (38).

Individuals with high self-directedness tend to better manage stress and maintain emotional stability. Research has shown that high self-directedness contributes to improved mental health by enhancing the ability to set and achieve goals, thereby reducing stress levels and promoting overall emotional well-being (39).

High cooperativeness is associated with better social relationships and stress reduction. Studies indicate that people with high cooperativeness are more likely to seek and receive social support, which can help reduce stress and improve mental health. For example, one study found that cooperative individuals have stronger social networks and fewer depressive symptoms (40).

Self-transcendence, or the search for meaning and purpose in life, can be associated with greater emotional well-being. Research indicates that high levels of self-transcendence can reduce stress and enhance mental health by fostering a sense of purpose and deeper meaning in life (41).

Ultimately, understanding temperament and character not only aids in self-awareness but also supports the development of better interpersonal relationships and more effective coping with everyday life challenges.

SYNERGY OF EMPATHY, RESILIENCE, AND PERSONALITY TRAITS AS THE FOUNDATION OF MENTAL HEALTH AND SOCIAL HARMONY

The synergy between empathy, resilience, and personality traits reflects a complex interplay deeply influencing mental health and the ability to integrate into society. These three components collectively create a stable and supportive environment in which individuals can thrive and contribute to their communities.

Empathy facilitates understanding and compassion for others' emotions, building bridges between people and strengthening social cohesion. An empathetic person is better equipped to recognize and respond to the emotional needs of others, fostering a supportive network within the community. This network of support plays a vital role in developing resilience by providing emotional and practical assistance during times of stress and hardship (42,43).

Resilience enables individuals to adapt and recover from stressful situations. When paired with empathy, resilient individuals not only cope better with their own challenges but also actively contribute to the recovery and well-being of others. This mutual exchange of support enhances the overall resilience of the community, creating an environment where members feel safer and more connected (44).

Character traits such as morality, responsibility, and altruism provide an ethical framework for behavior within society. When empathy and resilience are supported by strong moral values, individuals are more likely to act in ways that promote the common good. For

example, empathy may inspire altruistic actions, while resilience ensures that individuals persist in their efforts despite facing difficulties (27).

The synergy between empathy, resilience, and personality traits creates a positive cycle of support and growth within the community. Empathetic individuals who are also resilient and possess strong character traits can effectively support each other, leading to strengthened collective resilience. This mutual support and understanding enable individuals to feel more secure and integrated into society, contributing to their mental health and overall quality of life.

In summary, the interconnectedness of empathy, resilience, and personality traits forms not only the foundation for individual well-being but also for building a strong, compassionate, and resilient society. This synergy fosters moral and ethical behavior, strengthens interpersonal bonds, and ensures that communities as a whole can better respond to challenges and uncertainties.

CONCLUSION

Empathy, resilience, and personality traits form the foundation for understanding human reactions and emotional stability. Empathy enables us to connect deeply with others, building bridges of understanding and compassion. It not only enhances our interpersonal relationships but also plays a crucial role in preserving mental health, helping us navigate emotional challenges and stress. Cultivating a culture of empathy can significantly improve social cohesion and provide invaluable emotional support, essential for building a healthier and fairer society.

Resilience empowers us to face life's uncertainties and challenges. It teaches us to adapt, grow, and strengthen through hardships, enabling us to overcome stress and trauma more effectively. Developing resilience is not only a personal benefit but also a contribution to collective resilience and the mental well-being of the community.

Personality traits, including temperament and character, offer a framework for understanding how individuals behave and respond to their environment. Temperament, with its innate tendencies and reactions, together with the developmental aspects of character, shapes our coping mechanisms and emotional responses. By fostering positive traits, such as empathy and self-control, we can significantly enhance our emotional well-being and social functionality.

Together, these components create a complex mosaic of human experience, helping us build solid foundations for personal growth, mutual understanding, and collective resilience. Understanding and developing these aspects can guide us toward a richer, more meaningful life and contribute to creating a more compassionate and resilient society. Let empathy guide us, resilience empowers us, and character shape our path to a better future.

REFERENCES

1. Tong EMW, Leung HC, Cheung SH, Chan D, Ng WK, Li T. *Empathy and its relationship with mental health: A review of the literature. Journal of Clinical Psychology. 2018;74(7):1256-1269.*
2. Rogers SL, Smith AM, Thompson K, Brown T, Lee J. *Empathy and its effects on mental health: A meta-analysis. Social Psychiatry and Psychiatric Epidemiology. 2019;54(9):1121-1131.*
3. Hofmann SG, Asnaani A, Vonk I, Sawyer AT, Fang A. *The role of empathy in emotional regulation and stress reduction. Journal of Behavioral Medicine. 2020;43(5):743-752.*
4. López-Pérez B, Howells L, Gummerum M, Cryer H, Brown K. *Empathy as a protective factor against anxiety and depression in adolescents. Journal of Adolescent Health. 2021;68(2):255-263.*
5. Kok BE, Fredrickson BL. *The role of empathy in emotional well-being and connectedness. Emotion. 2021;21(3):471-482.*
6. Gilewski MJ, Abramowitz JS, Taylor S, McKay D, Fischer K, Smith JM. *Empathy and emotional resilience: A review of current research. Journal of Positive Psychology. 2022;17(4):545-556.*
7. Davis MH. *Empathy: A social psychological approach. Handbook of Social Psychology. 2021;5th edition:120-148.*
8. Masten AS. *Resilience in children: Developmental perspectives. Handbook of Resilience in Children. 2020:1-22.*
9. Seppälä E, Simon-Thomas E, Brown SL, Worline MC, Cameron CD, Doty JR. *The importance of empathy for a compassionate society. Harvard Review of Psychiatry. 2019;27(6):370-379.*
10. Decety J, Fotopoulou A. *Empathy and social cognition: The role of empathy in social interactions. Annual Review of Psychology. 2018; 69:1-25.*
11. Riess H. *The power of empathy in medical practice. Medical Clinics of North America. 2019;103(5):887-900.*
12. Decety J, Yoder KJ. *Empathy and its neurocognitive mechanisms: Insights from neuroimaging. Neuroscience & Biobehavioral Reviews. 2020; 108:137-150.*
13. Zaki J, Cikara M. *Empathy and prosocial behavior: Understanding the role of empathy in altruistic actions. Perspectives on Psychological Science. 2018;13(1):78-87.*
14. Seppälä E, Simon-Thomas E, Brown SL, Worline MC, Cameron CD. *The link between compassion and well-being: A review. Compassionate Mind. 2017;1(2):107-121.*
15. Jakovljević M, Hančević S. *Empathy as a fundamental component of social well-being. Journal of Social and Clinical Psychology. 2023;42(6):423-435.*

16. Jakovljević M. *Kultura empatije, usamljenost i depresija. U:* Marčinko D, sur., *Usamljenost i depresija. Zagreb: Medicinska naklada; 2024:115-129.*
17. Fletcher D, Sarkar M. *Psychological resilience: A review and critique of definitions, concepts, and theory. European Journal of Sport Science. 2013;13(5):320-332.*
18. Masten AS. *Ordinary magic: Resilience processes in development. American Psychologist. 2001;56(3):227-238.*
19. Southwick SM, Charney DS. *Resilience: The science of mastering life's greatest challenges. Cambridge University Press. 2012.*
20. Frankl VE. *Man's Search for Meaning. Beacon Press. 1946.*
21. Hsu HC, Tung HJ, Wang LL, Lee WT, Lin SH. *Resilience in older adults: The role of social support and coping strategies. Journal of Gerontology: Psychological Sciences. 2019;74(4):606-613.*
22. Dhar RL, Patel RC. *The impact of resilience on job stress and satisfaction among employees. Journal of Occupational Health Psychology. 2020;25(1):38-49.*
23. Zimmerman MA, Stewart SE, Morrel-Samuels S, Reischl TM, Miller ML. *Resilience in adolescence: The role of community and social support. Journal of Youth and Adolescence. 2021;50(7):1287-1300.*
24. Bonanno GA, Galea S, Bucciarelli A, Vlahov D. *Resilience and posttraumatic stress disorder: A review of the literature. Journal of Anxiety Disorders. 2019; 64:27-39.*
25. Bonanno GA. *The resilience paradox: Findings from studies of stress and trauma. Clinical Psychology Review. 2019; 68:30-39.*
26. Fletcher D, Sarkar M. *The role of resilience in recovery from trauma and adversity. Psychological Review. 2020;127(3):356-374.*
27. Tedeschi RG, Calhoun LG. *Posttraumatic growth: Conceptual foundations and empirical evidence. Psychological Inquiry. 2004;15(1):1-18.*
28. Garmezy N. *Resilience and vulnerability to adverse developmental outcomes associated with poverty. American Behavioral Scientist. 1991;34(4):416-430.*
29. Werner EE, Smith RS. *Overcoming the odds: High-risk children from birth to adulthood. Cornell University Press. 1992.*
30. Luthar SS, Cicchetti D, Becker B. *The construct of resilience: A critical evaluation and guidelines for future work. Child Development. 2000;71(3):543-562.*
31. Rutter M. *Implications of resilience concepts for scientific understanding. Annals of the New York Academy of Sciences. 2006;1094(1):1-12.*
32. Connor KM, Davidson JR. *Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). Depression and Anxiety. 2003;18(2):76-82.*
33. Ungar M, Ghazinour M, Richter J. *Resilience, trauma, and recovery: A cross-cultural perspective. Traumatology. 2013;19(4):255-266.*
34. Kim-Cohen J. *Resilience and developmental psychopathology. Child and Adolescent Psychiatric Clinics. 2007;16(2):271-283.*
35. Cyrulnik B. *Resilience: How your inner strength can set you free from the past. Penguin Random House. 2009.*
36. Zautra AJ, Hall JS, Murray KE. *Resilience: A new definition of health for people and communities. In:* Reich JW, Zautra AJ, Hall JS, eds. *Handbook of Adult Resilience. Guilford Press; 2010:3-29.*
37. Masten AS, Cutuli JJ, Herbers JE, Reed MG. *Resilience in development. In:* Snyder CR, Lopez SJ, eds. *Handbook of Positive Psychology. 2nd ed. Oxford University Press; 2011:117-131.*
38. Southwick SM, Litz BT, Charney D, Friedman MJ. *Resilience and mental health: Challenges across the lifespan. Cambridge University Press. 2011.*
39. Richardson GE. *The metatheory of resilience and resiliency. Journal of Clinical Psychology. 2002;58(3):307-321.*
40. Windle G. *What is resilience? A systematic review and concept analysis. Reviews in Clinical Gerontology. 2011;21(2):152-169.*
41. Luthar SS, Brown PJ. *Maximizing resilience through diverse perspectives on positive adaptation. American Journal of Orthopsychiatry. 2007;77(1):1-15.*
42. Masten AS. *Global perspectives on resilience in children and youth. Child Development. 2014;85(1):6-20.*
43. Rutter M. *Psychosocial resilience and protective mechanisms. American Journal of Orthopsychiatry. 1987;57(3):316-331.*
44. Henderson N, Milstein MM. *Resiliency in schools: Making it happen for students and educators. Corwin Press. 2003.*

Correspondence:
Matijana Jurišić
Dom zdravlja Tomislavgrad,
Dr. Mije Ferića 12, 88 240 Tomislavgrad
e-mail: jurisicmatijana@gmail.com

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2 *Review*

HERBAL THERAPIES IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASES: A HISTORICAL AND CONTEMPORARY REVIEW

Danijela Petrović[1], Helena Brekalo[1], Danijel Bevanda[2], Daniela Bevanda-Glibo[2], Milenko Bevanda[2]

[1] *Faculty of Agronomy and Food Technology, University of Mostar, 88 000 Mostar, Bosnia & Herzegovina*
[2] *Faculty of Medicine, University of Mostar, 88 000 Mostar, Bosnia & Herzegovina*
received: 04.09.2025; revised: 21.09.2025; accepted: 22.09.2025

SUMMARY

Inflammatory bowel diseases (ulcerative colitis and Crohn's disease) are chronic, relapsing disorders of the digestive tract, the etiology of which is complex and includes genetic, immunological, microbiological and environmental factors. Standard therapeutic options often have limited efficacy and significant side effects, which is why interest in complementary and alternative approaches, especially phytotherapy, is growing. Historically, medicinal plants have played a key role in the medical traditions of many civilizations, and modern research confirms the effectiveness of some herbal preparations in modulating the immune response, anti-inflammatory effects and maintaining intestinal homeostasis. This paper presents a historical overview of the use of plants in traditional medicine and modern knowledge about their role in the treatment of inflammatory bowel diseases. Special emphasis is placed on plants such as marshmallow, plantain, flax, licorice, sage, mint, cannabis and turmeric. Although the results of numerous studies confirm their potential in symptomatic relief and reducing inflammatory markers, additional randomized clinical trials are needed to confirm their safety and efficacy. The integration of phytotherapy into standard therapeutic protocols could represent a significant step forward in the holistic approach to patients with IBD.

Key words: *inflammatory bowel disease, ulcerative colitis, Crohn's disease, phytotherapy, herbal preparations*.

*****

INTRODUCTION

The connection between humans and plants dates back to the earliest history – from nutrition, through healing, to ritual and cultural use. The oldest civilizations, such as the Chinese, Egyptians, Indians, Greeks and Romans, knew a large number of medicinal plants whose use has shaped the foundations of medicine for centuries (1–4). Today, in the era of modern medicine, more and more research is focused on the potential of plants in the treatment of chronic diseases, including inflammatory bowel disease (IBD). IBD includes Crohn's disease and ulcerative colitis – chronic inflammatory diseases that significantly impair the quality of life of sufferers. Conventional therapies, although effective in many cases, often fail to lead to permanent remission or cause serious side effects. Therefore, interest in complementary and alternative medicine (CAM), especially phytotherapy, is growing (12–14).

The aim of this review is to unify historical and contemporary knowledge about the use of medicinal plants in the treatment of inflammatory bowel disease and to demonstrate their potential in modern medicine.

HISTORICAL OVERVIEW OF MEDICINAL PLANT USE

From the Sumerians and Egyptians to ancient Greece and Rome, herbal remedies have been used to treat digestive and inflammatory conditions. Hippocrates described more than 300 plants for therapeutic purposes, while Dioscorides and Galen laid the foundations of European herbal medicine (1,4,6). Monastic medicine played a significant role in the Middle Ages, and the Franciscans in Dubrovnik opened the first pharmacy in 1271, which operated continuously for centuries (10,11). Plants such as flax, licorice, mint, and sage have been used for centuries to treat digestive disorders, while turmeric and cannabis are part of the Eastern medical tradition (5,8,9). Interestingly, much of the traditional knowledge has been confirmed by modern scientific research, highlighting the continuity of the use of plants in medicine (7,22).

PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE

IBD is a multifactorial disease. Genetic predisposition, immune dysregulation, changes in the gut microbiota, and environmental factors are involved in its pathogenesis (15–19). In patients with IBD, the intestinal barrier is disrupted, leading to increased permeability, abnormal cytokine secretion, and inflammatory response (18). Standard therapy includes corticosteroids,

immunomodulators, and biologics, but side effects and resistance to therapy prompt the need for new therapeutic options (19,20). Toxicity often occurs in patients treated with biologic therapy (62). A significant number of patients with inflammatory bowel disease do not respond to anti-TNF therapy and require more effective treatment (63). Also, due to the lack of primary or secondary response to anti-TNF therapy in a certain number of patients, corticosteroid therapy must be included more often, which opens the possibility of steroid dependence.

HERBAL REMEDIES FOR INFLAMMATORY BOWEL DISEASE

Mallow root (Althaeae radix)

It contains high amounts of mucilage, which coats and soothes the lining of the digestive tract. It has been traditionally used for gastritis, enteritis, and irritable bowel syndrome, and clinical experience has shown its effectiveness in alleviating symptoms of IBD (38). Several studies have shown that mallow extract contains a variety of compounds, including phenolic derivatives, flavonoids, terpenoids, catalase enzymes, sulfite oxidase, fatty acids and certain sterols (especially essential fatty acids such as omega-3 and omega-6), beta-carotene, and vitamins C and E, which have anti-inflammatory and antioxidant properties (57, 58).

Psyllium seeds (Psyllium)

Acts as a mechanical laxative, improves stool regulation and reduces CRP levels in patients with irritable bowel syndrome. In IBD, it helps with constipation and diarrhea, contributes to the regulation of intestinal microbiota and reduces symptoms (39,40). The seeds contain the monosaccharides glucose, fructose, xylose and rhamnose, as well as the disaccharide sucrose and the trisaccharide planteose (59). Planteose acts as a reserve carbohydrate in the seeds (60). Research has identified biologically active substances such as polysaccharides, lipids, flavonoids, terpenes. Also, analyses have identified certain organic acids and alkaloids. The positive health effect is attributed to these biologically active substances, which were discovered in plantain extracts based on appropriate analyses. The outer shell of the seeds contains polysaccharides that swell in contact with water and form a highly viscous mucus.

Flaxseed (Linum usitatissimum)

Flaxseed is rich in fiber and omega-3 fatty acids, and has anti-inflammatory and laxative properties. Active ingredients in flaxseed also include lignin and protein, as well as a number of vitamins and minerals, such as vitamin B1 (thiamine), magnesium, copper, and manganese. Studies have shown a reduction in inflammatory markers and impr

ovement in symptoms in patients with ulcerative colitis (41).

Licorice root (Glycyrrhiza glabra)

Active substances in licorice root include triterpenoids and phenols, the most important of which is glycyrrhizin. It is fifty times sweeter than sugar and has potent anti-inflammatory, antioxidant, and immunomodulatory properties. Experimental models have shown suppression of NF-κB and TNF-α and protection of the colonic mucosa (42–45).

Sage (Salvia officinalis)

Its antiseptic and anti-inflammatory effects may alleviate symptoms of colitis. Active substances in sage include essential oils (composed of thujone and other compounds), phenolic acids (such as caffeic and ursolic acids), tannins, flavonoids, triterpenes, steroid compounds, and minerals (calcium, magnesium, iron, copper, zinc) and vitamins (B-groups, C, A). Its antiseptic and anti-inflammatory effects may alleviate symptoms of colitis. Preclinical studies suggest the possibility of preventing colon cancer (46,47).

Peppermint (Mentha piperita)

The main active ingredients of peppermint are compounds within its volatile essential oil, primarily menthol, which provides a cooling sensation and has therapeutic properties, and menthone, which contributes to the taste and aroma of mint. Other significant constituents include menthyl acetate, the compound responsible for the smell and taste of mint, and other terpenes such as limonene and 1,8-cineole. Peppermint essential oil has been shown to have antispasmodic and analgesic effects. Clinical trials have shown a reduction in abdominal pain and an improvement in quality of life in patients with irritable bowel syndrome and IBD (48–50).

Cannabis (Cannabis sativa)

Cannabinoids, primarily CBD and THC, but also lesser-known compounds such as CBG and terpenes that have synergistic effects, are attracting particular attention in the treatment of IBD. CBD is noted for its potent anti-inflammatory and immunomodulatory properties without psychoactive effects. Studies show that CBD reduces intestinal hyperpermeability and regulates T-lymphocyte activity, while THC acts primarily to reduce pain and improve appetite.Although small clinical trials have shown significant symptom relief in patients with Crohn's disease, the results for maintaining remission are not clear. The active ingredients (THC, CBD) act through the endocannabinoid system, modulating intestinal motility and inflammatory processes. Clinical studies have shown improvement in symptoms and a decrease in the need for corticosteroids in patients with Crohn's disease (51–54). There are more than 400 different structurally recognizable compounds in the biological structure of hemp. Among the ingredients are a large number of cannabinoids (depending on the cultivation and type of hemp, the number varies from 60 to 110), nitrosamines,

polycyclic aromatic hydrocarbons, aromatic amines, proteins, glycoproteins, enzymes, sugars, hydrocarbon compounds, alcohols, aldehydes, fatty acids, esters, steroids, terpenes, phenols, flavonoids, etc. Cannabinoids are not evenly distributed in the plant. The dried leaves of the female plant contain the highest amount of THC 2-3%, followed by the lower leaves where the content is less than 1% and the stem with a content ≤ 0.3%, while cannabinoids are not present in the seeds and roots. Differences in concentrations are due to the presence of glandular hairs.

Turmeric (Curcuma longa)

Recent research shows that curcumin also affects the expression of genes involved in the regulation of the immune response, in particular by modulating the balance between anti-inflammatory and pro-inflammatory cytokines. In addition to the NF-κB pathway, curcumin also inhibits the JAK/STAT signaling pathways, thereby reducing the expression of inflammatory mediators. Clinical meta-analyses highlight its potential in maintaining remission in ulcerative colitis, and the safety profile is considered favorable even with long-term use. However, the problem of low bioavailability is being addressed by new pharmaceutical forms such as nanoparticles and liposomes. Turmeric is also being investigated in the context of protecting the intestinal barrier, as it promotes the renewal of epithelial cells and reduces oxidative stress.

The main active ingredient of turmeric is curcumin, a polyphenol that gives turmeric its characteristic yellow color and strong antioxidant and anti-inflammatory properties. In addition to curcumin, turmeric also contains other active ingredients such as polyphenols, diterpenes, sesquiterpenes, sterols, triterpenoids and alkaloids. The active substance curcumin strongly inhibits inflammatory pathways (NF-κB, TNF-α, IL-6). Randomized studies have demonstrated induction of remission and reduction of endoscopic activity of ulcerative colitis (55).

DISCUSSION

It is important to emphasize that despite a large number of studies, the exact causes of IBD remain unknown. Although genetic predisposition, changes in the microbiota and dysregulation of the immune system are recognized in the pathogenesis, none of these factors can be considered the exclusive cause of the disease. It is precisely this unknown that opens up the possibility of using herbal preparations as supportive therapies, since they act in multiple ways and can contribute to reducing symptoms and improving quality of life. The emergence of IBD in newly industrialized regions coincides with the westernization of dietary habits, which potentially changes the gastrointestinal microbiota, which can impair the immune system leading to the occurrence of IBD. The Western diet consists of processed foods high in saturated fats, animal proteins, refined sugars, food additives combined with low intake of fruits and vegetables, fiber and raw foods (61). Inflammatory bowel disease (IBD) mainly includes ulcerative colitis (UC) and Crohn's disease (CD), with symptoms such as abdominal pain, diarrhea, and weight loss. Barnell et al. (64) reported that more than 50% of patients with Crohn's disease require resection at some point, and Regueiro et al. (65) reported that more than 30% of patients with Crohn's disease (CD) develop perianal fistulas. Due to the long duration of the disease and frequent relapses, IBD represents a major economic burden and psychological stress for the patient, and therefore the quality of life can be extremely impaired (66). In ulcerative colitis, more than 20% of patients progress to colectomy (67). Recent research suggests that herbal preparations, especially turmeric and hemp, can modulate key signaling pathways involved in chronic inflammation. However, well-designed, multicenter, larger-scale studies are needed to confirm their efficacy and safety. Herbal preparations in the treatment of inflammatory bowel diseases offer significant potential, but also challenges. Their value stems from their multicomponent composition that enables the synergistic action of various phytochemicals – flavonoids, phenolic acids, saponins, terpenes and essential oils (22,42). These compounds simultaneously act on various molecular pathways involved in the pathogenesis of IBD, including inhibition of NF-κB, reduction of pro-inflammatory cytokine expression (TNF-α, IL-1β, IL-6), modulation of oxidative stress and regulation of the intestinal microbiota (28–30,43). Clinical studies have particularly highlighted the effectiveness of curcumin, cannabis and probiotics in maintaining remission and improving the quality of life of patients (31,32,53,55). For example, randomized trials with curcumin showed significantly higher remission rates compared to placebo, while cannabis in studies of patients with Crohn's disease reduced the need for corticosteroids (53). Studies in cell cultures, animal models, and clinical trials have suggested that curcumin is a potential agent for the treatment of not only IBD, but also pancreatitis, arthritis, chronic anterior uveitis, and certain types of cancer. Curcumin has a significant effect on the repair of the intestinal mucosa and the maintenance of its morphology (68). Licorice and sage show promising results in experimental models of colitis, while plantain and flaxseed are useful in regulating stool and reducing CRP (39,41,42,46). Supplementation with peppermint oil, in addition to pharmacological standard treatments, is beneficial in patients with constipation-predominant IBD and in patients with bowel-emptying IBD (40). However, limitations are recognizable and obvious. Most studies are based on small samples, short duration, and large variations in dosage and formulation. Standardization of formulations and clear definition of active ingredients remain key research challenges (20,33,34). Also, the interactions of herbal preparations with conventional drugs have not been sufficiently investigated (42,51). Despite these limitations, the

potential of herbal therapies in IBD is undeniable. The use of complementary medicine among patients with IBD, especially in the form of herbal therapies, is widespread in the Western world, as well as in many Asian countries (69). Also, the most commonly used forms of treatment for children with IBD are medicinal plants (turmeric, cannabis), probiotics, fish oils, acupuncture, dietary nutrition and multivitamin therapy (70). Considering that when treating Crohn's disease (CD) with biological therapy, more than 50% of patients do not respond to therapy with deep remission, we are forced to look for other treatment modalities, even dual biological therapy (71,72). The greatest obstacle to optimal combination treatment remains toxicity (62). Herbal preparations should not replace conventional therapy, but complement it, especially in patients with milder forms of the disease or those who want a holistic approach to treatment (12,21,22). The integration of phytotherapy into standard therapeutic protocols could contribute to a more individualized and humane medicine (23,55,56).

CONCLUSION

Inflammatory bowel disease (IBD) remains a therapeutic challenge despite significant advances in pharmacotherapy. Medicinal plants, used for thousands of years in traditional medicine, are regaining importance thanks to modern scientific evidence. Herbal preparations such as mallow, plantain, flax, licorice, sage, mint, cannabis and turmeric have shown promising results in reducing symptoms and inflammatory markers in patients with IBD. Although herbal therapy cannot yet be considered a substitute for conventional drugs, it can represent a valuable complementary approach. Further research is needed to ensure the standardization, safety and efficacy of these preparations and their integration into official IBD treatment guidelines.

Acknowledgements: None.

Conflict of interests: None.

LITERATURE

1. Kušan F. *Medicinal plants. Zagreb: Školska knjiga; 1956.*
2. Bazala V. *History of natural sciences. Zagreb: JAZU; 1955.*
3. Videk M. *History of medicine. Zagreb: JAZU; 1960.*
4. Šantić Ž. *Medicinal plants through history. Mostar: University of Mostar; 1999.*
5. Parojčić D, et al. *Historical development of the use of plants in medicine. Belgrade: SANU; 2001.*
6. Vrgoč J. *History of pharmacy. Zagreb: Školska knjiga; 1931.*
7. Wong A. *Opium and its derivatives in medicine. J Med Hist. 1973; 17:112–21.*
8. Tartalja H. *History of Pharmacy and Pharmacognosy. Zagreb: Medicinska naklada; 1965.*
9. Atanacković M, Tucakov J. *Pharmacognosy. Belgrade: Medicinska knjiga; 1970.*
10. Peros V. *Franciscans and Medicine. Split: Franciscan Institute; 1963.*
11. Ribičić I. *Old Pharmacists and Franciscan Medicine. Sarajevo: Synopsis; 2004.*
12. Falkenberg T, et al. *Complementary and alternative medicine: relevance to public health. Scand J Public Health. 2012;40(5):447–52.*
13. Larson DB. *Why patients turn to alternative medicine. JAMA. 2007;297(14):1444–5.*
14. Peregoy J, et al. *Defining CAM: complementary vs alternative. Altern Ther Health Med. 2014;20(3):45–9.*
15. Scaldaferri F, et al. *Inflammatory bowel disease: pathogenesis and treatment. Dig Liver Dis. 2007;39(6):515–21.*
16. Orholm M, et al. *Familial occurrence of inflammatory bowel disease. N Engl J Med. 1991; 324:84–8.*
17. Mahida Y. *Immunology of inflammatory bowel disease. Gut. 1989;30(7):857–62.*
18. Zeeshan M, et al. *Intestinal barrier dysfunction in IBD. World J Gastroenterol. 2019;25(18):2181–90.*
19. Ramos GP, Papadakis KA. *Mechanisms of disease: inflammatory bowel disease. Mayo Clin Proc. 2019;94(1):155–65.*
20. Mountifield R, et al. *Perceptions of complementary and alternative medicine in IBD. J Crohns Colitis. 2015;9(4):327–34.*
21. Nguyen GC, et al. *Use of complementary and alternative medicine in IBD. Inflamm Bowel Dis. 2016;22(1):141–6.*
22. Tanović I. *Phytotherapy in modern medicine. Sarajevo: Avicenna; 2004.*
23. Inglis A, West P. *WHO support for traditional medicine. Bull World Health Organ. 1986;64(6):903–8.*
24. Fioramonti J, et al. *Probiotics and gut health. Dig Dis Sci. 2003; 48:1485–92.*

25. FAO/WHO. *Probiotics in food: health and nutritional properties and guidelines. Rome: FAO/WHO; 2001.*
26. Baumgart DC, et al. *Probiotic therapy in IBD. Gut. 2007; 56:365–71.*
27. Clausen MR, Mortensen PB. *Butyrate production and intestinal function. Scand J Gastroenterol. 1994; 29:462–8.*
28. Omenetti S, Pizarro TT. *The Treg/Th17 axis in IBD. Front Immunol. 2015; 6:639.*
29. Dalal SR, Chang EB. *The microbial basis of IBD. J Clin Invest. 2014; 124:4190–6.*
30. Lopez-Siles M, et al. *Faecalibacterium prausnitzii and health. Front Microbiol. 2017; 8:1223.*
31. Bibiloni R, et al. *VSL#3 in ulcerative colitis. Gastroenterology. 2005; 128:541–9.*
32. Kelesidis T, Pothoulakis C. *Saccharomyces boulardii in IBD. Curr Pharm Des. 2012; 18:2404–12.*
33. Damaskos D, Kolios G. *Prebiotics in IBD. Br J Nutr. 2008;100 Suppl 1: S54–7.*
34. Rasmussen HS, Hamaker BR. *Oligosaccharides and IBD. Curr Opin Clin Nutr Metab Care. 2017; 20:426–31.*
35. Larrosa M, et al. *Prebiotics and microbiota in colitis models. Br J Nutr. 2009; 101:541–50.*
36. Rose DJ, et al. *Resistant starch and microbiota. J Agric Food Chem. 2010;58(5):2441–9.*
37. Casellas F, et al. *Inulin in ulcerative colitis. Eur J Clin Nutr. 2007;61(6):802–9.*
38. Sadiković B. *Phytotherapy in gastrointestinal diseases. Zagreb: Medical Publication; 2010.*
39. Minihane AM. *CRP reduction by psyllium. Nutr Rev. 2015;73(9):574–88.*
40. Garg PK. *Psyllium in IBS. Clin Gastroenterol Hepatol. 2017; 15:112–7.*
41. Morshedzadeh N, et al. *Flaxseed in UC patients. Clin Nutr. 2019;38(1):392–9.*
42. Menegazzi M, et al. *Licorice extract in inflammation. Planta Med. 2008;74(3):261–7.*
43. Li Y, et al. *Glycyrrhiza and oxidative stress in IBD. Front Pharmacol. 2022; 13:842.*
44. Cao Y, et al. *Anti-inflammatory effects of licorice. Int Immunopharmacol. 2019; 68:242–50.*
45. Yuan H, et al. *Licorice extract in colitis models. World J Gastroenterol. 2006;12(26):4266–72.*
46. Jalalipour S, et al. *Sage in colitis rat model. J Ethnopharmacol. 2022; 284:114749.*
47. Pedro A, et al. *Sage tea and colon cancer prevention. Food Chem Toxicol. 2021; 150:112065.*
48. Kligler B, Chaudhary S. *Peppermint oil in IBS. Altern Ther Health Med. 2007;13(2):44–7.*
49. Cappello G, et al. *Peppermint capsules in IBS. Dig Liver Dis. 2007;39(6):530–6.*
50. Bastaki SM, et al. *Menthol in experimental colitis. Biomed Pharmacother. 2018; 107:1282–9.*
51. Baron TH, et al. *Cannabis in IBD. Mayo Clin Proc. 1990;65(3):377–81.*
52. Di Sabatino A, et al. *Endocannabinoid system in IBD. Gut. 2011; 60:472–81.*
53. Naftali T, et al. *Cannabis in Crohn's disease. Clin Gastroenterol Hepatol. 2011;9(10):752–7.*
54. Anthony JC, et al. *Prevalence of cannabis dependence. Am J Psychiatry. 1994; 151:1438–42.*
55. Banerjee R, et al. *Curcumin in ulcerative colitis. Aliment Pharmacol Ther. 2020;52(2):273–84.*
56. Song KH, et al. *Acupuncture in gastrointestinal disorders. World J Gastroenterol. 2019;25(31):4079–95.*
57. Benso B., Franchin M., Massarioli A. P., et al. *Anti-inflammatory, anti-osteoclastogenic and antioxidant effects of Malva sylvestris extract and fractions: in vitro and in vivo studies. PLoS One. 2016;11(9):p. e0162728. doi: 10.1371/journal.pone.0162728.*
58. Martins C., Campos M., Irioda A., Stremel D., Trindade A., Pontarolo R. *Anti-inflammatory effect of Malva sylvestris, Sida cordifolia, and Pelargonium graveolens is related to inhibition of prostanoid production. Molecules. 2017;22(11): p. 1883. doi: 10.3390/molecules22111883.*
59. Ahmed ZF, Rizk AM, Hammouda FM. *Phytochemical studies of egyptian Plantago species (Glucides). Journal of Pharmaceutical Sciences. 1965; 54:1060-1062.*
60. Rohrer DC. *The crystal and molecular structure of planteose dehydrate. Acta Crystallographica. 1972; 425-433.*
61. Altajar S, Moss A. *Inflammatory Bowel Disease Environmental Risk Factors: Diet and Gut Microbiota. Curr Gastroenterol Rep. 2020; 22:57.*
62. D'Haens G. *Risks and benefits of biologic therapy for inflammatory bowel diseases. Gut. 2007; 56:725–732.*
63. Van Assche G, Rutgeerts P. *Antiadhesion molecule therapy in inflammatory bowel disease. Inflamm Bowel Dis. 2002,8:291-300.*
64. Bernell O, et al. *Risk factors for surgery and postoperative recurrence in Crohn's disease. Ann Surg 2000; 231:38-45.*
65. Regueiro M, Mardini H. *Treatment of perianal fistulizing Crohn's disease with infliximab alone or as an adjunct to exam under anesthesia with seton placement. Inflamm Bowel Dis. 2003,9:98-103.*
66. Cohen RD. *The quality of life in patients with Crohn's disease. Aliment Pharmacol Ther. 2002; 16:1603-1609.*
67. Langholz E, et al. *Course of ulcerative colitis: analysis of changes in disease activity over years. Gastroenterology 1994:107:3-11.*
68. Jurenka JS. *Anti-inflammatory Properties of Curcumin, a Major Constituent of Curcuma longa: A Review of Preclinical and clinical Research. Altern Med Rev 2009; 14:141-53.*
69. D'Inca R, Garribba AT, Vettorato MG, Martin A, Martines D, Di Leo V, et al. *Use of alternative and complementary therapies by inflammatory bowel*

disease patients in an Italian tertiary referral centre. Dig Liver Dis. 2007; 39:524–9. doi: 10.1016/j.dld.2007.03.001.

70. Nousiainen P, Merras-Salmio L, Aalto K, Kolho KL. *Complementary and alternative medicine use in adolescents with inflammatory bowel disease and juvenile idiopathic arthritis. Complement Altern Med 2014; 14:124-31.*

71. Rutgeerts P, et al. *Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med 2005;353,2462-2476.*

72. Colombel JF, et al. *Adalimumab induces deep remission in patients with Crohn's disease. Clin Gastroenterol Hepatol. 2014; 12:414-422.*

Correspondence:
Professor Milenko Bevanda, MD, PhD
University of Mostar, Mostar, Bosnia and Herzegovina
Ministry of Health, Herzegovina-Neretva Canton,
Bosnia and Herzegovina
E-mail: milenko.bevanda@mef.sum.ba

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2 *Review*

METACOGNITION AND PHYSICAL ACTIVITY – MENTAL AND PHYSICAL HEALTH

Anica Kuzmić

Department of Physiotherapy, University North, Varazdin, Croatia
received: 04.03.2025; revised: 07.05.2025; accepted: 20.10.2025

SUMMARY

Metacognition and physical activity represent two important areas that can be interconnected to improve cognitive functions and overall human health. Metacognition refers to an individual's ability to understand and manage their cognitive processes, such as planning, monitoring, and adjusting thinking strategies. On the other hand, physical activity positively impacts physical health but can also have beneficial effects on mental processes, including metacognitive skills. The relationship between metacognition and physical activity lies in the fact that regular physical activity can enhance metacognitive abilities, such as attention, memory, concentration, and coping strategy development. Individuals who engage in regular physical activity demonstrate a better ability to reflect on their mental processes, which can lead to increased confidence in learning and problem-solving. Furthermore, physical activity can positively influence stress reduction and emotional well-being, which may improve and enhance metacognitive skills, such as self-awareness and emotional regulation. The implementation of physical activity into daily life offers a holistic approach to improving health, including cognitive aspects, and encourages the understanding and management of one's thought processes. Scientific research in this field is still exploring how different forms of physical activity affect specific metacognitive processes and how metacognition can be integrated into physical activity performances. The connection between metacognition and physical activity provides new opportunities for developing interventions that could enhance cognitive functions and the overall health of individuals.

Key words: *metacognition, physical activity, cognitive function*

*****

INTRODUCTION

Two key aspects of human life are metacognition and physical activity. Metacognition is the ability to think about one's thinking. It involves an individual's awareness of their thoughts, the thinking process, as well as the ability to plan and adapt thinking strategies. It plays an important role in learning, decision-making, and problem-solving by understanding one's cognitive processes (Stanton et al., 2021; Rivas et al., 2022). Physical activity is any bodily movement that requires energy expenditure. Due to its positive effects, it plays a crucial role in human life, not only for physical health but also for mental well-being (Tacchi et al., 2019; Briguglio et al., 2020). Regular physical activity can improve cardiovascular health, fitness, maintain a healthy body weight, and reduce the risk of many diseases. It can also reduce stress, depression, and anxiety, improve mood, and contribute to an overall increase in quality of life (Lasikiewicz et al., 2014; Warburton & Bredin, 2017; Firth et al., 2017). Physical activity is most commonly associated with physical health, while metacognition is linked to cognitive abilities and self-awareness (Stanton et al., 2021; Rivas et al., 2022). However, these aspects are interrelated, as physical activity can positively impact metacognition, and metacognition can influence physical activity. Engaging in regular physical activity can improve cognitive functions, including concentration, attention, and decision-making abilities. It can also reduce stress, which leads to improved metacognitive skills and better management of one's thoughts (Nuzum et al., 2020). Both physical activity and metacognition play significant roles in human daily life in various ways. In the workplace, metacognition can help employees manage their tasks, deadlines, and priorities more effectively, while physical activity can improve energy levels, productivity, and creativity, resulting in better work performance (Friedman & Miyake, 2017). Additionally, metacognition enables individuals to better understand their feelings and thoughts, which is crucial for decision-making, while physical activity helps reduce stress and improve mood, which can facilitate the process of making rational professional decisions (Awick, 2017). In education and learning, metacognition helps students better understand their learning strategies, set goals, manage time, and adapt their learning methods to achieve better results, while physical activity can improve concentration and cognitive abilities, facilitating learning and memory retention (Vrdoljak & Velki, 2012; Filipec et al., 2024). Metacognition enables individuals to better understand their emotional reactions and how to cope with them, while physical activity can improve mood and assist in dealing with emotional challenges (Erickson et al., 2012; Lasikiewicz et al., 2014; Warburton & Bredin, 2017). Together, metacognition and physical activity can improve and enhance the quality of life, contributing to better emotional, physical, and mental health in everyday life.

METACOGNITION: "KNOWLEDGE OF ONE'S OWN KNOWLEDGE"

Metacognition is a complex concept that refers to the ability to understand and manage one's cognitive processes. It involves awareness of one's memory, thoughts, perception, and problem-solving (Jankowski & Holas, 2014). This means that an individual is not only aware of visible external actions but also of their internal processes. The ability of metacognition represents more than mere awareness; it includes the ability to control and regulate one's cognitive processes (Rahnev, 2021). An example of this is recognizing a loss of concentration during learning and deciding to take a break. A person can reflect and ask themselves questions such as, "How am I thinking about this task?" or "Which strategy will I use to solve it?" This ability to think allows individuals to recognize their strengths and weaknesses and adapt their approach to achieve better outcomes (Jankowski & Holas, 2014; Szczepanik et al., 2020). It may include assessing one's understanding of the material during learning, planning time for tasks, setting goals for work efficiency, monitoring progress, and recognizing and correcting errors in thinking. Understanding and controlling one's cognitive abilities ensure successful coping with challenges in everyday life activities (Efklides, 2008; Kolesarić & Milić, 2014; Kuzmić & Filipec, 2022). Metacognition is not an innate ability; it develops over time and undergoes various developmental stages, especially during childhood and adolescence. During early childhood, children do not have full awareness of their cognitive processes, but around the age of four, they begin to develop a basic level of metacognitive awareness. An example of this is when a child is asked something they don't know and responds, "I don't know!" which signals the beginning of the ability to recognize their knowledge or lack thereof (Brinck & Liljenfors, 2013). As children grow, they begin to understand these abilities more and apply specific thinking methods regarding their actions and strategies for problem-solving. Later, during adolescence, metacognitive abilities become more sophisticated, and individuals become increasingly aware of their choice of strategies and techniques to improve cognitive processes. They develop the ability to assess their characteristics and think critically by setting realistic goals (Schneider, 2008). However, it is important to note that there is significant variation in the development of metacognition among individuals. For some, higher levels of metacognitive skills naturally develop, while others need to cultivate them through appropriate education and/or improvement through training and lifelong learning (Jackson & Kleitman, 2014; Faivre et al., 2018; Mazancieux et al., 2020; Abdelrahman, 2020). Understanding the process of metacognitive development and its formation throughout life can influence an individual's behavior and characteristics in various life situations, including its connection with physical activity.

METACOGNITION IN DAILY LIFE: THE POTENTIAL OF SELF-AWARENESS

Metacognition plays a crucial role in an individual's everyday life and can significantly affect their abilities, decisions, and emotional well-being. By using metacognitive abilities, individuals can better think about and analyze their problem-solving strategies and make better decisions. It also enables them to better assess their priorities and goals and make decisions aligned with their own needs and desires (Bhome et al., 2022). Individuals who are aware of their thoughts and feelings can better understand their reactions to stressful situations and apply coping strategies, such as recognizing their negative thoughts and redirecting them toward positive directions. Furthermore, metacognition can improve communication and interaction in social relationships. Understanding one's reactions and the ability to recognize the onset of conflict can ultimately contribute to better conflict resolution and the building of more positive interpersonal relationships. This can also be observed in everyday life during political and religious discussions. It is an essential characteristic, not only as an individual's ability to understand themselves but also to understand themselves about others by making fairer and more reasonable decisions (Jakovljević, 2005; Rollwage, 2018; Heyes et al., 2020). When metacognition is considered in the context of an individual's cultural background, the literature suggests that metacognitive abilities related to interpersonal relationships and personal functions are primarily enabled by cultural learning and are partially adaptive due to cultural selection (Heyes et al., 2020; Frith, 2023). A person's functioning in everyday life is also connected to metacognitive judgment abilities, including the monitoring of internal spatial cues and environmental signals. External environmental cues refer to the intake of global and local information from the external world, including auditory and visual signals (Chen et al., 2017), while internal spatial cues provide information about one's position in space (Stevens & Carlson, 2016). This confirms that metacognition plays a significant role in learning from the environment. For example, during daily human movement, individuals engage in monitoring environmental information by assessing and remembering paths, using a control mechanism to prevent loss of orientation. Environmental learning requires the encoding of verbal, visual, and spatial information, which occurs gradually and must be integrated over time. Depending on conditions, time, and motivation, various circumstances can affect the reliability of environmental cues. Relying on unreliable cues can undermine the accuracy of metacognitive judgment and the success of memory (Mason et al., 2022). Understanding one's cognitive processes and applying metacognitive strategies enables individuals to better understand themselves, make better decisions, and cope more effectively with life's challenges. This ability

can also positively impact the completion of everyday work tasks, as it facilitates better planning and management to achieve desired outcomes (Fleming & Bang, 2018; Shea & Frith, 2019).

PHYSICAL ACTIVITY

Physical activity is considered one of the basic human needs for functioning, to maintain and improve health. It encompasses a wide range of movements and includes all forms of human body movement that require effort and increase energy expenditure (Caspersen et al., 1985). People can engage in physical activities of varying intensity, duration, and type. For example, some may prefer moderate-intensity training in the gym, while others may prefer cycling or walking as forms of recreational physical activity. Physical activity also includes daily activities that are an integral part of life, such as climbing stairs, walking to the store, walking to work, or even performing household chores like cleaning and cooking. These everyday activities also contribute to the overall level of physical activity (Thomas et al., 2019; Miko, 2020). Engaging in physical activity has numerous physical and psychological benefits that contribute to overall health and well-being. It plays a vital role in preserving both physical and mental health and is a key component of a healthy lifestyle (Pearce, 2008; Pedersen & Saltin, 2015; Firth et al., 2020). Understanding what physical activity means, its benefits, and how it can be adapted to everyday needs helps individuals make informed decisions about their health.

INTEGRATION OF METACOGNITION IN PHYSICAL ACTIVITIES

The integration of metacognition in physical activities refers to an individual's ability to understand and manage their thoughts and thinking processes during performance. In applied contexts, it is typically associated with self-awareness and introspection aimed at improving performance and experience (Ngô, 2013). Some examples of integrating metacognition into physical activities include awareness of breathing, self-confidence and motivation, goal-setting, body monitoring, and performance analysis.

Breathing Awareness

One of the key components of metacognition in physical activities is breathing awareness. This involves an individual's focus and control over their breathing pattern during activity performance. Utilizing this awareness can improve the overall experience and performance quality of the physical activity. Understanding the rhythm and depth of breathing, along with controlling breath during exercise, can enhance endurance by optimizing breathing patterns. Breathing awareness helps individuals learn how to breathe properly during different physical activities. For example, during aerobic exercises such as running or cycling, deep and rhythmic breathing helps provide better oxygenation to the body, leading to increased endurance and reduced fatigue. Learning to breathe deeply and be controlled can calm the nervous system and reduce tension, which results in improved comfort and reduced stress. Additionally, during exercises or training, breathing awareness enables individuals to become more sensitive to signs of fatigue or physical overload. By noticing shallow and irregular breathing, a person can become aware that a break is needed or that the intensity should be reduced to prevent potential negative consequences (Baquet et al., 2003). Furthermore, breathing awareness can be used as a relaxation technique after activity or as part of meditation practices. Deep, focused, and controlled breathing aids in relaxing the mind, reducing muscle tension, and contributing to overall physical health. Properly directed breathing contributes to greater concentration and attention during everyday physical activities, training sessions, or sports competitions. This technique involves awareness of the way an individual breathes and the understanding that breathing is a critical part of the bodily process that influences performance quality, recovery, and overall experience during physical activities (Hölzel et al., 2011; Ngô, 2013). The integration of metacognition begins with becoming aware of the rhythm of breathing during exercise. For example, synchronizing breath with steps when walking, running, or the rhythm of movements in aerobic activities. Becoming aware of this rhythm improves oxygen supply to the body and enhances performance. Furthermore, an individual's awareness of the depth and control of their breath during various phases of physical activity allows for better adaptation, reduces fatigue, increases endurance, and contributes to better control of the body's response. For example, during intense physical activities, awareness of breathing can help individuals recognize moments of stress and apply relaxation breathing techniques to reduce tension and stress, contributing to physical and mental balance. Additionally, meditation techniques focusing on breathing can help calm the mind, achieve concentration, and enhance awareness during exercise (Marenus et al., 2023; Weng et al., 2021). Breathing awareness through the integration of metacognition contributes to a holistic approach to physical activity, where the focus is not only on physical performance but also on the mental processes that support and enhance it, improving the overall experience during physical activity performance.

Body Monitoring

In the context of metacognition, body monitoring in physical activities refers to the ability of an individual to consciously sense and interpret bodily sensations, movements, and other signs during performance. This ability enables a better understanding of one's body, awareness of proper movement execution and body positioning, as well as recognition its needs during

physical activity. By using metacognitive skills, a person can notice if they are performing a movement incorrectly or holding their body in an improper position. They can also consciously assess bodily sensations such as muscle tension, identify early signs of fatigue or discomfort, and ensure timely responses. By carefully monitoring their body, an individual can quickly identify potentially dangerous situations, such as overloading the musculoskeletal and/or cardiovascular system, and by responding promptly, reduce or avoid possible negative consequences such as injuries (Andersen et al., 2004). Additionally, body monitoring allows individuals to track their progress during performance by observing certain indicators. For example, one may notice gradual improvements in strength, endurance, or flexibility and use this information for further motivation and goal-setting. The integration of metacognition into physical activities fosters a deeper mental connection with the body, enhancing understanding of one's physical responses to stress, emotions, or fatigue. Through body monitoring via metacognition, individuals become more aware of their bodily needs, leading to improved safety, efficiency, and a more positive experience of physical activity (Williams, 2000; Andersen et al., 2004).

Setting Realistic and Specific Goals

Goal setting, in the context of metacognition and physical activities, refers to the process of defining realistic and specific goals related to physical fitness, exercise, or sports activities and managing thoughts and strategies to achieve these goals. These goals may vary, such as achieving a certain level of physical fitness, improving endurance, losing weight, or achieving a specific sports result. Metacognition enables individuals to reflect more deeply on their motives for achieving selected goals, why these goals are important, and how reaching them will impact their well-being. By becoming aware of metacognitive skills, an individual can track their progress and identify internal obstacles, such as negative thoughts or patterns that may hinder goal achievement. The integration of metacognition into goal-setting allows individuals to better understand their desires and needs, plan concrete steps and activities, and more effectively manage thoughts and strategies to achieve the set goals (Hall, 2008).

Self-confidence and Motivation

The integration of metacognitive skills into physical activities focuses on managing one's thoughts, emotions, and beliefs to improve self-confidence and maintain motivation during performance. Metacognition allows an individual to recognize negative thoughts and beliefs that may diminish motivation. This includes thoughts such as, "I'm not good enough, and I can't do this." Recognizing such negative thinking can represent the first step in countering or redirecting it toward positive and constructive solutions. This involves replacing negativity with affirmations like, "Every effort is a step forward, and I can do this" (Howie & Pate, 2012). By understanding and managing negative thoughts and doubts that may arise during physical activities, an individual can improve motivation and self-confidence. If a person are aware of their successes and achievements during exercise or other physical activities, they will develop greater self-assurance, monitor their progress, and feel more confident and motivated. The integration of metacognitive skills enables an individual to think more deeply about their motives and understand why they engage in specific physical activities, which helps maintain long-term motivation (Steeves et al., 2015). Additionally, individuals can use metacognitive skills to identify obstacles encountered on the path toward achieving set goals, and understanding these obstacles helps develop strategies for overcoming them, which also ensures sustained motivation. Awareness of one's thoughts and emotional state during physical activities leads to self-assessment. A person can track their thoughts and feelings to better understand their own needs and adjust their approach accordingly. This might also include planning rewards for achieving goals, which will motivate the individual to put in more effort to achieve their set objectives. The integration of metacognition into self-confidence and motivation during physical activities helps individuals become more aware of their thoughts and emotions, directing them toward the achievement of personal goals (Wells & Cartwright-Hatton, 2004; Bélanger, 2017).

Performance Analysis

Performance analysis refers to an individual's metacognitive ability to carefully and critically evaluate their performance during physical activities, identify their strengths and weaknesses, and develop strategies for improvement. Before beginning performance, a person can set clear goals as references for specific exercises or sports competitions and carefully track their performance (time, number of repetitions, technical characteristics), as well as their overall sense. Additionally, an individual's ability to critically reflect on their performance after completing the activity helps identify areas that need improvement and plan for progress. This includes identifying areas where the person feels confident and those that require further development (Mišigoj-Duraković, 2018; Zhang et al., 2020). By using metacognitive skills, a person becomes aware of both their mind and body, recognizing fatigue, pain, negative thoughts, and emotions that may arise. Instead of becoming discouraged by negative thoughts or self-criticism, a person can apply metacognition to focus on constructive feedback aimed at improvement and think about necessary self-help strategies. Based on performance analysis through metacognition, an individual can develop a plan for future physical activities or competitions, which may include setting goals for improvement, developing specific training regimens, and working on technical aspects of

performance. This allows individuals to mentally prepare, including visualizing successful performances, fostering positive self-confidence, and focusing on control during exercise. Performance analysis through metacognition helps individuals improve their physical activities by better understanding their performance and developing strategies for improvement. One can track their progress and assess whether the strategies applied are effective by comparing new performances with previously achieved results. This awareness also helps increase satisfaction and reduce stress during physical activities, allowing individuals to become more aware of their emotions and thoughts (Williams, 2000; Bao et al., 2024).

Planning Daily Activities

Metacognition can improve physical activity in everyday life, particularly for individuals who are not professional athletes but wish to engage in regular exercise to maintain a healthier lifestyle, regardless of their physical fitness level. It helps individuals plan their physical activities more effectively by setting priorities for performing exercises and incorporating physical activities into their daily schedule (Mišigoj-Duraković & Duraković, 2006). For example, an individual can use their metacognitive skills to design a weekly workout plan that fits into their family and work obligations. In everyday life, there are often obstacles that can hinder physical activity due to daily responsibilities.

Metacognition enables individuals to recognize these obstacles and develop strategies to overcome them, by identifying negative thoughts such as, "I'm too tired," or "I don't have time," and applying techniques to counter these thoughts (Rhodes et al., 2018). By understanding priorities, individuals can better manage their resources and time to ensure that physical activity remains a regular part of their daily life. Maintaining motivation for regular exercise in daily life is often challenging, but metacognition can help individuals understand their motivations and recognize how positive thoughts about the importance of physical activity can boost their motivation. Individuals who apply metacognitive skills regularly assess their activities to determine whether they have achieved their goals, allowing them to adjust their plans and strategies according to their needs in specific life circumstances. The metacognitive approach enables better understanding of one's behavior, thoughts, and emotions related to physical activity, which leads to positive changes in lifestyle (Loprinzi & Nooe, 2016).

„THE MIND AND BODY SPEAK THE SAME LANGUAGE" - PROMOTING AWARENESS OF METACOGNITION IN PHYSICAL ACTIVITIES

Promoting awareness of metacognition can help individuals become more conscious of their emotions and thoughts related to physical activity. Increased awareness provides the potential to improve health and well-being by fostering positive lifestyle changes and daily habits. It contributes to a broader understanding of how awareness of one's emotions and thoughts can be beneficial for maintaining an active lifestyle and achieving specific goals. Cognitive processes are often automatic, much like breathing. Therefore, it is essential to consider whether individuals pay attention to their thoughts, how they think, whether they understand them, and what decisions they make. Metacognition plays a crucial role in this by facilitating the interaction between the brain, mind, body, and behavior, integrating effective strategies through which mental, social, and behavioral factors can influence health (Jakovljević & Ostojić, 2015). Education and fostering collaboration across various disciplines such as education, public health, psychology, psychiatry, and sports sciences are necessary to integrate metacognition and expand the understanding of the effects of physical activity and a healthy lifestyle. This could involve lectures, workshops, and/or online materials explaining what metacognition is and how it can be applied to enhance physical activity and overall health. Furthermore, collaboration with media, physical activity experts (e.g., physiotherapists), and other promoters of healthy lifestyles within the fitness industry is crucial for raising awareness about metacognition and how it can improve physical activity and/or athletic performance. Integrating metacognition education into school curricula, especially for younger generations, is important to highlight the significance of understanding one's emotions and thoughts in the context of physical activity. Students could be taught how to develop positive metacognitive strategies and recognize and control negative thoughts that hinder them from being active. Collaboration with mental health professionals, applying metacognitive techniques, can also contribute to improved mental health, both for individuals struggling with depression, anxiety, and stress, as well as for the general population (Jakovljević & Muck-Šeler, 2013). Promoting funding and supporting research projects focused on metacognition and physical activity will encourage further research and the development of metacognitive approaches. This may include the availability and application of practical apps and the development of digital tools that assist individuals in applying metacognitive techniques during physical activities. Furthermore, organizing initiatives and campaigns to educate the wider public about the concept of metacognition in physical activities can provide concrete and useful practical recommendations. This would help individuals and professionals (educators, coaches, decision-makers) utilize metacognitive strategies during physical activities in their work or daily lives. This may involve developing strategies for monitoring one’s thoughts, emotions, and physical sensations during performance, as well as recognizing negative patterns of thinking that may interfere with specific physical activities. It is essential to encourage and motivate people to develop positive metacognitive

strategies to cope with negative emotions and thoughts, paying attention to fears, frustrations, and low self-confidence that may arise during the execution of certain activities. Additionally, providing information on available educational methods for applying metacognitive skills to achieve better mental and physical health is necessary.

CONCLUSION

Metacognition, as an important factor in physical activities, can be crucial for achieving and maintaining physical activity, as well as for increasing motivation and overcoming barriers to engaging in physical activities. Improving metacognitive skills can have a positive impact on the overall health and well-being of individuals. Greater awareness of one's emotions and thoughts can reduce stress, anxiety, and depression, contributing to better physical and mental health. Additionally, metacognition can serve as a tool for prevention and intervention in the fight against physical inactivity and its negative consequences. Various metacognitive techniques need to be integrated into programs for the prevention of obesity, cardiovascular diseases, and other health issues associated with a lack of physical activity. Developing metacognitive skills can encourage individuals to establish healthy habits and maintain long-term lifestyle changes, as well as overcome challenges that typically lead to the abandonment of physical activity. It is crucial to include different populations and groups in the promotion of metacognition in physical activities by providing tailored approaches for individuals, as well as synthesizing key insights and emphasizing the importance of metacognition in physical activity for practical application in their lives. Finally, it is essential to highlight the transdisciplinary nature of the field, aimed at restoring cognitive, physical, behavioral, and affective functions that can contribute to achieving healthcare not only for individuals but also for public health and global health protection at the population level (Jakovljević & Bevanda, 2024).

Acknowledgments: None.

Conflict of interest: None to declare.

REFERENCES

1. Abdelrahman RM: *Metacognitive awareness and academic motivation and their impact on academic achievement of Ajman University students. Heliyon. 2020; 6(9):1-8.*

2. Andersen LB, Hasselstrøm H, Grønfeldt V, Hansen SE, Karsten F*: The relationship between physical fitness and clustered risk, and tracking of clustered risk from adolescence to young adulthood: eight years follow-up in the Danish Youth and Sport Study. Int J Behav Nutr Phys Act. 2004; 8;1(1):1-4.*

3. Awick EA, Ehlers DK, Aguinaga S, Daugherty A., Kramer AF et al: *Effects of a randomized exercise trial on physical activity, psychological distress and quality of life in older adults. General Hospital Psychiatry. 2017; 49:44–50.*

4. Bao L, Soh KG, Mohd Nasiruddin NJ, Xie H, Zhang J: *Unveiling the Impact of Metacognition on Academic Achievement in Physical Education and Activity Settings: A Comprehensive Systematic Review and Meta-Analysis of Qualitative Insights. Psychol Res Behav Manag. 2024; 8(17):973-987.*

5. Baquet G, van Praagh E, Berthoin S: *Endurance training and aerobic fitness in young people. Sports Med. 2003;33(15):1127–1143.*

6. Bélanger M, Phillips EW, O'Reilly C, Mallet B, Aube S, Doucet M, et al: *Longitudinal qualitative study describing family physicians' experiences with attempting to integrate physical activity prescriptions in their practice: 'It's not easy to change habits'. BMJ Open 2017;7(7): e017265.*

7. Bhome R, McWilliams A, Price G, Poole NA, Howard RJ, Fleming SM et al: *Metacognition in functional cognitive disorder. Brain Commun. 2022; 4(2):fcac041*

8. Brinck I & Liljenfors R: *The developmental origin of metacognition. Infant and Child Development. 2013;22(1): 85–101.*

9. Briguglio M, Vitale JA, Galentino R, Banfi G, Zanaboni Dina C, Bona A, et al: *Healthy eating, physical activity, and sleep hygiene (HEPAS) as the winning triad for sustaining physical and mental health in patients at risk for or with neuropsychiatric disorders: considerations for clinical practice. Neuropsychiatr Dis Treat. 2020; 16:55–70.*

10. Caspersen CJ, Powell KE, Christenson GM: *Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985; 100:126-31*

11. Chen X, McNamara TP, Kelly JW, Wolbers T: *Cue combination in human spatial navigation. Cognitive Psychology. 2017; 95:105–144.*

12. Efklides, A: *Metacognition: Defining its facets and levels of functioning in relation to selfregulation and co-regulation. European Psychologist. 2008; 13(4): 77-287.*

13. Erickson KI, Hillman C, Stillman CM, Ballard RM, Bloodgood B, Conroy DE et al,: *Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. Med. Sci. Sports Exerc. 2019; 51(6):1242-1251.*

14. Faivre N, Filevich E, Solovey G, Kühn S, Blanke O: *Behavioral, Modeling, and Electrophysiological Evidence for Supramodality in Human Metacognition. The Journal of Neuroscience. 2018; 38(2): 263–277.*

15. Filipec M, Kuzmić A, Ćurlin M & Pavao Vlahek P: *Cognitive emotional regulation in physiotherapy students in Croatia. Health Psychology and Behavioral Medicine. 2024;12(1): 2419842: 1-15.*

16. Firth J, Stubbs B, Rosenbaum S, Vancampfort D, Malchow B, Schuch F, et al: *Aerobic exercise improves cognitive functioning in people with schizophrenia: a systematic review and meta-analysis. Schizophr Bull. 2017; 43:546–56.*

17. Firth J, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E, et al: *A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. World Psychiatry. 2020; 19:360-80.*

18. Fleming SM & Bang D: *Shouldering responsibility. Science. 2018; 361:449–450.*

19. Friedman NP & Miyake A: *Unity and diversity of executive functions: individual differences as a window on cognitive structure. Cortex. 2017; 86:186–204.*

20. Frith CD: *Consciousness, (meta)cognition, and culture. Q J Exp Psychol (Hove). 2023; 76(8):1711-1723.*

21. Hall PA, Fong GT, Epp LJ, Elias LJ: *Executive function moderates the intention-behavior link for physical activity and dietary behavior. Psychol Health. 2008; 23(3):309–326.*

22. Heyes C, Bang D, Shea N, Frith CD, Fleming SM: *Knowing Ourselves Together: The Cultural Origins of Metacognition. Trends Cogn Sci. 2020; 24(5):349-362.*

23. Rollwage M: *Metacognitive failure as a feature of those holding radical beliefs. Curr. Biol. 2018; 28:4014–4021.e8.*

24. Howie EK & Pate RR: *Physical activity and academic achievement in children: a historical perspective. J Sport Health Sci. 2012; 1:160–9.*

25. Hölzel BK, Lazar SW, Gard T, Schuman-Olivier Z, Vago DR, Ott U: *How Does Mindfulness Meditation Work? Proposing Mechanisms of Action From a Conceptual and Neural Perspective. Perspect Psychol Sci. 2011; 6(6):537-59.*

26. Jackson SA, Kleitman S: *Individual differences in decision-making and confidence: capturing decision tendencies in a fictitious medical test. Metacogn. Learn. 2014; 9:25–49.*

27. Jakovljević M: *Current status of religion and spirituality in psychiatry. Psychiatr Danub 2005; 17(3-4):138-40*

28. Jakovljević M & Muck-Šeler D: *Serotonin u zdravlju i bolesti // Serotonin i depresija: mitovi i činjenice. Zagreb: Pro Mente. 2013. str. 25-59.*

29. Jakovljević M & Ostojić L: *Professionalism in contemporary medicine: If it is an important academic issue, then surely it is a "hot" issue as well. Psychiatria Danubina 2013; 25 (Suppl 1), 6-17.*

30. Jakovljević M & Bevanda M: *Integrative Medicine: Between Wishful Thinking and Reality. Medicina Academica Integrativa, 2024;1(1): 4-10.*

31. Jankowski T & Holas P*: Metacognitive model of mindfulness. Conscious Cogn. 2014; 28: 64-80.*

32. Kolesarić V & Milić M: *Promjene metakognitivnih procesa (zabrinjavajućih misli) u studentskoj populaciji utvrđene "Upitnikom Metakognicije". Suvremena psihologija. 2014; 17: 167-180.*

33. Kuzmić A & Filipec M: *Metakognicija - koncept suvremenog učenja // Fizioterapija u sportu, rekreaciji i wellnessu. Vukovar: Veleučilište Lavoslav Ružička u Vukovaru. 2022. str.146-153.*

34. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL: *Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014; 72:123–37.*

35. Loprinzi PD & Nooe A: *Executive function influences sedentary behavior: a longitudinal study. Health Promot Perspect. 2016; 6(4):180–4.*

36. Marenus MW, Cahuas A, Hammoud D, Murray A, Friedman K, Ottensoser H, et al: *Web-Based Physical Activity Interventions to Promote Resilience and Mindfulness Amid the COVID-19 Pandemic: A Pilot Study. Int J Environ Res Public Health. 2023; 20(8):5463.*

37. Mason LA, Thomas AK, Taylor HA: *On the proposed role of metacognition in environment learning: recommendations for research. Cogn Res Princ Implic. 2022; 7(1):2-15.*

38. Mazancieux A, Fleming SM, Souchay C, Moulin CJA: *Is there a G factor for metacognition? Correlations in retrospective metacognitive sensitivity across tasks. Journal of Experimental Psychology: General. 2020; 149(9):1788–1799.*

39. Miko HC, Zillmann N, Ring-Dimitriou S, Dorner TE, Titze S, Bauer R: *Effects of Physical Activity on Health].Gesundheitswesen. 2020; 82 (3):184-195.*

40. Mišigoj-Duraković M i sur.: *Tjelesno vježbanje i zdravlje. Znanje. Zagreb. 2018.*

41. Mišigoj-Duraković M & Duraković Z: *Poznavanje razine tjelesne aktivnosti i njezinih komponenti u funkciji kvalitete rada // Kvaliteta rada u područjima edukacije, sporta i sportske rekreacije : zbornik radova /* Findak V (ur.). *Zagreb: Hrvatski kineziološki savez (HKS), 2006. str. 53-59*

42. Ngô TL: *Review of the effects of mindfulness meditation on mental and physical health and its mechanisms of action. Sante Ment Que. 2013; 38(2):19-34.*

43. Nuzum H, Stickel A, Corona M, Zeller M, Melrose RJ, Wilkins SS: *Potential Benefits of Physical Activity in MCI and Dementia. Behav Neurol. 2020; 2020:7807856.*

44. Pearce PZ: *Exercise is medicine. Curr Sports Med Rep. 2008;7(3):171-5.*

45. Pedersen BK & Saltin B: *Exercise as medicine–evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports. 2015; 25:1-72.*

46. Rahnev D: *Visual metacognition: Measures, models, and neural correlates. Am Psyhol. 2021; 76(9):1445-1453.*

47. Rhodes RE, Williams DM & Conner MT: *Affective determinants of health behaviour: Common themes, future directions, and implications for health behavior change. In: Williams DM, Rhodes RE & Conner MT, eds.*

Affective Determinants of Health Behavior. New York, NY: Oxford University Press; 2018. p. 485-498.

48. Rivas SF, Saiz C, Ossa C: *Metacognitive Strategies and Development of Critical Thinking in Higher Education. Front Psychol. 2022; 13:913219:1-13.*

49. Schneider W: *The development of metacognitive knowledge in children and adolescents: Major trends and implications for education. Mind, Brain, and Education, 2008; 2(3):114–121.*

50. Shea N, Frith CD: *The Global Workspace Needs Metacognition. Trends Cogn Sci. 2019; 23(7):560-571.*

51. Stanton JD, Sebesta AJ, Dunlosky J: *Fostering Metacognition to Support Student Learning and Performance. CBE Life Sci Educ. 2021; 20(2):fe3:1-7.*

52. Steeves JA, Liu B, Willis G, Lee R, Smith AW: *Physicians' personal beliefs about weight-related care and their associations with care delivery: the U.S. National Survey of Energy Balance Related Care among Primary Care Physicians. Obes Res Clin Pract 2015; 9: 243–55.*

53. Stevens CA & Carlson RA: *Are you sure the library is that way? Metacognitive monitoring of spatial judgments. Journal of Experimental Psychology: Learning, Memory, and Cognition. 2016;42(7):1034–1049.*

54. Szczepanik JE, Brycz H, Kleka P, Fanslau A, Zarate CA Jr, Nugent AC: *Metacognition and emotion - How accurate perception of own biases relates to positive feelings and hedonic capacity. Conscious Cogn. 2020; 82:102936.*

55. Tacchi MJ, Heggelund J, Scott J: *Predictive validity of objective measures of physical fitness for the new onset of mental disorders in adolescents and young adults. Early Interv Psychiatry. 2019; 13:1310–8.*

56. Thomas E, Battaglia G, Patti A, Brusa J, Leonardi V, Palma A, et al: *Physical activity programs for balance and fall prevention in elderly: A systematic review. Medicine (Baltimore). 2019; 98(27):1-9.*

57. Vrdoljak G & Velki T: *Metacognition and Intelligence as Predictors of Academic Success. Croatian Journal of Education. 2012: 14 (4);799 – 815.*

58. Zhang YP, Hu RX, Han M, Lai BJ, Liang SB, Chen BJ, et al: *Evidence base of clinical studies on Qi Gong:a bibliometric analysis. Complement Ther Med. 2020; 50:1-8.*

59. Warburton DER & Bredin SSD: *Health benefits of physical activity: a systematic review of current systematic reviews. Curr Opin Cardiol. 2017; 32(5):541–56.*

60. Wells A & Cartwright-Hatton S: *A short form of the metacognitions questionnaire: properties of the MCQ-30. Behav Res Ther. 2004;42(4):385–396.*

61. Weng HY, Feldman JL, Leggio L, Napadow V, Park J, Price CJ: *Interventions and Manipulations of Interoception. Trends Neurosci. 2021; 44(1):52-62.*

62. Williams AM: *Perceptual skill in soccer: implications for talent identification and development. J Sports Sci. 2000;18(9):737-50.*

Correspondence:
Anica Kuzmić, Univ. Mag. Physioth., Senior Lecturer,
Department of Physiotherapy, University North, 42 000 Varaždin, Croatia
E-mail: akuzmic@unin.hr

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2 *Research paper*

ECONOMIC ASPECTS OF TREATMENT AND MANAGEMENT OF CLOSTRIDIOIDES DIFFICILE INFECTIONS IN UNIVERSITY CLINICAL HOSPITAL MOSTAR

Svjetlana Grgić[1,2,3], Nives Vasilj[1,2,3], Roberta Perković[3], Mirela Mabić[4]

[1] University Clinical Hospital Mostar, 88 000 Mostar, Bosnia and Herzegovina
[2] School of Medicine, University of Mostar, 88 000 Mostar, Bosnia and Herzegovina
[3] Faculty of Health Studies, University of Mostar, 88 000 Mostar, Bosnia and Herzegovina
[4] Faculty of Economics, University of Mostar, 88 000 Mostar, Bosnia and Herzegovina
received: 07.03.2025; revised: 11.07.2025; accepted: 11.07.2025

SUMMARY

Treatment of Clostridioides difficile infections in University Clinical Hospital Mostar from an economic perspective Clostridioides difficile is the most prominent pathogen directly tied to a healthcare system and proven to be one of the main causes of high economic impacts. It results in a frequent need for hospitalization, including the treatment of sepsis and post-acute care, and requires an extended number of days spent at the hospital. In addition to the costs of the medicine and laboratory analysis, extended hospitalization is the key component of the high healthcare expenses. The rational use of antibiotics, mandatory implementation of general hygiene measures, like washing hands, and disinfecting surfaces can significantly contribute towards hospital's overall expenses. This is particularly important for those in contact with an infected patient or with a patient suspected of having CDI. These basic measures establish security systems in the prevention of CDI. Proper managing and forecasting of the costs on the annual level for each individual healthcare institution is a necessary measure. Developing an accurate estimate of the funds needed for the treatment and prevention of CDI and its best therapies for each form of the disease, is a secure way to prevent recurring episodes that cause a significant economic burden on healthcare institutions.

Key words: *Clostridioides difficile, infection, treatment, healthcare expenses, hospital treatmet*

*****

INTRODUCTION

The first important document on the treatment and management of Clostridioides difficile, previously known as Clostridium difficile infection (CDI), was published by the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) in 2009. The same document was updated in 2014. The latest guideline update from 2021 established that the definition of CDI treatment remains unchanged, while the definition of treatment response for severe CDI is modified (1). The Infectious Diseases Society of America (IDSA) together with the Society for Healthcare Epidemiology of America (SHEA) significantly changed their recommendations for treating initial CDI episodes in 2017, as well as the overall approach to healthcare due to the high costs of treating with newer drugs, which they determined have lower disease recurrence rates when applied (2). Demographic aging of the population along with widespread use of antibiotics, especially in hospital settings, has led to a high frequency of CDI in both developed and developing countries and is considered the leading cause of hospital-acquired infections globally. Antibiotic use can be accompanied by numerous adverse effects, most commonly occurring in the gastrointestinal system (3). Depending on the type of antibiotic, epidemiological circumstances, and the population from which the patient originates, diarrhea occurs in 25 to 50% of patients receiving antibiotic treatment. Although a decrease in CDI incidence has been observed in recent years, the occurrence of more severe clinical forms of the disease is still present (2). Factors that lead to significant increases in morbidity, mortality, prolonged hospital stays, frequent readmissions, increased treatment costs result in additional burden on healthcare systems of each individual country (4). Proper antibiotic selection during the first episode of illness is crucial for reducing the main risk factor, which are recurrent and recurring episodes, based on which treatment strategy is determined for each individual patient (5).

Clostridioides difficile is a ubiquitous spore-forming bacterium that can be found in water, soil, the digestive system of numerous domestic animals, and in the digestive system of healthy children and adults. O'Tolle and Hall discovered the bacterium Clostridioides difficile in newborn feces in 1935 and named it Bacillus difficilis due to its extremely complicated and difficult cultivation (7). With the discovery of antibiotics and their increasingly frequent use during the 20th century, there was an increase in the incidence of diarrhea caused by C. difficile, which occurs particularly often after clindamycin use. Clindamycin-associated colitis began to

be more intensively studied in the 1970s when the extreme importance of C. difficile toxins in disease pathogenesis was proven (8). From that period until today, due to the increase in incidence of severe forms of the disease and the increasingly frequent occurrence of recurrent disease, the medical and economic significance of C. difficile infection has grown and has been characterized as an "urgent threat" to public health according to data from the Centers for Disease Control and Prevention (9). The aim of this study is to examine the impact of new approaches to CDI treatment on economic expenditures of treatment and treatment outcomes of patients at the Clinic for Infectious Diseases of the University Clinical Hospital Mostar compared to treatment with therapy not recommended by the latest guidelines in the time period from January 1, 2018, to May 31, 2023, covering the period before the SARS-COV-2 pandemic, during the SARS-COV-2 pandemic, as well as the period after the SARS-COV-2 virus pandemic.

SUBJECTS AND METHODS

The purpose of this study is to determine how much the treatment and management as well as the provision of healthcare for mild CDI, moderately severe CDI, severe CDI, and recurrent CDI economically burden the hospital institution and to define healthcare when treating CDI. The purpose of the study can also be characterized as applicative due to possible practical value because the obtained data can determine the costs that go toward treating this infection as a complication of hospital treatment and predict the funds that need to be secured annually for infection treatment so that economic expenditures can be controlled in a planned manner, which is important for every healthcare institution.The conducted study included all patients with confirmed CDI diagnosis who were treated at the Clinic for Infectious Diseases of the University Clinical Hospital in Mostar from January 1, 2018, to May 31, 2023. Demographic data (age, gender) and epidemiological data were analyzed - first episode of illness, recurrent episodes of illness (rCDI), number of days of hospital stay, type of admission to the Clinic (admission from home conditions, transfer from other clinics, departments, hospitals), admissions from residential institutions, previous hospital stay within the past four months, applied antibiotic therapy, total monetary amount of treatment. A variable that was also analyzed was whether the patient had SARS-COV-2 infection due to the time period of the conducted study since the pandemic was declared during the time period covered by the conducted study. The study is retrospective cohort by its characteristics. Data for 208 patients were used in the conducted study. The study itself was divided into collecting data about the studied group obtained from medical documentation, hospital information system and data from the Billing Unit of University Clinical Hospital Mostar and the Information Technology Service of University Clinical Hospital Mostar, entering the obtained data into the computer, statistical data processing, tabular presentation and interpretation of the obtained data.

Statistical analysis of data was performed using IBM SPSS Statistics for Windows, version 25 (Armonk, NY: IBM Corp.). Categorical variables were expressed as number and percentage, and numerical variables as median and first and third quartiles. Normality of distribution of numerical variables was tested using the Kolmogorov-Smirnov test. Differences in prevalence were tested using the Chi-square test, and for testing differences in numerical variables, the Mann-Whitney U test and Kruskal Wallis H test were used. The statistical significance threshold was set at alpha=0.05. P values that could not be expressed to three decimal places were expressed as $p<0.001$.

RESULTS

In the period from January 1, 2018, to May 31, 2023, at the Clinic for Infectious Diseases of the UniversityClinical Hospital Mostar, a total of 208 patients were treated for infections caused by the bacterium Clostridioides diffiile (Table 1). The oldest patient was 93 years old, and the youngest was 17 years old. The mean age of patients was 74.5, and half of the patients were between 66 and 81 years old. The mean length of stay in the department was 9.0 days, with half of the patients staying between 6 and 12 days. Among CDI patients, those with the first episode significantly predominated ($\chi2=7.692$; $p=0.006$) (Table 2). Analysis of the number of CDI patients by year showed significantly higher representation of these patients in the period 2020–2022 than in other years from the observed period ($\chi2=89.000$; $p<0.001$) (Table 3). No significant difference was found in the distribution of CDI patients by gender ($\chi2=1.558$; $p=0.212$) (Table 3). Most CDI patients had more than one diagnosis ($\chi2=38.942$; $p<0.001$) (Table 4). In 151 patients, the primary diagnosis was enteritis caused by Clostridium difficile (code A04.7). Most patients were hospitalized within 4 months of admission to another department ($\chi2=108.173$; $p<0.001$) (Table 5). Most CDI patients had recovered from coronavirus disease (were SARS-COV-2 positive) ($\chi2=10.173$; $p=0.001$) (Table 6). A statistically significant difference was found in the distribution of patients by disease severity ($\chi2=40.856$; $p<0.001$). Half of the patients had moderately severe disease caused by Clostridium difficile (Table 7). A statistically significant difference was found in the distribution of patients by therapy ($\chi2=62.923$; $p<0.001$). Most patients were treated with a combination of metronidazole and vancomycin (Table 8). Most patients felt improvement after therapy ($\chi2=239.433$; $p<0.001$) (Table 9). Deterioration was found in two patients with severe disease (Table 9). No statistically

significant difference was found in treatment outcome by therapy ($\chi2$=4.616; p=0.289; Fisher's exact test) (Table 10).

Table 1. Distribution of CDI patients by year

Year	n	%
2018	16	7,7
2019	18	8,7
2020	36	17,3
2021	72	34,6
2022	56	26,9
2023	10	4,8
total	208	100,0

Table 2. Distribution of patients by disease episode

Episode	n	%
First	124	59,6
Recurrent	84	40,4
Total	208	100,0

Table 3. Distribution of patients by gender

Gender	n	%
Male	95	45,7
Female	113	54,3
Total	208	100,0

Table 4. Distribution of patients by number of diagnose

Number of diagnoses	n	%
One	59	28,4
Multiple	149	71,6
Total	208	100,0

Table 5. Distribution of patients by hospitalization within 4 months

Hospitalized within 4 months	n	%
No	29	13,9
Yes	179	86,1
Total	208	100,0

Table 6. Distribution of patients by recovered SARS COV 19 disease

Had SARS COV 19	n	%
no	81	38,9
yes	127	61,1
Total	208	100,0

Table 7. Distribution of patients by disease severity

Disease severity	n	%
Mild	73	35,1
Moderate	105	50,5
Severe	30	14,4
Total	208	100,0

Table 8. Distribution of patients by therapy

Therapy	n	%
Metronidazol	60	28,8
Combination	120	57,7
Vankomicin	28	13,5
Total	208	100,0

Table 9. Distribution of patients by outcome

Clinical outcome	n	%
Mortality	33	15,9
Clinical improvement	173	83,2
Clinical deterioration	2	1,0
Total	208	100,0

Table 10. Treatment outcome by type of therapy

	Metronidazol		Kombinirano		Vankomicin	
Outcome	n	%	n	%	n	%
Mortality	11	18,3	19	15,8	3	10,7
Clinical improvement	47	78,3	101	84,2	25	89,3
Clinical improvement	2	3,3	0	0,0	0	0,0
Total	60	100,0	120	100,0	28	100,0

No statistically significant difference was found in the distribution of patients who continued therapy after initial treatment ($\chi2$=0.347; p=0.841) (Table 11).

Table 11. Continuation of treatment by type of therapy

	Metronidazol		Combined		Vankomicin	
Extended therapy	n	%	n	%	n	%
No	15	25,0	28	23,3	8	28,6
Yes	45	75,0	92	76,7	20	71,4
Total	60	100,0	120	100,0	28	100,0

Total treatment costs and therapy costs by year are shown in Table 12. Total hospital treatment costs and therapy costs by type of therapy are shown in Table 13

Table 12. Total treatment costs and therapy costs by year

Year	Treatment costs (BAM)	Therapy costs (BAM)
2018	36422,81	1475,60
2019	43934,52	1611,05
2020	87193,05	13855,05
2021	277624,64	39373,05
2022	198187,63	42360,90
2023	33808,61	7873,05
Total	677171,26	106548,70

.

Table 13. Treatment and therapy costs by type of therapy

	Total	C [Q1-Q3]*
Treatment costs (BAM)		
Metronidazol	169915,91	1645,51 [1127,03; 3012,09]
Combined	428054,98	2774,37 [1895,60; 4335,80]
Vankomicin	79200,37	2203,40 [1430,90; 3597,51]
Therapy costs (BAM)		
Metronidazol	3357,40	27,30 [22,43; 39,00]
Combined	83037,60	597,45 [348,28; 991,78]
Vankomicin	20153,70	646,83 [448,00; 925,65]

*C [Q1-Q3] – Median [first quartile; third quartile]

A statistically significant difference was found in hospital treatment costs by type of therapy (Kruskal-Wallis H=14.579; p=0.001). Hospital treatment costs for patients treated with metronidazole alone were significantly lower than hospital treatment costs for patients treated with combination therapy (Mann-Whitney U=181.500; p<0.001). Hospital treatment costs by therapy are shown in Figure 1.

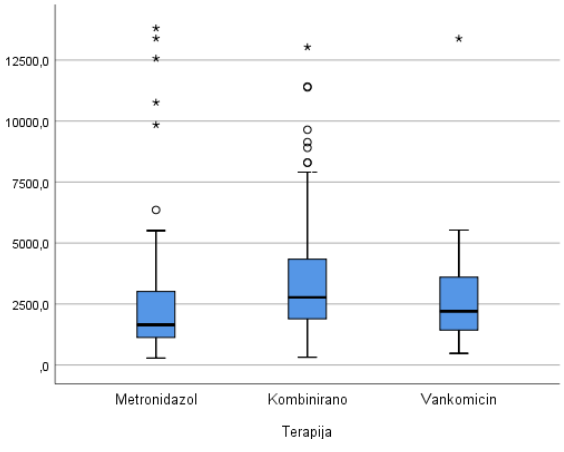

Figure 1. Hospital treatment costs by therapy

A statistically significant difference was found in therapy costs by type of therapy (Kruskal-Wallis H=115.440; p<0.001). Therapy costs for patients treated with metronidazole alone were significantly lower than therapy costs for patients treated with combination therapy (Mann-Whitney U=181.500; p<0.001) as well as therapy costs for patients treated with vancomycin (Mann-Whitney U=37.000; p<0.001). Therapy costs by therapy are shown in Figure 2.

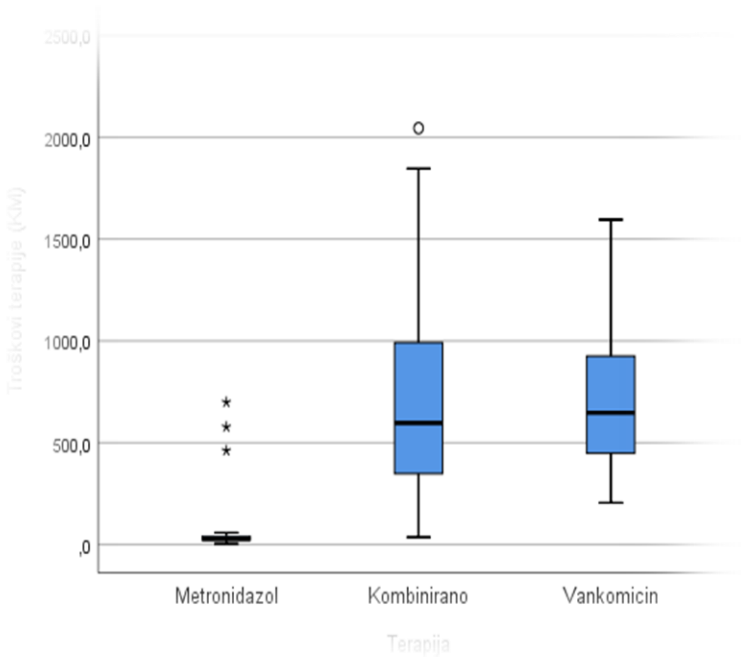

Figure 2. Therapy costs by therapy

Analysis of the share of therapy costs in treatment costs shows a mean value of 14.45%, with therapy costs representing between 3.15% and 26.48% of total treatment costs for half of the patients.

DISCUSSION

In our study, the number of CDI patients we monitored by year showed significantly higher representation in the period 2020–2022 than in other years of the observed period. During 2020, 17.3% of the total number were treated, in 2021, 34.6% were treated, and during 2022, 26.9%. Since the above-mentioned period coincides with the SARS-COV-2 virus pandemic period, we can conclude that during pandemic years, the number of CDI infections at the Clinic for Infectious Diseases of the University Clinical Hospital Mostar was on the rise. According to Kelly R Reveles and colleagues, hospitals during the pandemic suffered high numbers and flow of patients in general and intensive care departments, and inadequate staff as well as lack of personal protective equipment and prioritizing COVID-19 over traditional healthcare-associated infections, especially early in the pandemic and during waves, increased hospital antibiotic prescribing (2). In a systematic review and meta-analysis by Langford and colleagues, 62.4% of all COVID-19 patients received at least 1 antibiotic. Among them, the most commonly prescribed antibiotics were fluoroquinolones (20.0%), macrolides (18.9%), β-lactam/β-lactamase inhibitors (15.0%), and cephalosporins (15.0%), with 8.6% of COVID-19 patients having concomitant bacterial infection, suggesting that many of these prescribed antibiotics may not have been necessary (24). Of the total 208 patients, 59.6% had their first episode of illness, while the remaining 40.4% developed recurrent episodes of illness. Most CDI patients had more than one diagnosis. In 151 patients, the primary diagnosis was enteritis caused by Clostridioides difficile bacterium (A04.7). The majority of patients, 86.1%, were hospitalized within 4 months in the hospital system. According to Jessica A. Bowman et al., a strong risk factor is hospitalization and contact with healthcare personnel, which is why the burden of this infection mainly affects older patients with comorbidities who have been treated with antibiotic therapy in the recent past (13).

Khanna et al. in their studies conducted in the USA showed that patient movement between healthcare institutions directly affects CDI occurrence. They used a network approach and showed that increased transmission in University hospitals was 4.5% (21). By analyzing disease severity, we found that there is a significant statistical difference in patient representation. Half of the patients had moderately severe disease 50.5%, mild disease was present in 35.1% of patients, while severe disease developed in 14.4% of patients. In CDI treatment, antibiotic therapy with metronidazole, vancomycin, or a combination of these two antibiotics was applied depending on the patient's clinical condition,

first or repeated episode of illness, where we reached the following results: 28.8% of patients were treated with metronidazole. Of the total patients treated with metronidazole, 78.3% improved, 18.3% died, and deterioration was recorded in 3.3% of patients. Patients treated with a combination of intravenous metronidazole and oral vancomycin represent 57.7% of the total number treated, where improvement was recorded in 84%, deaths were 15.8%, and there were no deteriorated patients on combination therapy. Oral vancomycin therapy was received by 13.5% of the total number of treated patients, of which improvement was recorded in 89.3%, there were no deteriorated patients, while those with fatal outcome were 10.7%, which indicates that the lowest mortality rate occurs when patients are treated with vancomycin capsules according to prescribed doses and sufficient treatment duration. After discharge from the hospital system, follow-up of patients who continued therapy according to the scheme was continued, where it was noticed that the proportion of patients treated with metronidazole in hospital conditions required continuation of therapy in 75.0%. In patients treated with a combination of both antibiotics, continuation of treatment after improvement and discharge from the hospital system was recorded in 76.7% of patients. The best and fastest recovery during hospital treatment was shown in situations when patients were treated with oral vancomycin capsules.

It is important to note that during the observed period, we were repeatedly faced with a shortage of vancomycin capsules, and patients were treated with substitutes suggested by guidelines (vancomycin solution powder orally, vancomycin enemas rectally), whose effectiveness is difficult to measure due to the drug's passage through the upper digestive system, direct effect of gastric acid on the orally taken drug preparation, and passage of the drug through the duodenum and jejunum. A limitation in the research was also a certain number of patients whose health condition did not allow the use of oral vancomycin capsules due to lack of swallowing ability. Despite the mentioned limitations, the fastest recovery was recorded in patients on vancomycin monotherapy (capsules, suspension, enema) during hospitalization, with extended vancomycin treatment scheme applied in 71.5% of patients. In statistical data processing, no statistically significant difference was proven between the use of metronidazole, combination of metronidazole and vancomycin, and vancomycin monotherapy after hospital discharge, but we believe that the above-mentioned limitations significantly influenced the research results. A statistically significant difference was found in therapy costs by type of therapy. Metronidazole therapy costs are significantly lower than combination therapy costs and vancomycin costs. Low metronidazole treatment costs are justified by the fact that metronidazole itself is significantly cheaper to procure compared to vancomycin. Metronidazole was the preferred choice in 28.8%. According to ESCMID guidelines, it is still the choice in the absence of vancomycin and fidaxomicin, but for milder forms of disease and in our conditions is still effective due to good sensitivity of Clostridium difficile toxin B (TcdB) to the drug.

In the observed period, we noticed that combination therapy of both drugs represents the greatest economic burden for the institution. With this observation, we must emphasize that treated patients very often had other comorbidities - as many as 71.6% had more than one medical diagnosis, average age of 74.5 years, patients spent from at least 6 days to a maximum of 12 days in the hospital system, on average staying 9 days in the hospital. According to H.E. Burton et al., about 25% of patients treated with vancomycin and metronidazole develop disease recurrence. From 40 to 60% of patients after the first recurrence develop subsequent episodes, which represents the biggest obstacle to recovery, and enormous resources are spent in this vicious cycle of infection-reinfection, increasing morbidity, mortality, reducing quality of life and work capacity (20). In the observed period at the Clinic for Infectious Diseases UKB Mostar, there were 40.4% recurrent infections, which suggests that in the future we need to consider the use of fidaxomicin because previous research has shown that fidaxomicin has minimal effects on intestinal flora and pronounced preventive effect on sporulation and regrowth of C. difficile spores compared to vancomycin and metronidazole (20). Analyzing data for the observed period, funds spent on treatment amount to 106,548.70 BAM, and the amount spent on overall treatment is 677,171.26 BAM, which tells us that the economic burden of CDI treatment is significant, serious, and included treatment of sepsis, provision of post-acute care, prolonged treatment, and complications of prolonged bed rest. We analyzed therapy costs in relation to overall treatment costs where we recorded a mean value of 14.45%, with therapy costs representing between 3.15% and 26.48% of total treatment costs for half of the patients.

CONCLUSION

1. In our study, a statistically significant difference in treatment costs by type of therapy was proven.
2. The best and fastest recovery of patients during hospital treatment in our institution was shown in cases when patients were treated with oral vancomycin capsules.
3. Vancomycin capsule monotherapy proved significantly more cost-effective from an economic perspective than combination therapy of vancomycin and metronidazole for both first and recurrent episodes of illness.
4. Funds should be allocated not only for medications but also for comprehensive patient care, considering the extended number of days of stay in the

institution and frequent recurrent episodes of illness. A certain portion of economic resources should be allocated and directed toward education of healthcare and non-healthcare staff, working on improving control and supervision of hospital infections.

5. Services in the system that assess necessary resources for diagnosis A04.7 should be encouraged to reshape structural limitations and reprogram financial resources annually in a way that prioritizes the most effective approaches to treating patients with as few recurrent episodes of illness as possible.
6. Prevention of recurrent episodes of illness must be at the center of daily patient care, and in this way, the most cost-effective treatment strategy can be identified.

REFERENCE

1. Joffrey van Prehn, Elena Reigadas, Erik H. Vogelzang i sur: *The guideline committee of the European Study Group on Clostridioides difficile, European Society of Clinical Microbiology and Infectious Diseases, 2021 27 Suppl 2:S1-S21. doi: 10.1016/j.cmi.2021.09.038.*
2. Bainum TB, Reveles KR, Hall RG 2nd, Cornell K, Alvarez CA. *Controversies in the Prevention and Treatment of Clostridioides difficile Infection in Adults: A Narrative Review. Microorganisms.2023; 3;11:3 doi: 10.3390/microorganisms11020387*.
3. Mathur H, Rea MC, Cotter PD, Ross RP, Hill C. *The potential for emerging therapeutic options for Clostridium difficile infection. Gut Microbes. 2014; 696-710. doi: 10.4161/19490976.2014.983768.*
4. Johnson S, Lavergne V, Skinner AM, Gonzales-Luna AJ, Garey KW, Kelly CP, Wilcox MH. *Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021; Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults. Clin Infect Dis. 2021;73:e1029-e1044. doi: 10.1093/cid/ciab549.*
5. Comparcini D, Simonetti V, Segala FV. *Nurses' Knowledge, Attitudes and Practices on the Management of Clostridioides difficile Infection: A Cross-Sectional Study. Antibiotics (Basel). 2023 7;12:529. doi: 10.3390/antibiotics12030529.*
6. Depestel DD, Aronoff DM. *Epidemiology of Clostridium difficile infection. J Pharm Pract. 2013, 464-75. doi: 10.1177/0897190013499521.*
7. Reveles KR, Yang M, Garcia-Horton V, Edwards ML, Guo A, Lodise T, Bochan M, Tillotson G, Dubberke ER. *Economic Impact of Recurrent Clostridioides difficile Infection in the USA: A Systematic Literature Review and Cost Synthesis. Adv Ther. 2023. doi: 10.1007/s12325-023-02498-x.*
8. Khanna S, Lett J, Lattimer C, Tillotson G. *Transitions of care in Clostridioides difficile infection: a need of the hour. Therap Adv Gastroenterol. 2022; 15:17562848221078684. doi: 10.1177/17562848221078684.*
9. Reveles KR, Frei AL, Strey KA, Young EH. *Prevalence and Health Outcomes of Clostridioides difficile Infection During the Coronavirus Disease 2019 Pandemic in a National Sample of United States Hospital Systems. Open Forum Infect Dis. 2022; 9:ofac 441. doi: 10.1093/ofid/ofac441.*
10. Nelson RE, Jones M, Leecaster M, Samore MH, Ray W, Huttner A, Huttner B, Khader K, Stevens VW, Gerding D, Schweizer ML, Rubin MA. *An Economic Analysis of Strategies to Control Clostridium Difficile Transmission and Infection Using an Agent-Based Simulation Model .PLoSOne 2016 ;31;11:e0152248. doi: 10.1371/journal.pone.0152248.*
11. Nagy E. *What do we know about the diagnostics, treatment and epidemiology of Clostridioides (Clostridium) difficile infection in Europe? J Infect Chemother 2018: 164-170. doi: 10.1016/j.jiac.2017.12.003.*
12. Bowman JA, Utter GH. *Evolving Strategies to Manage Clostridium difficile Colitis. J Gastrointest Surg. 2020:484-491. doi: 10.1007/s11605-019-04478-5.*
13. Cornelius J Clancy, Deanna Buehrle, Michelle Vu, Marilyn M Wagener, M Hong Nguyen, *Impact of Revised Infectious Diseases Society of America and Society for Healthcare Epidemiology of America Clinical Practice Guidelines on the Treatment of Clostridium difficile Infections in the United States , Clinical Infectious Diseases, 2021;72(11):1944 – 1949, doi:10.1093/cid/ciaa484*
14. Burton HE, Mitchell SA, Watt M. *A Systematic Literature Review of Economic Evaluations of Antibiotic Treatments for Clostridium difficile Infection. Pharmacoeconomics. 2017; 35: 1123-1140. doi: 10.1007/s40273-017-0540-2.*
15. Okumura H, Ueyama M, Shoji S, English M. *Cost-effectiveness analysis of fidaxomicin for the treatment of Clostridioides (Clostridium) difficile infection in Japan. J Infect Chemother. 2020;26:611-618. doi: 10.1016/j.jiac.2020.01.018.*
16. Reveles KR, Frei AL, Strey KA, Young EH. *Prevalence and Health Outcomes of Clostridioides difficile Infection During the Coronavirus Disease*

2019 Pandemic in a National Sample of United States Hospital Systems. Open Forum Infect Dis. 2022; 25;9:ofac441. doi: 10.1093/ofid/ofac441.

17. Madoff SE, Urquiaga M, Alonso CD, Kelly CP. *Prevention of recurrent Clostridioides difficile infection: A systematic review of randomized controlled trials. Anaerobe. 2020; 61:102098. doi: 10.1016/j.anaerobe.2019.102098.*
18. Khanna S, Lett J, Lattimer C, Tillotson G. *Transitions of care in Clostridioides difficile infection: a need of the hour. Therap Adv Gastroenterol. 2022; 15:17562848221078684. doi: 10.1177/17562848221078684.*
19. Bishop EJ, Tiruvoipati R. *Management of Clostridioides difficile infection in adults and challenges in clinical practice: review and comparison of current IDSA/SHEA, ESCMID and ASID guidelines. J Antimicrob Chemother.2022;78:21-30. doi: 10.1093/jac/dkac404.*
20. Martínez-Meléndez A, Camacho-Ortiz A, Morfin-Otero R, Maldonado-Garza HJ, Villarreal-Treviño L, Garza-González E. *Current knowledge on the laboratory diagnosis of Clostridium difficile infection. World J Gastroenterol 2017; doi: 10.3748/wjg.v23i9.1552*

Correspondence:
Svjetlana Grgić, MD, PhD, Associate Professor
Clinic for Infectious Diseases; University Clinical Hospital Mostar;
University of Mostar School of Medicine
Kralja Tvrtka, BA - 88000 Mostar, Bosnia and Herzegovina
e-mail: svjetlanag@gmail.com

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

Research paper

BREAST RADIOLOGICAL TREATMENT IN THE SCREENING PROGRAM

Andrej Galić

Clinical Department of Radiology, University Clinical Hospital Mostar, 88 000 Mostar, Bosnia and Herzegovina

received: 02.07.2025; revised: 15.07.2025; accepted: 08.11.2025

ABSTRACT

Introduction: *The breast is a symmetrical, paired organ located in the chest. Complete development of the breast occurs during pregnancy. There are many different pathological processes that occur in the breast including malignancy. The Cantonal Breast Cancer Early Detection Program is the first such program implemented in Bosnia and Herzegovina.*

Objective: *The main objective of this paper is to define and explain radiological diagnostic procedures used in the detection of various diseases and changes in the breast. To prove that mammography remains the gold standard in the early detection of breast cancer, despite newer methods and imaging techniques. The paper will also present the results and advantages of the "Breast Cancer Early Detection Program".*

Materials and methods: *The study was conducted as a cross-sectional study. Data were collected retrospectively from official data sources provided by the Ministry of Health, Labor and Social Welfare through the Radiological Information System for the University Clinical Hospital in Mostar for our county.*

Results: *In the first and second phases from 2019 to 2022, mammography was performed on 933 patients at the University Clinical Hospital Mostar, of whom 9 had a positive result. In the third phase of the program (2022-2024), mammography was performed on 2,499 patients. Of these, 18 had positive results.*

Conclusions: *Despite technological advances, mammography remains the gold standard in early detection of breast cancer. Similar breast cancer screening programs are being implemented in a few countries, including Turkey, Morocco, India, and Saudi Arabia. The results of these programs, as well as the challenges they face, further emphasize the importance and relevance of our county-level program implemented in HNZ/K County.*

Key words: *breast, screening, mammography, early detection, health.*

*****

INTRODUCTION

The breast is a symmetrical, paired organ located on the chest. In males, it develops until puberty and is usually not sensitive to hormonal influences. Towards the end of the first month of embryonic development, the mammary streaks develop along the ventrolateral side of the trunk, from the base of the arm to the base of the leg. (1) Estrogens during puberty cyclically stimulate the growth of the stroma and ducts, as well as the deposition of fat that increases the volume of the breast. Complete development of the breast occurs during pregnancy. The placenta secretes large amounts of estrogen during pregnancy, which lead to branching and growth of the duct system, enlargement of the stroma and deposition of fat. At least four other hormones influence the growth of the duct system: growth hormone, prolactin, glucocorticoids of the adrenal glands and insulin. (2) There are many different pathological processes that occur in the breast. Breast diseases can be divided into benign and malignant (breast cancer). Benign breast diseases include cysts, lumps, fibroadenomas, nipple discharge, infections and gynecomastia. (3) Breast pain and cysts often occur together and are included under the common name fibrocystic disease. It is unlikely that fibrocystic disease is associated with the risk of breast cancer. (4) Mammography is the basic examination for the early detection of breast cancer and is accepted as a screening method in asymptomatic women over 40 years of age because it is the only method of breast examination that has been proven to reduce cancer mortality. (5) Mammography involves exposing the breast to X-rays that are unevenly attenuated based on the characteristics of the breast tissue, which determines its sensitivity. (6) The sensitivity of mammography is higher in involutively changed breasts (breasts with a higher proportion of fatty tissue). The radiation dose absorbed by the breast depends on the thickness of the breast tissue, and the absorbed dose increases with breast thickness. (7) The Cantonal Breast Cancer Early Detection Program is the first such program implemented in Bosnia and Herzegovina. (8) The main objective of this paper is to define and explain radiological diagnostic procedures used in the detection of various diseases and

changes in the breast, and to present their advantages and disadvantages. To prove that mammography remains the gold standard in early detection of breast cancer, despite newer imaging methods and techniques. The paper will also present the results and advantages of the "Early Breast Cancer Detection Program".

SUBJECTS AND METHODS

The study was conducted as a cross-sectional study. The participants were not actively involved, and their personal data remained fully protected. The data were collected retrospectively from official data sources provided by the Ministry of Health, Labor and Social Care through RIS (Radiology Information System) for the University Clinical Hospital in Mostar for our county. It included data from 01.01.2019. until 31.12.2024. Initially, the program was planned in two phases. The first phase starts in 2019 and ends in December 2022. Given the number of women included in the program (32,444) and the planned response rate of 60%, the first phase (2019-2020) covers approximately 19,500 women. The second phase also lasted two years (2021-2022). Inclusion criteria were exclusion from phase 1, age 45 to 69 years. In the first and second phases from 2019 to 2022, mammography examinations were performed for 933 patients at the University Clinical Hospital Mostar. In the third phase of the program (2022-2024), mammography examinations were performed for 2,499 patients at the University Clinical Hospital Mostar. In the period from 01.01.2019 to 31.12.2024, 3,432 patients underwent mammography, 27 of whom had a positive result after the images were reviewed and read by at least two and at most four doctors. The SPSS for Windows and Microsoft Office Excel 2010 software systems were used for statistical data processing.

RESULTS

In the first and second phases from 01.01.2019 to 31.12.2022, mammography examinations were performed for 933 patients at the University Clinical Hospital Mostar of whom 9 had a positive result.

Institution	Total patients	Positive result
University Clinical Hospital Mostar	933	9

Table 1. The total number of examined patients and the number of positive results for first and second phases

BI - RADS category L-D breast	Total result
4-4	8
5-5	1

Table 2. BI - RADS category L-D breast and total result for first and second phases

4 - 4 means that both doctors gave a category 4, which means that this change is for biopsy.

5 - 5 means that both doctors gave a category 5, which means that this change is more than 94% malignant.

In the third phase of the program (2022-2024), mammography examinations were performed for 2,499 patients at the University Clinical Hospital Mostar. Of these, 18 had positive results.

Institution	Total patients	Positive result
University Clinical Hospital Mostar	2499	18

Table 3. The total number of examined patients and the number of positive results for third phases

BI - RADS category L-D breast	Total result
4 - 4	10
2 - 4 - 4	1
3 - 4 - 4	2
4 - 1 - 4	3
5 - 4	2

Table 4. BI - RADS category L-D breast and total result for third phases

4 – 4, means that both doctors gave a category 4, which means that this change is for biopsy.

2 - 4 - 4, this means that the first doctor assigned a score of 2, indicating a benign finding—something is present, but the doctors are confident it has benign characteristics. As a result, no further routine follow-up is required. However, the second doctor later assigned a score of 4, suggesting a different assessment, this means that something existed and that it is for biopsy, and the third final finding is 4 this means that something existed and that it is for biopsy, but since this is a cancer screening

program and if one doctor thinks that this is for biopsy, a biopsy is always done so that there is no false reading.

3 - 4 - 4, 3 means that it is a benign finding, but a more recent or additional follow-up is needed, for example with ultrasound, if any asymmetry is observed, then the magnet and if the lymph nodes are highlighted and they need to be further investigated. Soon all 3 BI RADS systems will be omitted due to problems with reading the findings. On the second finding, the doctor put a 4, which means that there are changes and that a biopsy is needed.

4 - 1 - 4, 4 means that a biopsy is needed, the second finding is 1, which means that it is a good finding that there is nothing pathological in the finding, neither good nor bad, the structure of the breast is completely normal, there is no inverted nipple, no lymph nodes, the breast is normal, there are no microcalcifications, no shadowing, but the last finding is 4, which means that it is going to be biopsied again.

5 - 4, 5 means that the first doctor thinks that it is certain that it is a malignant change, the second doctor gave a score of 4, which means that the patient is referred for an urgent biopsy.

DISCUSSION

The study was conducted as a cross-sectional study. The participants were not actively involved, and their personal data remained fully protected. All patients were first imaged with mammography. After reading the findings, depending on the stage, patients were referred for additional tests such as biopsy, ultrasound or magnetic resonance imaging.

BI - RADS category L-D breast and total score for the first and second phase of the program, most doctors gave a score of 4 in the mammogram reading, which means that patients are referred for an urgent biopsy. As a result, we have improved health and the possibility of early detection of breast cancer, which is also the point of the entire program.

The data were collected retrospectively from official data sources provided by the Ministry of Health, Labor and Social Care through RIS (Radiology Information System) for the University Clinical Hospital in Mostar for our county. It included data from 01.01.2019. until 31.12.2024. the target population consisted of patients older than 40 to 65 years and in that period 3,432 patients underwent mammography, 27 of whom had a positive result.

Similar breast cancer screening programs are being implemented in several countries, such as Turkey, Morocco, India, and Saudi Arabia, with the aim of increasing early detection of the disease. The results of these programs, as well as the challenges they face, further emphasize the importance and relevance of our county-level program implemented in HNZ/K County.

CONCLUSIONS

The County Breast Cancer Screening Program is the first such program to be implemented in Bosnia and Herzegovina. The research was part of this program, which includes all women aged 45 to 69, regardless of health insurance status, and the goal of the program is to detect breast cancer at an early stage, which will reduce breast cancer mortality by 23-31%, prolong the life of breast cancer patients and improve the quality of life of breast cancer patients. All patients were first scanned with mammography. Mammography remains the gold standard for early detection of breast cancer despite technological advances. After reading the findings, depending on the calcification in the BI RADS system, patients are referred for additional tests such as biopsy, ultrasound or magnetic resonance imaging. In total, in our county, in the period from 01.01.2019. until December 31, 2024, 3,432 patients underwent mammography examinations at the University Clinical Hospital Mostar, 27 patients had a positive result after reviewing the images and readings by at least two and at most four doctors.

Acknowledgements: None.

Conflict of interests: None.

LITERATURE

1. Orrantia-Borunda E, Anchondo-Nuñez P, Acuña-Aguilar LE, Gómez-Valles FO, Ramírez-Valdespino CA, Stanisławek A. *Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. Cancers. 2021 Aug;13(17):4287.*
2. Kerlikowske K, Abraham L, Sprague BL, Sattayapiwat O, Nyante SJ, Tice JA, Miglioretti DL. *Mammographic calcifications association with risk of advanced breast cancer. Breast Cancer Res Treat. 2025 Aug;212(3):555-567.*
3. Toan DTT, Son DT, Hung LX, Minh LN, Mai DL, Hoat LN. *Knowledge, Attitude, and Practice Regarding Breast Cancer Early Detection Among Women in a Mountainous Area in Northern Vietnam. Cancer Control. 2019 Jan-Dec;26(1):1073274819863777.*
4. Ostapenko V, Mikalauskas T, Bruzas S, Mudenas A, Sabonis J, Tutkus J, Meskauskas R, Miliauskas P, Jackevicius A, Grinyte L. *Neuzciuopiami krūties navikai [Mamography and core biopsy value in diagnosis of nonpalpable breast tumors]. Medicina (Kaunas). 2004;40(12):1165-9.*
5. Couto LS, Freitas-Junior R, Correa RS, Peixoto JE, Almeida CD, Rodrigues DCN, Glassman LM, Soares LR. *Mean glandular dose in digital mamography in women with breast implants. J Radiol Prot. 2019 Apr;39(2):498-510.*

6. Brandão RF, Soares LE, Borges LR, Bakic PR, Tingberg A, Vieira MAC. *Exploring the impact of image restoration in simulating higher dose mammography: effects on the detectability of microcalcifications across different sizes using model observer analysis. J Med Imaging (Bellingham). 2025 Nov;12(Suppl 2):S22013.*
7. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249.*
8. Health Insurance Institute of HNZ/K. *County program for early detection of breast cancer 2019–2022 presented [Internet]. Mostar: ZZO HNZ/K; 2018 [cited 2025 Jul 2]. Available from: https://www.zzo.ba/hr/novost/predstavljen-zupanijski-program-ranog-otkrivanja-karcinoma-dojke-2019-2022*

Correspondence:
Andrej Galić, mag. rad. techn.,
Faculty of Health Studies, University of Mostar,
88 000 Mostar, Bosnia & Herzegovina;
e-mail: galicandrej@icloud.com, andrej.galic@fzs3.sum.ba

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

Special article

NAVIGATING THE LEGAL AND ETHICAL BOUNDARIES OF EMBRYO STATUS: A BALKAN PERSPECTIVE WITH A FOCUS ON BOSNIA AND HERZEGOVINA

Asad Herić

Department of Obstetrics and Gynecology, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina

received: 03.05.2025; revised: 17.07.2025; accepted: 17.07.2025

SUMMARY

The status of the human embryo remains one of the most debated issues at the intersection of science, ethics, and law. This paper explores the ethical, legal, and scientific perspectives on the embryo, with a particular focus on Bosnia and Herzegovina. A comparative analysis of legal frameworks across the Balkans highlights inconsistencies and gaps in regulation, particularly regarding embryo research and extended in vitro culture. Religious perspectives, predominantly shaped by monotheistic traditions, further complicate policy-making in this domain. By integrating scientific findings, ethical debates, and legal texts, this paper aims to provide a comprehensive overview of the current status of the embryo, emphasizing the need for legislative reforms in Bosnia and Herzegovina. The discussion underscores the importance of harmonizing national laws with European standards, such as the SOHO Directive and ESHRE guidelines, while considering the region's unique socio-cultural and religious landscape. The paper concludes with recommendations for policy changes, advocating for the extension of embryo culture up to the 14th day and the introduction of regulated research within IVF laboratories. These proposed changes aim to balance ethical concerns with scientific progress and align Bosnia and Herzegovina's legislation with contemporary European practices.

Keywords: *embryo status, bioethics, reproductive law, embryo research, Bosnia and Herzegovina.*

*****

INTRODUCTION

The birth of Louise Joy Brown in 1978 (Edwards and Steptoe, 1978) marked a turning point in reproductive medicine, heralding the success of in vitro fertilization (IVF). While IVF provided new hope for infertile couples, it also sparked ethical, legal, and religious debates regarding the moral and legal status of embryos, reproductive autonomy, and the broader implications of assisted reproductive technologies (ART) (Kamel, 2013; Roy et al., 2017). A central ethical dilemma is whether embryos should be regarded as persons with inherent rights or as biological entities subject to medical intervention and research.

Bioethics, emerging as a multidisciplinary field in the 20th century, has played a crucial role in shaping discussions on reproductive medicine. Ethical principles such as autonomy, justice, and informed consent challenge traditional paternalistic approaches, particularly in relation to embryo status (Jonsen, 2000; Jones, 1987). From a biological standpoint, human development is a continuous process without a universally agreed-upon starting point for life (Johnson, 2016). However, defining the embryo's moral or legal status extends beyond biology into cultural, religious, and philosophical domains.

In the Balkans, perspectives on the embryo's status vary, influencing legislation, ethical norms, and access to ART. Despite medical advancements, legal inconsistencies persist. This perspective article aims to synthesize scientific, religious, and legal viewpoints to critically assess the status of the human embryo in contemporary bioethical and legislative discourse. The analysis includes a comparative overview of regulations across Balkan countries, with a special focus on Bosnia and Herzegovina, particularly the Federation of Bosnia and Herzegovina. Recommendations for legal reform are proposed based on the argument that embryo status should be reconsidered in light of scientific progress and ethical reasoning, balancing embryo protection with patient-centred care in reproductive medicine.

METHODS

This study employs a qualitative analysis of scientific literature, religious texts, and legal documents. Scientific sources were selected through systematic searches in PubMed and Web of Science, focusing on publications from the last two decades discussing embryonic development, viability, and ethical considerations in assisted reproduction. Religious perspectives were drawn from theological texts and analyses of official monotheistic religions positions. Legal documents, including national laws, bylaws, and international legal instruments, were examined to compare regulatory frameworks in Bosnia and Herzegovina, Croatia, Slovenia, Montenegro, North Macedonia, and Serbia.

The first research segment explores scientific and medical perspectives on embryonic development. Peer-

reviewed studies from biomedical databases, embryology textbooks, and professional guidelines in reproductive medicine were reviewed to define key developmental stages, including fertilization, zygote, morula, and blastocyst formation.

Ethical and religious perspectives were analysed through theological and philosophical sources, including primary texts (the Bible, Qur'an, and Talmud) and interpretations from scholars within Catholicism, Orthodoxy, Islam, and Judaism. Official doctrinal statements, encyclicals, and scholarly theological discussions were examined alongside secondary bioethical analyses contextualizing religious views within contemporary ethical debates.

The legal status of embryos was assessed through national laws, regulations, and judicial decisions related to ART in Balkan countries. Legal documents were sourced from government websites, ministry archives, and legal databases. Comparative legal analysis was conducted to highlight differences in embryo recognition, protection, and use in ART among countries.

Additionally, international guidelines were considered, including the European Society of Human Reproduction and Embryology (ESHRE) position on embryo ethics and the new Directive on Substances of Human Origin (SoHO). The study employs a comparative approach to identify key similarities and conflicts across scientific, ethical, religious, and legal perspectives, concluding with recommendations for Bosnia and Herzegovina.

SCIENTIFIC AND MEDICAL VIEW OF EARLY EMBRYONIC DEVELOPMENT

Early Development and the Embryogenic Phase

The earliest stages of human development lay the groundwork for cellular differentiation and organogenesis (Shahbazi, 2020). These stages determine not only embryonic development but also the supporting structures necessary for implantation and placental formation. Before the embryo fully develops, the product of fertilization is referred to as the conceptus, which includes both embryonic and extraembryonic components (Su, 2015; Jones, 2018; Johnson, 2016).

Fertilization occurs when a sperm cell fuses with an oocyte, forming a zygote – a single-cell entity carrying genetic material from both parents (Okabe, 2014). The zygote undergoes a series of mitotic divisions called cleavage, resulting in blastomeres that initiate the early stages of embryonic differentiation (Johnson, 2016). By day three or four post-fertilization, the zygote develops into a morula, a compact cluster of 16–32 cells. As division continues, it transforms into a blastocyst – a hollow structure with an inner cell mass (the future embryo) and an outer trophoblast layer, which will contribute to the placenta (Gauster et al., 2022; Coticchio et al., 2019; Ivec et al., 2011). During the first 14–16 days, the conceptus undergoes differentiation into embryonic and extraembryonic structures. The inner cell mass consists of pluripotent cells, which give rise to the embryo, while outer trophoblast cells support implantation and placenta formation (Shahbazi et al., 2024; Zheng et al., 2022; Johnson, 2016).

Why "Conceptus" is a More Appropriate Term than "Embryo"

The term conceptus more accurately describes the pre-embryonic stage because it includes both embryonic and extraembryonic structures. Referring to this early-stage entity as an embryo can be misleading, as the biological "oneness" of an individual is not yet established. Until approximately day 14 post-fertilization, the conceptus retains the potential for twinning, meaning individuality has not been definitively determined. This is the rationale behind the widely accepted 14-day rule in embryo research, marking the onset of the primitive streak, the first sign of organized development and a precursor to the nervous system. Before this, the conceptus remains a cluster of different cells with multiple developmental possibilities.

Scientific Advances and Ethical Considerations

Recent embryological and regenerative medicine advancements have intensified discussions about embryo viability and extended culture, particularly regarding stem cell research. This debate underscores the challenge of balancing scientific innovation with ethical constraints (Rugg-Gunn et al., 2023; Amadei et al., 2022). In Bosnia and Herzegovina, legal frameworks currently prohibit embryo culture beyond Day 6, despite scientific findings suggesting that certain embryos may develop successfully if cultured to Day 7 (Hammond et al., 2018; Hernandez-Nieto et al., 2019; Insogna et al., 2021).

Aligning legal definitions with contemporary scientific knowledge is essential to prevent unnecessary restrictions on reproductive medicine. Legal framework should balance ethical concerns with the potential for clinical advancements, ensuring that legislative barriers do not impede scientific progress and patient outcomes in ART.

RELIGIOUS AND ETHICAL PERSPECTIVE

The moral and legal status of the human embryo has been a central ethical and religious question for centuries. Different monotheistic religions offer diverse perspectives on when life begins, the moral status of embryos, and the ethical permissibility of ART. These religious perspectives have influenced ethical debates and legal frameworks across societies. This chapter examines these perspectives through sacred texts, theological interpretations, and ethical implications.

The Christian Perspective

Christianity's views on the embryo's moral status derive from biblical scripture, Church tradition, and theology. The three main branches, Catholicism, Eastern Orthodoxy, and Protestantism, present varying interpretations regarding the beginning of human life and the embryo's moral and legal standing.

Catholicism

The Catholic Church asserts that life begins at conception, granting full moral status to the embryo. This belief is grounded in Psalm 139:13: "For you created my inmost being; you knit me together in my mother's womb.". Donum Vitae (1987) affirms: "From the moment of its conception, life must be guarded with the greatest care while abortion and infanticide are unspeakable crimes.". Other references, such as Jeremiah 1:5 ("Before I formed you in the womb I knew you, before you were born, I set you apart.") and Psalm 139:16 ("Your eyes saw my unformed body; all the days ordained for me were written in your book before one of them came to be."), further reinforce this position. Dignitas Personae (2008) explicitly states that embryos have full moral status from conception, leading to opposition to IVF due to embryo destruction and the separation of conception from the marital act.

Eastern Orthodoxy

Orthodox Christianity generally upholds that human life begins at conception and emphasizes the sanctity of life. However, theological discussions allow for nuanced perspectives on ART. While the Greek Orthodox Church expresses ethical concerns about embryo manipulation, it does not entirely prohibit IVF, particularly when performed within marriage and without embryo destruction. Unlike Catholicism, Orthodoxy does not have a centralized doctrinal authority, and ethical positions often depend on pastoral guidance.

Protestantism

Protestant perspectives on embryonic status vary significantly due to the emphasis on personal interpretation of Scripture. Evangelical and conservative denominations often align with Catholic beliefs on life beginning at conception, while liberal branches may allow ART under specific conditions. Some Protestants reference Genesis 2:7 ("Then the Lord God formed a man from the dust of the ground and breathed into his nostrils the breath of life, and the man became a living being.") to argue that life begins with the first breath, leading to more permissive stances on embryo research and ART.

The Islamic Perspective

Islamic bioethics is shaped by the Qur'an, Hadith, and Fiqh (Islamic jurisprudence). Scholars widely agree that ensoulment (ruh) occurs at either 40- or 120-days post-conception, as referenced in Surah Al-Mu'minun (23:12-14): "And indeed, We created humankind from an extract of clay. Then placed each as a drop in a secure place, then We developed the drop into a clinging clot, then developed the clot into a lump, then developed the lump into bones, then clothed the bones with flesh, then We brought it into being as a new creation. So Blessed is Allah, the Best of Creators." A Hadith states: "Each of you is gathered in your mother's womb for forty days as a drop, then as a clot for the same period, then as a lump for the same period. Then the angel is sent to breathe the soul into him." (Sahih al-Bukhari, Hadith 3208; Sahih Muslim, Hadith 2643).

Islamic scholars conclude:

- Before ensoulment, the embryo lacks full human status and rights.
- IVF is permissible within marriage if third-party gametes are not involved.
- Embryo destruction before ensoulment is debated but is not equated with murder under Shariah law.

The Islamic Organization for Medical Sciences (IOMS) and Fiqh Councils in Egypt and Saudi Arabia permit ART while emphasizing the ethical responsibility to limit the number of embryos created to avoid unnecessary destruction.

The Jewish Perspective

Jewish perspectives on embryo status are based on the Torah, Talmud, and Rabbinic teachings. Judaism does not attribute full personhood to the embryo in its early stages. The Talmud states that the foetus is maya be-alma ("mere water") until 40 days post-conception (Yevamot 69b). The Mishnah (Ohalot 7:6) views a foetus as part of the mother rather than an independent entity.

Exodus 21:22-23 states: "If people are fighting and hit a pregnant woman and she gives birth prematurely but there is no serious injury, the offender must be fined... But if there is serious injury, you are to take life for life.". This suggests that a foetus does not hold the same legal status as a born human. The Talmud (Sanhedrin 91b) states that a foetus attains nefesh (personhood) only at birth.

Jewish law (Halakha) generally permits and even encourages assisted reproduction, particularly to fulfil the commandment of pru urvu ("Be fruitful and multiply" Genesis 1:28). However, ethical concerns about embryo destruction vary among Rabbinic authorities.

Comparative Ethical Considerations

Religious perspectives on embryo status led to diverse ethical positions:

- Catholicism grants absolute protection to embryos, whereas Islam and Judaism take a more gradual approach.
- Catholicism strictly limits ART, while Islam and Judaism permit it under conditions.
- Catholicism and Orthodox Christianity oppose embryo destruction, whereas some Islamic and Jewish scholars allow conditional embryo use in research.

Secular bioethicists also shape the debate. Peter Singer argues that personhood is tied to cognitive capacity rather than biological development, asserting that early-stage embryos lack sentience and therefore moral status (Singer, 1993). In contrast, Leon Kass emphasizes the intrinsic moral worth of human life from its earliest stages, cautioning against a purely utilitarian approach (Kass, 2002).

Conclusion

Religious and ethical perspectives on embryo status are deeply rooted in theological and philosophical traditions. While monotheistic religions recognize the embryo's significance, their interpretations of its moral and legal status differ, influencing national laws and ART policies. Understanding these perspectives is essential for ethical and legally sound reproductive medicine policies in diverse societies.

LEGAL FRAMEWORKS

International Legal Frameworks on Embryo Status

The moral and legal status of the human embryo has been debated extensively, leading to various international legal instruments and ethical guidelines designed to balance scientific progress with respect for human dignity. This section examines key frameworks addressing the protection of human embryos.

European Convention on Human Rights and Biomedicine - Oviedo Convention

The Oviedo Convention, adopted by the Council of Europe in 1997, is the first legally binding instrument to protect human rights in the biomedical field. It focuses on safeguarding human dignity and ensuring respect for human rights in biology and medicine. While the Convention does not define the moral or legal status of the embryo, it establishes a framework that has led to varying embryo-related laws across Europe, affecting reproductive treatments and embryo research policies.

European Court of Human Rights (ECHR) Rulings

The ECHR has ruled on cases involving embryo status, reproductive rights, and ART, reflecting the margin of appreciation that allows member states to regulate bioethical issues according to their national contexts. In Evans v. United Kingdom (2007), the Court ruled that destroying embryos created via IVF after one partner withdrew consent did not violate the applicant's right to family life under Article 8, highlighting the legal uncertainty of embryo status and its subjectivity to national discretion.

European Union Directives and Recommendations

The EU has developed regulations, such as the SoHO Regulation (Regulation (EU) 2024/1938), to ensure high standards for the safety and quality of substances of human origin, including reproductive cells and embryos. However, it does not define the embryo's moral or legal status, leaving this to national legislation.

Position of Professional Organizations

The European Society of Human Reproduction and Embryology (ESHRE) has contributed to the ethical discourse on the moral status of embryos. ESHRE's 2024 position paper argues that embryos have a limited moral status, shaped by local ethical, cultural, and legal factors. It advocates for extending the permissible research period to 28 days post-fertilization, citing scientific benefits and the need for ethical oversight.

Comparative Legal Analysis of Embryo Status in the Balkan Countries

This section compares the legal frameworks governing embryo creation, use, and research in six Balkan countries: Bosnia and Herzegovina (specifically the Federation of Bosnia and Herzegovina, FBiH), Croatia, North Macedonia, Montenegro, Serbia, and Slovenia. Key areas of comparison include embryo surplus, freezing policies, storage duration, and research regulations.

All countries allow the creation of surplus embryos in IVF, but only Croatia limits the number of oocytes that can be collected in an IVF cycle to 12. Surplus embryos can be frozen in all countries, but destruction of surplus embryos is forbidden in Croatia and allowed in the others analysed countries.

Duration of in-lab embryo cultivation varies from six days in Bosnia and Herzegovina and Croatia, 14 days in North Macedonia, Montenegro, Slovenia, while in Serbia it is stated that it is forbidden to allows human development outside the womb.

Storage duration varies from (mandatory) indefinite storage in Croatia to maximally allowed 15 years in Montenegro. Other countries have 10 years in max.

In Bosnia and Herzegovina and Slovenia, embryos must be disposed of after ten years, whereas Montenegro, North Macedonia, and Serbia permit scientific research on embryos with the couple's consent. Croatia, in contrast, mandates indefinite storage or donation to other couples. While research on donated embryos is legally permitted in Montenegro, North Macedonia, and Serbia, Slovenia allows research only if it does not affect the

outcome of the procedure. In Bosnia and Herzegovina and Croatia, embryo research remains strictly prohibited.

Legal Status of the Embryo in Bosnia and Herzegovina (Federation of Bosnia and Herzegovina – FBiH)

This section provides an overview of the legal framework governing embryo status in FBiH, focusing on implications for ART, embryo freezing, and research.

The law in FBiH defines the embryo as a fertilized egg capable of development from the moment the nuclei merge. It treats all stages of embryo development uniformly, without distinguishing between early and later phases.

IVF is available to both married and non-married couples. There are no age restrictions for IVF, but public funding has age caps for state-supported treatments. A formal diagnosis of infertility is required.

Freezing surplus embryos is allowed, with proper storage and traceability. The default storage period is five years, extendable for another five years upon request. Once the storage period expires, embryos are automatically destroyed. Donation for reproduction or research is prohibited, with disposal being the only legally permitted option.

The law prohibits all forms of embryo research, including:

- Development of embryos outside the womb beyond six days

- Creation of embryos for research

- Any scientific or experimental procedures on embryos

Violations are punishable by 3 to 10 years in prison.

FBiH's restrictive stance, including the prohibition on embryo research and donation, hinders scientific advancement. In contrast, Slovenia allows embryo cultivation up to 14 days and permits controlled research. These legal restrictions prevent the development of new ART techniques and limit FBiH's ability to align with European scientific standards. Legal reforms are necessary to foster scientific progress and bring Bosnia and Herzegovina closer to international practices.

COMPARATIVE AND ANALYTICAL APPROACH

This chapter synthesizes scientific, ethical, religious, and legal perspectives on embryo status, highlighting key conflicts and areas for legal reform. It discusses the biological and philosophical distinction between the conceptus and the embryo, examines religious perspectives on embryo development, and analyses legal contradictions in Bosnia and Herzegovina, particularly the six-day limit on embryo culture and the prohibition of embryo research. The chapter concludes with a call for legal reform in light of scientific advancements.

Biological and Philosophical Perspective: The Conceptus vs. the Embryo

The debate over when life begins is central to discussions on embryo status. Biologically, life is a continuous cycle that has remained unbroken since the first living cell billions of years ago and continues through the gametes inherited from both parents. Death, not fertilization, marks the interruption of life (Brown, 2018). However, a meaningful distinction is the point of biological unity, when the embryo begins to develop as a single organism. Prior to Day 14, the conceptus is undifferentiated and can potentially split into twins or fuse with another conceptus. This period is marked by the lack of biological unity (Alvarez-Diaz, 2007).

Day 14 is recognized as the key developmental milestone because the primitive streak forms, signalling the onset of a unified organism. Scientific consensus allows embryo culture up to Day 14, with some experts advocating for an extension to 28 days to gain more insights into early development (ESHRE, 2024). This evolving understanding challenges current legal restrictions based on outdated notions of embryo status.

Scientific vs. Religious Perspectives on Embryo Status

Religious perspectives on embryo status vary significantly. Christianity, especially Catholicism and Orthodoxy, holds that the embryo is fully human from conception., which contrasts with scientific milestones, when biological unity is established. Islam recognizes gradual development, with ensoulment occurring later (at 40 or 120 days), aligning more closely with scientific perspectives. Judaism also follows a gradual approach, with the embryo regarded as "mere water" until after 40 days.

These religious views highlight the ethical dilemma of whether national policies should prioritize scientific evidence or religious doctrine when it comes to embryo research and regulation. The divergence between scientific and religious interpretations poses significant challenges for legal frameworks.

Legal Contradictions in Bosnia and Herzegovina

Bosnia and Herzegovina impose a six-day limit on embryo culture, which is at odds with modern reproductive medicine. Clinical studies suggest that

extending embryo culture to Day 7 can enhance IVF outcomes, yet the legal framework remains restrictive. This discrepancy raises concerns about Bosnia's adherence to contemporary medical standards.

Ethical Paradox: The Destruction of Surplus Embryos

A major ethical contradiction exists in Bosnia and Herzegovina's policy on surplus embryos. Embryos not used by the couple must be destroyed, even if they are viable. Moreover, research on embryos is prohibited, even though such research could advance IVF treatments and benefit future patients. This raises an ethical question: If embryos must be destroyed, why not use them for scientific research that could improve medical practices?

The Case for Legal Reform

Given the scientific evidence supporting the benefits of extending embryo culture and allowing controlled research, Bosnia and Herzegovina's restrictive policies appear outdated. Measured legal reforms could lead to significant medical advancements.

DISCUSSION

This chapter summarizes key findings, outlines legal recommendations, and proposes changes to Bosnia and Herzegovina's laws regarding embryo culture and scientific research. It emphasizes the need for a balanced approach that promotes scientific progress while maintaining ethical standards and social acceptability.

Legal Recommendations for Bosnia and Herzegovina

Bosnia and Herzegovina's current legal framework restricts embryo culture to Day 6 and imposes a complete ban on scientific research involving embryos. These limitations hinder medical progress and reduce the potential for improved IVF outcomes. Scientific evidence indicates that:

• Extending embryo culture to Day 7 can enhance IVF success rates in selected clinical cases.

• Permitting strictly regulated research on surplus embryos can lead to improved assisted reproductive technology (ART) protocols.

Several European countries, including Slovenia, the United Kingdom, and Belgium, allow embryo research under strict ethical oversight. Based on this, the following legal amendments are proposed:

Amendment to Article 47, Paragraph 1

Current text:

"(1) In the process of medically assisted reproduction, it is prohibited to allow in vitro development of embryos older than six days." Translation: "(1) U postupku biomedicinski potpomognute oplodnje zabranjeno je: a) omogućiti vantjelesni razvoj embriona starijih od šest dana.").

Proposed amendment:

"(1) In the process of medically assisted reproduction, it is prohibited to allow in vitro development of embryos beyond day seven, or after hatching from the zona pellucida." Translation: "(1) U postupku biomedicinski potpomognute oplodnje zabranjeno je: a) omogućiti vantjelesni razvoj embriona starijih od sedam dana, odnosno nakon oslobađanja iz zone pelucide.".

Justification:

Extending embryo culture to Day 7 is supported by clinical evidence as beneficial in selected cases, improving pregnancy rates. Harmonizing the legal framework with European standards, where culture is permitted up to 14 days, should be a long-term goal. Extending to Day 7 represents an initial and realistic step.

Amendment to Article 47, Paragraph 3

Current text:

"(3) Scientific or research work on embryos is prohibited." Translation: "(3) Zabranjen je naučni ili istraživački rad na embrionu."

Proposed amendment:

"(3) Scientific or research work is prohibited if it may have negative implications for the treatment outcome or embryo itself." Translation: "(3) Zabranjen je naučni ili istraživački rad koji može imati negativne implikacije na ishod liječenja ili na sami zametak."

Justification:

The absolute ban on embryo research is overly restrictive and prevents IVF advancements. The reform would allow ethical research without endangering treatment outcomes or embryo itself.

Amendment to Article 65

Current text:

"… or conducts scientific or research work on embryos shall be punished by imprisonment from three to ten years." Translation: "... ili obavlja naučni, odnosno istraživački rad na embrionu, bit će kažnjen kaznom zatvora od tri do 10 godina."

Proposed amendment:

"... or conducts scientific or research work without prior consent of the Commission and Ethics Committee shall be punished by imprisonment for a term of three to 10 years." Translation: "... ili obavlja naučni, odnosno istraživački rad bez prethodne saglasnosti Komisije I Etičkog komiteta bit će kažnjen kaznom zatvora od tri do 10 godina."

Justification:

This change removes the absolute criminalization of embryo research while still penalizing unethical practices.

Balancing Science, Ethics, and Law

To balance scientific progress with ethical oversight, Bosnia and Herzegovina should establish national or institutional ethics committees to review research proposals. Countries like Slovenia, the UK, and Belgium have successfully implemented ethical oversight mechanisms to ensure that research advances without moral or legal compromise.

CONCLUSION

Key findings include:

- Religious traditions define life's beginning based on spiritual beliefs.
- Scientific advancements necessitate legal adaptation.
- Bosnia and Herzegovina's restrictive framework is out of step with modern practices.

Proposed reforms:

- Extend embryo culture to Day 7 (preferably aligning with the 14-day European standard).
- Allow controlled embryo research that does not compromise treatment outcomes or embryo itself.
- Harmonize legal terminology and establish Ethical committees.

Implementing these reforms will align Bosnia and Herzegovina with recent medical and ethical standards, ensuring reproductive rights and scientific progress.

Acknowledgements: None.

Conflict of Interest: None to declare

REFERENCES

1. Steptoe PC & Edwards RG: *Birth after the reimplantation of a human embryo. Lancet 1978; 2:366.*

2. Kamel RM: *Assisted reproductive technology after the birth of Louise Brown. J Reprod Infertil 2013; 14:96-109.*

3. Jones HW Jr & Schrader C: *The process of human fertilization: implications for moral status. Fertil Steril 1987; 48:189-92.*

4. Roy MC, Dupras C & Ravitsky V: *The epigenetic effects of assisted reproductive technologies: ethical considerations. J Dev Orig Health Dis 2017; 8:436-42.*

5. Jonsen AR: *A short history of medical ethics. Oxford University Press, New York, 2000.*

6. Johnson M: *Essential Reproduction, 8th ed. Wiley-Blackwell, Oxford, 2016.*

7. Shahbazi MN: *Mechanisms of human embryo development: from cell fate to tissue shape and back. Development 2020; 147:dev190629.*

8. Su RW & Fazleabas AT: *Implantation and establishment of pregnancy in human and nonhuman primates. Adv Anat Embryol Cell Biol 2015; 216:189-213.*

9. Jones HW Jr & Schrader C: *And just what is a pre-embryo? Fertil Steril 1989; 52:189-91.*

10. Okabe M: *Mechanism of fertilization: a modern view. Exp Anim 2014; 63:357-65.*

11. Liu J: *The "life code": A theory that unifies the human life cycle and the origin of human tumors. Semin Cancer Biol 2020; 60:380-97.*

12. Gauster M, Moser G, Wernitznig S, Kupper N & Huppertz B: *Early human trophoblast development: from morphology to function. Cell Mol Life Sci 2022; 79:345.*

13. Coticchio G, Lagalla C, Sturmey R, Pennetta F & Borini A: *The enigmatic morula: mechanisms of development, cell fate determination, self-correction and implications for ART. Hum Reprod Update 2019; 25:422-38.*

14. Ivec M, Kovacic B & Vlaisavljevic V: *Prediction of human blastocyst development from morulas with delayed and/or incomplete compaction. Fertil Steril 2011; 6:1473-78.*

15. Shahbazi MN & Pasque V: *Early human development and stem cell-based human embryo models. Cell Stem Cell 2024; 31:1398-1418.*

16. Zheng Y, Yan RZ, Sun S, Kobayashi M, Xiang L, Yang R, et al.: *Single-cell analysis of embryoids reveals lineage diversification roadmaps of early human development. Cell Stem Cell 2022; 29:1402-19.*

17. Rugg-Gunn PJ, Moris N & Tam PPL: *Technical challenges of studying early human development. Development 2023; 150:dev201797.*

18. Amadei G, Handford CE, Qiu C, De Jonghe J, Greenfeld H, Tran M, et al.: *Embryo model completes gastrulation to neurulation and organogenesis. Nature 2022; 610:143-53.*

19. Hammond ER, Cree LM & Morbeck DE: *Should extended blastocyst culture include Day 7? Hum Reprod 2018; 33:991-97.*

20. Hernandez-Nieto C, Lee JA, Slifkin R, Sandler B, Copperman AB & Flisser E: *What is the reproductive potential of day 7 euploid embryos? Hum Reprod 2019; 34:1697-1706.*

21. Insogna IG, Lanes A, Ginsburg ES & Racowsky C: *Quality of embryos on day 7 after medium refreshment on day 6: a prospective trial. Hum Reprod 2021; 36:1253-59.*

22. Singer P: *Practical ethics, 2nd ed. Cambridge University Press, Cambridge, 1993.*

23. Howard J: *The moral status of the human embryo according to Peter Singer: individuality, humanity, and personhood. Linacre Q 2005; 72:212-28.*

24. Kass LR: *Life, Liberty, and the Defense of Dignity: The Challenge for Bioethics. Encounter Books, San Francisco, 2002.*

25. Bahadur G: *The moral status of the embryo: the human embryo in the UK Human Fertilisation and Embryology (Research Purposes) Regulation 2001 debate. Reprod Biomed Online 2003; 7:12-6.*

26. *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine. Oviedo, 1997.*

27. Evans v. United Kingdom, *No. 6339/05, European Court of Human Rights, Judgment of 10 April 2007. Available from: https://hudoc.echr.coe.int/eng#{%22itemid%22:[%22001-80046%22]}.*

28. European Parliament and Council of the European Union: *Regulation (EU) 2024/1938 of 13 June 2024 on standards of quality and safety for substances of*

human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC. Off J Eur Union 2024; L1938:1-XX. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1938.

29. Writing Group of the ESHRE Ethics Committee; Pennings G, Dondorp W, Popovic M, Chuva de Sousa Lopes S & Mertes H: *Ethical considerations on the moral status of the embryo and embryo-like structures. Hum Reprod 2024; 39:2387-91.*

30. Federal Ministry of Health of Bosnia and Herzegovina: *Zakon o liječenju neplodnosti biomedicinski potpomognutom oplodnjom [Law on the Treatment of Infertility with Biomedically Assisted Fertilization]. Official Gazette of FBiH 2018; 59. Available from: https://fmoh.gov.ba/uploads/file_manager/5e8c653ea279da7f4d6d06f2746220c21eb2a8bb.pdf.*

31. Blackshaw BP & Rodger D: *Defining life from death: Problems with the somatic integration definition of life. Bioethics 2020; 34:549-54.*

32. Brown MT: *The somatic integration definition of the beginning of life. Bioethics 2019; 33:1035-41.*

33. Brown MT: *The Moral Status of the Human Embryo. J Med Philos 2018; 43:132-58.*

34. Alvarez-Díaz JA: *El estatus del embrión humano desde el gradualismo [The status of the human embryo from a gradualistic perspective]. Gac Med Mex 2007; 143:267-77.*

35. Neaves W: *The status of the human embryo in various religions. Development 2017; 144:2541-43.*

36. Carlson BM: *Human Embryology and Developmental Biology. 5th ed. Elsevier, Philadelphia, 2014.*

37. Elder K & Dale B: *In Vitro Fertilization. 4th ed. Cambridge University Press, Cambridge, 2020.*

Correspondence:
Asad Herić
Department of Obstetrics and Gynecology, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina
e-mail: asadheric@yahoo.com

THE ARGUMENT FOR ESTABLISHING A NEW JOURNAL OF ANESTHESIA AND INTENSIVE CARE

Tina Tomić Mahečić, Robert Baronica, Dora Karmelić, Ivan Šitum, Ante Erceg, Slobodan Mihaljević

UHC Zagreb, Department of Anesthesia and Intensive Care Medicine, Kišpatićeva 12, Zagreb, Croatia

received: 03.05.2025; revised: 14.07.2025; accepted: 14.07.2025

SUMMARY

The field of anesthesia and intensive care is an essential component of modern healthcare. It significantly impacts patient outcomes in elective and emergency medical settings. Integrating anesthesia and intensive care practices is crucial for patient survival, recovery, and overall healthcare efficiency.

Despite their importance in clinical settings, there is a lack of scientific and published work in this field of expertise, particularly in smaller countries. This significant gap requires establishing a new national and regional journal focused on anesthesia and intensive care medicine. Such a journal should address specific national and regional issues, encourage and promote research, and facilitate collaboration within the community.

This article makes a compelling case for establishing a New Journal of Anesthesia and Intensive Care (NJAIC), the Academic Alliance for Anesthesia and Intensive Care Medicine. It outlines its benefits for practitioners, researchers, and healthcare institutions.

Keywords: *Journal, Anesthesia, Intensive Care Medicine*

*****

CURRENT LANDSCAPE OF ANESTHESIA AND INTENSIVE CARE JOURNALS

Globally, numerous medical journals are dedicated to anesthesia and intensive care. Prestigious publications such as *Anesthesia & Analgesia*, *the British Journal of Anaesthesia*, and *Intensive Care Medicine* have significantly contributed to spreading clinical research and best practices (Lauritsen & Moller 2004, Andrès & Lavigne 2024).

However, these journals are often oriented towards broad international audiences, leaving a gap in context-specific research and regional issues. Although they provide valuable information, these journals may not address the unique clinical and administrative challenges faced by healthcare systems at the national and regional levels, where local policies, regulations, and patient demographics play crucial roles in medical care (Rivas-Ruiz 2019). Consequently, due to strict audit principles, quality articles and research from smaller countries and regions can easily be rejected.

IMPORTANCE OF A NATIONAL PERSPECTIVE

It is widely recognized that medical journals are vital for spreading new knowledge and clinical practices. They enable researchers and practitioners to share the latest findings, methodologies, and innovative ideas in a peer-reviewed format (Kaynar 2022). Establishing a national or regional journal focused on anesthesia and intensive care medicine illustrates the enthusiasm and creativity of the dedicated medical community. A journal like this would encourage local researchers, enhance visibility, and ensure global representation. The *New Journal of Anesthesia and Intensive Care (NJAIC), the Academic Alliance for Anesthesia and Intensive Care Medicine,* would provide an invaluable platform for addressing the unique needs of the local healthcare system. Such a journal can focus on issues relevant to healthcare professionals operating within the same regulatory and economic frameworks, including training practices and continuing medical education, as well as specific regional disease burden and resource allocation. This context-specific approach would allow for more targeted research, evidence-based guidelines, and recommendations immediately applicable within the local healthcare setting.

Establishing a new journal would highlight our country's strong foundation and tradition in anesthesia and intensive care practice in the region, emphasizing the capacity of local professionals to contribute meaningful research and clinical advancements.

The successes of modern Croatian anesthesia and intensive care medicine are recognized in European and global contexts. The best example of this is transplantation medicine, where we rank among the leaders in the number of donated organs and transplanted patients per million inhabitants. In our country, we perform transplantation of all solid organs (heart, lungs, liver, kidneys, pancreas), and simultaneous transplants (e.g., heart/liver or heart/kidney) are also successfully conducted (*https://www.transplant-observatory.org/wp-content/uploads/2025/02/2023-data-global-report-20022025.pdf*). All these procedures require

exceptionally well-organized anesthesia and intensive care. Anesthesia and intensive care medicine related to transplantation procedures represent some of the most challenging and complex practices in the field, highlighting the exceptional quality of our specialists (Mah et al. 2023).

Additionally, several anesthesiology and intensive care societies operate in our country, promoting the profession both domestically and internationally (e.g., Croatian Society of Anesthesiology, Reanimatology, and Intensive Care Medicine (HDARIM), Croatian Society of Intensive Care Medicine (HDIM), Croatian Society of Regional Anesthesia and Analgesia (HDRAA), and others). These societies actively organize annual meetings, workshops, and courses at national and international levels.

Today's profession's successes are built upon the strong tradition and history of anesthesiology in Croatia; the first successful anesthesia in Croatia was performed in 1847 in Zadar, just five months after the first public demonstration of ether anesthesia in Boston (Šakić 2011).

Moreover, national collaboration and research efforts may be essential for solving public health crises like the COVID-19 pandemic and earthquakes in Zagreb. Crises like these require rapid adaptation of anesthesia and intensive care practices. National-level insights into the deployment of intensive care units (ICUs), the management of ventilator shortages, and the training of anesthesiologists and intensivists during such crises highlight the need for a dedicated platform to exchange ideas, data, and clinical experiences continuously.

Furthermore, this journal could serve as a channel for disseminating national or institutional guidelines that can be directly adopted and implemented across hospitals and healthcare systems (Suzuki et al.2006).

THE ROLE OF A NEW JOURNAL IN RESEARCH AND EDUCATION

A dedicated new journal would encourage anesthesiologists to conduct research relevant to their unique clinical settings and challenges. Resource-limited settings often produce innovative solutions that deserve broader recognition (van Zyl et al. 2021). The journal could serve as an educational tool for training medical students and early-career professionals, familiarizing them with current research trends and practices.

Croatia, a country with approximately 700 anesthesiologists, has a unique opportunity to strengthen its medical community by launching a scientific journal focused on anesthesia and intensive care. The journal should cover all kinds of scientific work, including original research investigations, review articles, case reports, case series, interviews with experts, guidelines from national anesthesiological and intensive care medicine societies, and other areas of perioperative medicine. The most important areas of interest for this journal would include general and regional anesthesia, mechanical ventilation, hemodynamic monitoring, management of coagulation and bleeding, volume and fluid management, the use of ultrasound in everyday clinical practice, transplantation medicine, treatment of different types of shock, antimicrobial prophylaxis and therapy, parenteral and enteral nutrition, treatment of delirium, and many others.

This initiative would provide a platform to highlight the country's expertise and promote regional collaboration and research partnerships among academic institutions, healthcare providers, and industry stakeholders to inspire innovation despite resource constraints.

Anesthesia and intensive care are disciplines characterized by complex, highly technical practices that require ongoing education and training (Chin et al. 2024). The journal would provide a valuable resource for practitioners and clinicians looking to stay updated on the latest clinical guidelines, techniques, equipment, and innovations.

By focusing on national standards and regional medical practices, the journal would provide accessible, relevant, and practical information for medical students, residents, anesthesiologists, intensivists, and all other perioperative physicians. In addition to the national standardization of medical practice, one of the most critical roles of this journal could be to promote regional scientific and clinical collaboration with neighboring countries. This may improve the quality of care in every country, reduce existing costs through resource sharing, and improve patient outcomes. For example, medical journal editors in the Eastern Mediterranean Region have emphasized the importance of pooling resources for training editors, reviewers, and researchers and minimizing expenses through gift and exchange programs. Collaborations with academic institutions or government agencies can provide essential financial or infrastructural support for journal operations (Larsson & Larsson 2020).

SUPPORTING THE ANESTHESIA AND INTENSIVE CARE WORKFORCE

The *New Journal of Anesthesia and Intensive Care (NJAIC), the Academic Alliance for Anesthesia and Intensive Care Medicine*, could play a pivotal role in supporting the professional development of the national workforce. The journal could publish career development articles, interviews with leading professionals, and insights into the latest anesthesia and intensive care trends.

Addressing the specific challenges and issues related to anesthesia, intensive care specialists, and nurses is essential due to the increasing pressure on healthcare systems worldwide, including practitioner shortages and burnout. Moreover, the journal could offer a platform for promoting professional networking and collaboration, which is vital for career advancement and knowledge sharing. By highlighting national conferences, workshops, and training programs, the journal could

become an essential resource for development initiatives and policy advocacy at the national and regional levels.

Small countries such as Croatia, with limited budgets, have employed innovative strategies to support the publication of medical journals, ensuring that their researchers and practitioners can share knowledge and contribute to global medical science. Many small countries adopt open-access publishing models using platforms like the "Open Journal System" (OJS) (Iyandemye & Thomas 2019). This cost-effective and user-friendly system allows journals to be free for authors and readers. For example, the “Journal of Health Informatics in Developing Countries” uses OJS and relies on the goodwill of editorial teams and international collaborations to sustain operations.

As we know, article processing charges (APCs) can often be prohibitive for researchers in low-resource settings (Saloojee & Pettifor 2024).

The journal could adopt tiered pricing or seek subsidies from international organizations to address this. The journal may also pursue funding from international grants, academic institutions, or public-private partnerships to cover operational costs. Utilizing online publishing platforms can help reduce costs associated with print editions while increasing global reach (Mondal & Mondal 2024).

The plan is to ensure high-quality peer review processes that will enhance credibility and attract submissions from international researchers. Transitioning to an open-access model can maximize the number of readers and minimize barriers for researchers from low- and middle-income countries and underrepresented regions. After enhancing the journal’s reputation and impact, the plan is to ensure indexation and presentation in international databases, attracting submissions from a broader range of researchers (Fassoulaki et al. 2001).

Collaborations with international organizations and initiatives like HINARI (Health InterNetwork Access to Research Initiative), developed by the World Health Organization (WHO), are essential (Saric 2016). These initiatives provide low-cost or free access to high-quality scientific journals for developing countries. This program helps researchers stay updated and improve their chances of publishing internationally by offering access to current knowledge.

Non-profits like PREPSS (Pre-Publication Support Services) offer pre-publication support, including peer review and editing services, to researchers from low- and middle-income countries (LMICs) without charging fees (Newton 2020).

These strategies demonstrate that even with financial constraints, small countries can successfully publish medical journals by leveraging technology, fostering collaborations, and adopting flexible financial models (Logullo et al. 2024).

Launching a *New Journal of Anesthesia and Intensive Care (NJAIC), the Academic Alliance for Anesthesia and Intensive Care Medicine* is an academic success and a statement of scientific enthusiasm and innovation. It validates the expertise of local professionals, supports collaboration, and elevates the country's place in global medical research. By addressing challenges such as funding and accessibility, this initiative can become a cornerstone for advancing anesthesia practice locally and internationally.

By providing a dedicated platform for local research and clinical experiences, the journal can become a cornerstone for advancing anesthesia and intensive care practices. It can help identify best practices, highlight areas for improvement, and drive evidence-based changes in patient care.

CONCLUSION

Establishing a *New Journal of Anesthesia and Intensive Care (NJAIC), the Academic Alliance for Anesthesia and Intensive Care Medicine* is a timely, powerful, and essential initiative for the healthcare community. By focusing on the specific needs of national healthcare systems, providing a platform for innovative research, supporting professional development, and improving patient outcomes, the journal would play an instrumental role in advancing both the scientific and clinical aspects of anesthesia and intensive care. As the fields continue to evolve, a new journal would help bridge the gap between international advancements and national and regional healthcare systems' unique needs, allowing a more unified, informed, and collaborative community of practitioners.

REFERENCES

1. Andrès E, Lavigne T: *Medical Journals: Role, Place, Issues, and Future Challenges. J Clin Med. 2024 Apr 2;13(7):2059. doi: 10.3390/jcm13072059. PMID: 38610823; PMCID: PMC11012967*
2. Chin H, Ingerman Å, Block L, Hergès HO. *Navigating the complex dynamics of anesthesiologists' professional identity formation in the context of their specialty training program: a phenomenographic perspective. BMC Med Educ. 2024 May 15;24(1):539. doi: 10.1186/s12909-024-05527-7. PMID: 38750505; PMCID: PMC11097508.*
3. Fassoulaki A, Sarantopoulos C, Papilas K, Patris K, Melemeni A. *Academic anesthesiologists' views on the importance of the impact factor of scientific journals: a North American and European survey. Can J Anaesth. 2001 Nov;48(10):953-7. doi: 10.1007/BF03016583. PMID: 11698312.*
4. Iyandemye J, Thomas MP. *Low-income countries have the highest percentages of open access publication: A systematic computational analysis of the biomedical literature. PLoS One. 2019 Jul 29;14(7):e0220229. doi: 10.1371/journal.pone.0220229. PMID: 31356618; PMCID: PMC6663019.*

5. Kaynar AM. *Editorial: Insights in intensive care medicine and anesthesiology: 2022. Front Med (Lausanne). 2024 Jun 18;11:1404342. Doi: 10.3389/fmed.2024.1404342. PMID: 38957304; PMCID: PMC11217530).*
6. Larsson, J.; Larsson, L. *Integration, Application and Importance of Collaboration in Sustainable Project Management. Sustainability* ***2020****, 12, 585. https://doi.org/10.3390/su12020585*.
7. Lauritsen J, Moller AM: *Publications in anesthesia journals: quality and clinical relevance. Anesth Analg. 2004 Nov;99(5):1486-1491. Doi: 10.1213/01.ANE.0000136468.92993.CF. PMID: 15502053.*
8. Logullo P, de Beyer JA, Kirtley S, et al. *Open access journal publication in health and medical research and open science: benefits, challenges, and limitations BMJ Evidence-Based Medicine 2024;****29:****223-228.*
9. Mah J, Johnston-Webber C, Prionas A, Bušić M, Streit S, Wharton G, et al. *Organ Donation in Croatia: The Importance of a National Champion, a Comprehensive Plan, and International Collaborations. Transpl Int. 2023 May 25;36:11011. doi: 10.3389/ti.2023.11011. PMID: 37305341; PMCID: PMC10249501.*
10. Mondal, H, Mondal, S. *The Paradigm Shift in Scientific Publications. Preventive Medicine Research & Reviews 1(2):p 64-66, Mar–Apr 2024. | DOI: 10.4103/PMRR.PMRR_38_23.*
11. Newton CR. *Research and open access from low- and middle-income countries. Dev Med Child Neurol. 2020 May;62(5):537. doi: 10.1111/dmcn.14513. PMID: 32249939; PMCID: PMC7613490.*
12. Rivas-Ruiz R. *La importancia de las revistas médicas nacionales en un mundo global [The importance of national medical journals in a global world]. Rev Med Inst Mex Seguro Soc. 2019 Dec 30;57(6):334-336. Spanish. PMID: 33001606.*
13. Saloojee H, Pettifor JM. *Maximizing Access and Minimizing Barriers to Research in Low- and Middle-Income Countries: Open Access and Health Equity. Calcif Tissue Int. 2024 Feb;114(2):83-85. doi: 10.1007/s00223-023-01151-7. Epub 2023 Nov 14. PMID: 37962622; PMCID: PMC10803444.*
14. Saric, K. *HINARI Access to Research in Health program networks to sustain and expand success. J Med Libr Assoc. 2016 Oct;104(4):338-341. doi: 10.3163/1536-5050.104.4.018. PMID: 27822161; PMCID: PMC5079501.*
15. Suzuki K, Edelson A, Iversen LL, Hausmann L, Schulz JB, Turner AJ. *A Learned Society's Perspective on Publishing. J Neurochem. 2016 Oct;139 Suppl 2:17-23. doi: 10.1111/jnc.13674. Epub 2016 Aug 17. PMID: 27534728.*
16. Šakić K. *Introduction of anaesthesia in Croatia // Periodicum biologorum, 113 (2011), 2; 123-123.*
17. van Zyl C, Badenhorst M, Hanekom S, Heine M. *Unravelling 'low-resource settings': a systematic scoping review with qualitative content analysis. BMJ Glob Health. 2021 Jun;6(6):e005190. doi: 10.1136/bmjgh-2021-005190. PMID: 34083239; PMCID: PMC8183220.*

Correspondence:
Tina Tomić Mahečić, MD, PhD
UHC Zagreb, Department of Anesthesia and Intensive Care Medicine, Kišpatićeva 12, Zagreb, Croatia
e-mail: ttomic@kbc-zagreb.hr

Medicina Academica Integrativa, 2025; Vol. 2, No. 1-2

SUPRAVENTRICULAR TACHYCARDIA-INDUCED CARDIOGENIC SHOCK IN A NEONATE: A CASE REPORT

Iva Mandić, Svjetlana Mikulić, Helena Karlović,
Marija Novaković Bošnjak, Marjana Jerković Raguž
Clinic for Children's Diseases, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina
received: 11.07.2025; revised: 27.10.2025; accepted: 27.10.2025

*****

INTRODUCTION

Shock is defined as the failure to deliver adequate oxygenated blood to tissues, re-sulting in a mismatch between oxygen supply and demand. Oxygen delivery is primarily determined by arterial oxygen content (dependent on hemoglobin con-centration and oxygen saturation) and cardiac output, which is the product of stroke volume and heart rate (Marcdante et Kliegman, 2019). Shock can be broadly classified into three progressive phases: com-pensated, uncompensated, and irreversible. In the compensated phase, cardiac ou-tput is maintained via sympathetic activation, increasing heart rate and systemic vascular resistance (Mardešić et al., 2016). Based on the underlying pathogenesis, shock can be classified: hypovolemic, cardiogenic, distributive (septic) and obstructive shock. Cardiogenic shock is pathophysiologically characterized by impai-red systolic function and reduced cardiac output, typically resulting from congenital heart defects, cardiomyopathies, or arrhythmias (Brissaud et al., 2016).

We report the case of a neonate admitted to our clinic in a state of cardiogenic shock caused by supraventricular tachycardia (SVT). On admission, the infant presented in sinus rhythm, which initially masked the underlying arrhythmia and complicated the diagnostic process. The diagnosis of SVT was confirmed only after haemodynamic stabilization, emphasizing the diagnostic challenges associated with undifferentiated shock in neonates.

CASE DESCRIPTION

A 27-day-old female neonate was brought to the emergency department due to respiratory distress, poor general condition, and grunting. The parents reported that the infant had awakened during the night with a high-pitched cry and assumed a fetal position, followed by labored breathing and peripheral cyanosis.

The infant was born at term (40 weeks' gestation) after a pregnancy complicated by gestational diabetes. Apgar scores were normal; birth weight was 3600 g, and length was 56 cm. She had shown normal neurological and clinical development and had been breastfed regularly.

On admission, the neonate was in shock. Clinical examination revealed mottled skin, cold and livid extremities, capillary refill time of 3 seconds, and bradycardia (~100 bpm). She was in respiratory distress, with narrow, isocoric pupils, and a soft anterior fontanelle level with the skull.. Pulmonary auscultation was unremarkable. Cardiac examination revealed a rhythmic, bradycardic heart rate with clearly audible tones and no murmurs. The abdomen was distended. The patient was hypotonic. She was immediately intubated and placed on mechanical ventilation. Initial venous blood gas analysis demonstrated severe mixed acidosis (pH 6.57, pCO_2 9.46 kPa, pO_2 4.9 kPa, SpO_2 15%, HCO_3^- 6.4 mmol/L, BE – 31.7, lactate >20 mmol/L). Boluses of crystalloids and sodium bicarbonate were administered, along with dopamine and dobutamine.

Septic shock was initially suspected. Lumbar puncture excluded meningitis, and laboratory markers were within normal ranges. Empiric triple antibiotic therapy (ampicillin, amikacin, and ceftazidime) was initiated. Chest X-ray was unremarkable.

Following hemodynamic stabilization, the patient showed improved vital signs (SpO_2 93%, HR 130 bpm, BP 84/36 [52] mmHg). Several hours later, she developed a narrow-complex tachycardia >250 bpm. ECG confirmed SVT at >300 bpm, which was successfully terminated with adenosine and amiodarone. Echocardiography revealed normal cardiac anatomy, while abdo-minal ultrasound showed a small amount of free fluid between bowel loops. On the first day of hospitalization, propranolol, gastric protection, neuroprotection (phe-nobarbital), and analgesia/sedation were initiated. Laboratory findings revealed markedly elevated proBNP (55,707 pg/mL), troponin (778 ng/L), and signifi-cantly elevated AST, ALT, and LDH le-vels.

On day two, the patient experienced a brief episode of bradycardia, which responded promptly to resuscitation. Serial echocardiography revealed a small pleural effusion, which later resolved. On day five, during extubation, the patient experienced a tonic-clonic seizure that ceased following administration of phenobarbital. EEG demonstrated mildly dysrhythmic patterns, and levetiracetam was added to the treatment. Cranial ultrasound was normal.

The infant was discharged in stable condi-tion on day 13 with continued beta-blocker and antiepileptic therapy.

DISCUSSION

Cardiogenic shock in neonates, although rare, is a critical emergency with high morbidity and mortality. It most commonly arises from congenital heart defects, myocarditis, or arrhythmias such as su-praventricular

tachycardia (SVT). The immature neonatal myocardium is particu-larly vulnerable to volume and pressure overload, and even mild myocardial dysfunction can result in profound circulatory failure. Unlike in older children and adults, neonates often present with non-specific signs - such as poor feeding, irritability, vomiting, or cyanosis - which can delay diagnosis. (Brissaud et al., 2016). Early recognition and differentiation from other types of shock are crucial for survival and favorable long-term outcomes.

A study conducted at the British Columbia Children's Hospital revealed that, in neonates presenting with undifferentiated decompensated shock, cardiogenic causes - particularly arrhythmias like SVT are mo-re frequently identified than infectious etiologies (Chan et al., 2019). This finding underscores the importance of maintaining a high index of suspicion for arrhythmic causes of shock even in the absence of classical signs of infection.

SVT is among the most common ar-rhythmias requiring emergency cardiovas-cular intervention in neonates. Its inciden-ce is estimated at 0.06 per 1,000 live births within the first month of life and 0.25 per 1,000 by the end of the first year (Kamel et al., 2022). Clinical manifestations of SVT are often nonspecific, which can delay diagnosis and appropriate manage-ment. If left untreated, sustained SVT can lead to myocardial dysfunction, hemodynamic compromise, cardiogenic shock, and ultimately heart failure.

Several case reports have highlighted SVT as a primary cause of cardiogenic shock in neonates. A report by Viveiros et al. described a neonate who, similarly to our patient, initially presented in sinus rhythm and developed SVT only after hemodynamic stabilization. Conversely, a Croatian case report presented a neonate diagnosed with SVT and cardiogenic shock upon ad-mission, illustrating the variability in clinical presentation of this condition (Viveiros et al., 2013; Doder et al., 2022).

Further supporting these observations, a retrospective study by Gilljam et al. (2008) found that nearly half (48%) of neonates under 30 days old with SVT exhibited signs of heart failure. Importantly, the same study demonstrated that by one year of age, 52% of these infants remained free of arrhythmia without requiring further antiarrhythmic therapy. These findings highlight the potential for spontaneous resolution of SVT during infancy, particularly in cases without underlying structural heart disease.

Additionally, neonates diagnosed with SVT before 60 days of age and without a Wolff-Parkinson-White (WPW) pattern on electrocardiogram are considered to have a low risk of recurrence. In 90% of such cases, SVT does not recur by one year of age. In those treated with antiarrhythmic therapy, recurrence rates fall to only 5% after cessation of treatment, emphasizing the importance of individualized management strategies based on risk stratification (Mah et al., (2017).

In our case, the initially misleading presentation in sinus rhythm delayed recognition of the underlying arrhythmic cause. The patient's rapid deterioration and development of SVT after stabilization emphasize the diagnostic challenges associated with undifferentiated shock in neonates. Early ECG monitoring and consideration of arrhythmia, even in the absence of typical features, were pivotal in achieving a favorable outcome.

CONCLUSION

This case, therefore, highlights the need for comprehensive assessment and timely intervention in neonates with cardiogenic shock, especially when the etiology is not immediately apparent. Although SVT-induced cardiogenic shock is rare, it is a critical diagnosis that can be made with prompt electrocardiographic evaluation and appropriate pharmacologic intervention. Early diagnosis and treatment are key to preventing long-term sequelae, including developmental delays and organ dysfunction.

Acknowledgements: None.

Conflict of Interest: None to declare.

Contribution of individual authors:

Iva Mandić: conception, writing the first draft, manuscript preparation, execution.
Svjetlana Mikulić: conception, organization, manuscript preparation, analysis, design.
Helena Karlović: organization, review and critique.
Marija Novaković Bošnjak: organization, review and critique
Marjana Jerković Raguž: organization and critique.

REFERENCES

1. Marcdante KJ, Kliegman RM, editors. *Nelson essentials of pedia-trics. 8th ed. Philadelphia (PA): Elsevier; 2019.*

2. Brissaud O, Botte A, Cambonie G, Dauger S, de Saint Blanquat L, Durand P, Gournay V, Guillet E, Laux D, Leclerc F, Mauriat P, Boulain T, Kuteifan K. *Experts' recommendations for the management of cardiogenic shock in children. Ann Intensive Care. 2016 Dec;6(1):14.*

3. Mardešić D, urednik. *Pedijatrija. 8. izdanje. Zagreb: Školska knjiga; 2016.*

4. Kamel O, Hammouda T, Tarek A, Ali W. *Recovery of cardiogenic shock with ablation of incessant tachycardia in a neonate. Glob Cardiol Sci Pract. 2022 Jun 30;2022(1-2)*

5. Chan KH, Sanatani S, Potts JE, Harris KC. *The relative incidence of cardiogenic and septic shock in neonates. Paediatr Child Health. 2019 Jun 24;25(6):372-377.*

6. Viveiros E, Aveiro AC, Costa E, Nunes JL. *Cardiogenic shock in a neonate. BMJ Case Rep. 2013 Jun.*

7. Gilljam T, Jaeggi E, Gow RM. *Neonatal supraventricular tachycardia: outcomes over a 27-year period at a single institution. Acta Paediatr. 2008;97:1035–1039.*
8. Doder V, Skokić F, Kapidžić M, Fetić I. *Cardiogenic shock caused by supraventricular tachycardia in a neonate – a case report. Medicina Fluminensis.*

Correspondence:
Iva Mandić, MD,
Clinic for Children's Diseases, University Clinical Hospital Mostar, Bijeli Brijeg bb, 88000 Mostar, Bosnia and Herzegovina.
e–mail: ivacvitkovic.mandic@gmail.com

ALLERGENIC PLANTS IN THE ENVIRONMENT AND THEIR MEDICAL SIGNIFICANCE: UNIVERSITY TEXTBOOK REVIEW

*****

Authors: Danijela Petrović, Branko Krišto, Milenko Bevanda, Aldin Boškailo

Publisher: Sveučilište u Mostaru (University of Mostar)

Place and year of publishing: Mostar, 2025.

Number of pages: 319.

ISBN: 978-9926-28-094-9

*****

The University of Mostar recently published the university textbook „Alergene biljke u okolišu i njihov medicinski utjecaj: sveučilišni udžbenik“ („Allergenic Plants in the Environment and Their Medical Significance: University Textbook“) by Professors Danijela Petrović, PhD, Branko Krišto, MD, PhD, Milenko Bevanda, MD, PhD and Associate Professor Aldin Boškailo, PhD.

CONTENT AND STRUCTURE

The book is a comprehensive professional publication that systematically covers various aspects of allergenic plants - from botany, through aerobiology, to clinical implications for human health. The main segments covered in the book:

1. Plant species - the authors analyze in detail the most common allergenic plants in the environment: grasses, trees, and weeds.

2. Pathophysiology of allergic reactions - the book explains the mechanisms by which pollen (and other plant allergens) trigger immune reactions in humans.

3. Diagnostics and therapy - practical recommendations for medical professionals are provided: how to recognize allergies, how to diagnose, and how to treat and prevent allergic conditions.

4. Prevention - the emphasis is also on education and practical advice on how to reduce exposure to allergenic plants.

5. Pollen calendar - the book provides a pollen calendar, which is very important for understanding seasonal allergy patterns.

6. Illustrations and visuals - the book contains original illustrations, which helps both scientists and laypeople to recognize allergenic plants.

The book has an interdisciplinary approach; it combines botany, medicine (allergology), and public health, which is rare in the literature in this region. It is not only an academic publication - it also serves as a manual for doctors, but also for the general public who want to understand allergic reactions triggered by plants. Allergies are, according to the authors and promoters of the book, a significant health problem of the 21st century, so the book can serve as a tool for raising awareness and planning preventive measures.

Since the authors are from Bosnia and Herzegovina and Mostar, the book is adapted to local plant species and climatic conditions, which is a great advantage because it provides relevant information for the region. The authors are recognized experts (professors and researchers), which gives the book necessary authority. Regarding practical applicability of the textbook, readers can learn how to recognize allergenic plants in the environment and how to reduce the risk. In addition to experts, the book is useful for students, but also for patients who want to better understand plant-caused allergies. The illustrations and calendar give the book special value - they improve understanding and help visualize plant allergens.

CONCLUSION

The book "Allergenic Plants in the Environment and Their Medical Significance" by Danijela Petrović, Branko Krišto, Milenko Bevanda and Aldin Boškailo represents a very important and useful contribution to the knowledge of plant allergens in the region. The book is excellently designed as a bridge between botany, medicine and public health and offers scientific insights and practical advice at the same time.

For anyone interested in allergies, pollen, public health or ecology, this book can serve as an indispensable resource. It is particularly relevant for clinicians, students and scientists, but also for a wider audience who want to better understand how environmental plants affect human health.

Correspondence: Daniela Bevanda Glibo, MD, PhD
School of Medicine, University of Mostar, Mostar,
Bosnia and Herzegovina
E-mail: daniela.bevanda-glibo@mef.sum.ba

EFFECTIVENESS OF COGNITIVE BEHAVIORAL THERAPY AND YOGA IN MANAGING ANXIETY AND STRESS IN SCHOOL GOING CHILD WITH PRIMARY DYSMENORRHEA

Insiya Juzer & Vinodhkumar Ramalingam

Saveetha College of Physiotherapy, SIMATS, Chennai, Tamil Nadu, India

*****

Dear Editor,

We would like to share our experience with the Medicina Academica Integrativa audience regarding the common symptoms of anxiety and stress experienced by adolescent girls during menstruation due to dysmenorrhea. Dysmenorrhea is categorized into primary and secondary types. Primary dysmenorrhea involves severe cramping in the lower abdomen before or during menstruation, lasting 8-72 hours and peaking on the first or second day. Additionally, the pain is often accompanied by systemic symptoms like nausea, vomiting, diarrhoea, fatigue, and insomnia. In contrast, a number of distinct pathological conditions, such as endometriosis, adenomyosis, fibroids (myomas), and pelvic inflammatory disease, can cause secondary dysmenorrhea pain. (Iacovides, Avidon & Baker 2015)

The severity of dysmenorrhea varies, affecting women differently. While some experience mild to moderate discomfort, others endure extreme pain, leading to negative effects on emotions, social life, and physical well-being. Dysmenorrhea is also linked to anxiety and stress, commonly found in school girls. Anxiety and depression levels, which have been linked to a variety of pains, are believed to be linked to dysmenorrhea as well. Menstrual cycle issues and dysmenorrhea are more common in those with emotional and behavioural issues (Sahin et al. 2018). Many girls experience embarrassment and social withdrawal due to fear of pain and discomfort, leading to heightened stress, avoidance behaviors, and a negative self-image. This often results in school absenteeism among young women, impacting various aspects of life. Reports indicate high rates of absenteeism due to dysmenorrhea. The perceived severity of the pain and its related morbidities influence the frequency of absenteeism from school. Research has also indicated that even individuals who are able to attend school could struggle to focus or engage in their coursework. The academic achievement of the student will be impacted by school absences, particularly if they become a regular occurrence (Ezebialu, Ezenyeaku & Umeobika 2021)

Cognitive Behavioral Therapy (CBT) has been shown to improve mood swings, academic performance, and participation in daily physical activities, while also enhancing attention, concentration, and tolerance to pain (Akbar et al. 2024; Hassan et al. 2021). Yoga, as an alternative therapy, reduces dysmenorrhea pain, lowers stress, and enhances physical and mental well-being through practices like asanas, pranayama, and meditation (Rakhshaee 2011). Yoga combines breathing exercises, meditation, and physical activities to strengthen muscles and relieve tension.

Regular yoga practice encourages relaxation, reduces stress reactions, and helps individuals feel less anxious. Consistent practice also teaches the mind to feel more in control, manage emotions, and remain present. Notably, both yoga and CBT reduce dysfunctional thought processes, but yoga may lessen the likelihood of these thoughts occurring in the first place. Whereas, CBT teaches individuals to recognize and replace dysfunctional thoughts. The combination of yoga and CBT may be beneficial, as yoga can reduce the propensity for negative thoughts, while CBT can substitute maladaptive thoughts. This integrated approach may effectively lessen anxiety, highlighting the potential benefits of combining yoga and CBT.

This case study was approved by the Institutional Scientific Review Board (ISRB number: 01/009/2023/ISRB/SR/SCPT). Informed assent was obtained, and the subject's anonymity was preserved. A 16-year-old girl diagnosed with dysmenorrhea experienced severe cramping, pain, and discomfort, leading to heightened anxiety and stress. This resulted in minimum 2 and maximum 4 days of school absenteeism per cycle, affecting her academic performance and social life. Initial assessments were conducted using the Generalized Anxiety Disorder-7 (GAD-7) and Perceived Stress Scale (PSS) revealed moderate anxiety (14/21) and high stress (28/40). A 12-week integrated intervention combining Cognitive Behavioral Therapy (CBT) and Yoga was administered, consisting of three 40-minute sessions per week. The intervention included CBT principles, yoga asanas, and relaxation techniques.

Post-intervention assessments showed significant improvement, with decreased GAD-7 (6/21) and PSS (11/40) scores, indicating mild anxiety and low stress. School absenteeism reduced to 2 days in 3 months, and the participant reported increased confidence and reduced anxiety, leading to improved participation in school activities. This case study demonstrates the effectiveness of combining CBT and yoga in managing psychological distress associated with primary dysmenorrhea in school children. The findings of this study contribute to the application of CBT and yoga in future research.

Authors contribution: Design of the study, Literature search and analyses, Manuscript writing- I.J., Interpretation of data, Critical revision of manuscript- V.R., Final approval of the version- V.R., Agreement to be accountable for all aspect of the work- I.J.

Acknowledgements: None.

Conflict of Interest: None to declare

REFERENCES

1. Akbar SA, Ramana K, Srinivasan V, Suganthirababu P. *Efficacy of cognitive behavioral therapy on mental health in hospital housekeeping staff. Psychiatr Danub. 2024;36(3–4):400–401. https://doi.org/10.24869/psyd.2024.400*

2. Ezebialu I, Ezenyeaku C, Umeobika J. *Prevalence of dysmenorrhea and its contribution to school absenteeism among Nigerian undergraduate students. Ann Health Res. 2021;7(1):59–66. https://doi.org/10.30442/ahr.0701-07-116*

3. Hassan SI, Gouda AMI, El-Monshed AH, Abd-Ella NY. *Effect of cognitive behavioral therapy on depression, anxiety, stress, achievement, and coping strategy among young female students with primary dysmenorrhea. Egypt J Health Care. 2021;12(2):1383–1395. https://doi.org/10.21608/ejhc.2021.184416*

4. Iacovides S, Avidon I, Baker FC. *What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update. 2015;21(6):762–778. https://doi.org/10.1093/humupd/dmv039*

5. Rakhshaee Z. *Effect of three yoga poses (cobra, cat and fish poses) in women with primary dysmenorrhea: a randomized clinical trial. J Pediatr Adolesc Gynecol. 2011;24(4):192–196. https://doi.org/10.1016/j.jpag.2011.01.059*

6. Sahin N, Kasap B, Kirli U, Yeniceri N, Topal Y. *Assessment of anxiety-depression levels and perceptions of quality of life in adolescents with dysmenorrhea. Reprod Health. 2018;15(1):53. https://doi.org/10.1186/s12978-018-0453-3*

Correspondence:
Dr. Vinodhkumar Ramalingam, MPT, Ph.D.
Department of Physiotherapy, Saveetha College of Physiotherapy
Saveetha Institute of Medical and Technical Sciences, Chennai, India
e-mail: vinodhkumar.scpt@saveetha.com