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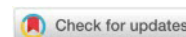
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THE IMPACT OF SOCIAL MEDIA ON YOUTH MENTAL HEALTH: A MULTIDIMENSIONAL APPROACH

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Abstract: Despite a substantial body of research, findings concerning the complex and multi-layered impact of social media on youth health continue to exhibit a high degree of inconsistency. The literature frequently presents conflicting, and at times even diametrically opposed, conclusions regarding both the positive and negative effects of social media use. This heterogeneity of results underscores the fact that the multidimensional nature of the relationship between social media use and youth health remains insufficiently clarified, both theoretically and empirically, particularly with respect to contextual factors that shape patterns of use, as well as the implications such patterns have for behavior within digital, or virtual, environments.

Against the backdrop of these theoretical and empirical ambiguities, the primary aim of the present study is to provide a systematic analysis of existing scientific evidence on the effects of social media use on the mental health of young people. At the same time, the study seeks to identify key gaps in the current body of knowledge and to delineate directions and opportunities for future research in this field. Particular emphasis is placed on the need for a more in-depth understanding of the mechanisms through which different patterns of social media use give rise to divergent mental health outcomes.

In this context, the effective mitigation of potential health risks associated with social media use among youth, alongside the recognition, affirmation, and optimal utilization of its positive aspects, can be achieved only through the long-term, systematic, and interdisciplinary advancement of media literacy. Furthermore, it is essential to foster the development of an inclusive, safe, and supportive digital environment that promotes responsible technology use and empowers young individuals to engage in critical thinking and constructive participation within the contemporary media landscape.

Keywords: mental health, health risks, social media, media literacy, infodemic

Field: Medical Sciences and Health

1. INTRODUCTION

Social media environments are replete with opportunities for social comparison, which renders the investigation of both short-term and long-term exposure to comparison-relevant content an ongoing research imperative. Empirical findings indicate that frequent use of social networking platforms is associated with lower levels of self-esteem, particularly in the domain of personal attributes. For instance, Facebook users have been found to report reduced self-confidence, a relationship mediated by increased exposure to social comparison processes. Additionally, experimental studies examining brief exposure to social media profiles demonstrate that participants' self-esteem and relative self-evaluations tend to decline when target profiles contain elements conducive to unfavorable comparisons, such as lower levels of social activity or the presence of unhealthy lifestyle habits (Vogel et al., 2014).

Of particular concern is the observation that the predominant body of evidence regarding the detrimental effects of social media on youth continues to rely heavily on subjective self-report measures. In contrast, only a negligible number of studies substantiate these findings using more clinically objective indicators, such as symptoms of mental disorders.

A relevant theoretical perspective emphasizes that the key determinant of the valence of adolescents' exposure to social media influences, and of the balance between potential risks and benefits, is not the duration of use per se, but rather the qualitative nature of engagement with these platforms (Davila et al., 2012; Feinstein et al., 2013).

Lloyd (2014) summarizes the positive implications of social media use among young people across several domains, with particular emphasis on benefits for individuals from minority communities, persons with disabilities, and those living with chronic illnesses. Specifically, social media provide opportunities for meaningful connections with others who share similar life circumstances, despite geographical distance. Moreover, it is suggested that policymakers and healthcare professionals could leverage social media as a tool for fostering engagement and support in the domain of mental health. However, as Dimitrovska (2026) warns, unhealthy lifestyles may lead to adverse health outcomes, not only through their direct clinical consequences but also by imposing substantial economic and societal burdens on healthcare

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systems, including increased healthcare expenditures, reduced productivity, and the erosion of overall living standards.

Media hyperproduction has led to an exponential increase in the volume of information circulating within the digital environment, a substantial portion of which consists of misinformation, misinterpreted content, and unverified rumors. Okray (2022) highlights findings indicating that the phenomenon of the infodemic is associated with a higher prevalence of various mental health disturbances, including depersonalization and derealization, anxiety, depression, and suicidal ideation. Such trends carry potentially serious societal implications, as they undermine individuals' capacity to make rational, evidence-based decisions.

Moreover, a transformation of discursive patterns within online support communities for individuals with mental disorders has been observed, characterized by a marked increase in content reflecting negative affective states, such as hopelessness, helplessness, loneliness, and even themes related to suicide.

A considerable proportion of individuals with mental health conditions do not utilize mental health services to obtain treatment. At the same time, there is compelling evidence that individuals with mental and psychosocial difficulties are becoming increasingly aware and are seeking greater influence and control over life events and treatment processes. In this context, social media, encompassing emails, video calls, text messaging, helplines, and social networking platforms, have emerged and expanded against the backdrop of exponential technological growth.

The proliferation of redesigned technologies has the potential to facilitate patient-centered services, support empowerment strategies, and enable the personalization of care, while simultaneously reducing associated costs. Additionally, there is a growing interest in the application of social media within the domain of mental health care and promotion (Di Napoli et al., 2015).

2. SOCIAL MEDIA: POSITIVE IMPLICATIONS VS. NEGATIVE IMPLICATIONS

Social media constitute an integral component of adolescents' everyday lives. However, their increasing pervasiveness simultaneously raises concerns regarding potential adverse implications. Contemporary research, as well as parental perspectives, suggests that continuous digital connectivity, prolonged use of social networking platforms during late evening hours, and the pressures inherent in online interactions may exert detrimental effects on young people's psychological well-being, academic performance, and overall health status (Richter, 2026).

In examining the emotional experiences of younger users in the context of social media engagement, Christodoulou et al. (2026) identify three key thematic domains. First, the authors address the emotional consequences of social media use, including phenomena such as disengagement and intermittent withdrawal as coping strategies in response to feelings of exhaustion, fatigue, and psychological strain. Second, an increasing level of distrust toward social media platforms and online informational content is highlighted, manifesting as heightened skepticism toward misinformation, algorithmically curated content, and contemporary artificial intelligence technologies. Third, the prevalence of aggressive communication patterns within social networks is analyzed, with users frequently exposed to hostile digital environments and consequently developing various defensive mechanisms to avoid such contexts.

The findings further indicate a dynamic transformation of behavioral patterns over time: earlier models characterized by active participation and content sharing have gradually given way to greater caution, distrust, and social withdrawal. This shift is interpreted as an adaptive response aimed at protecting individuals from emotional exhaustion and the adverse effects of exposure to unreliable or harmful information. While the existing literature predominantly focuses on younger cohorts, the present study makes a significant contribution by directing attention to the comparatively underexplored population of middle-aged individuals.

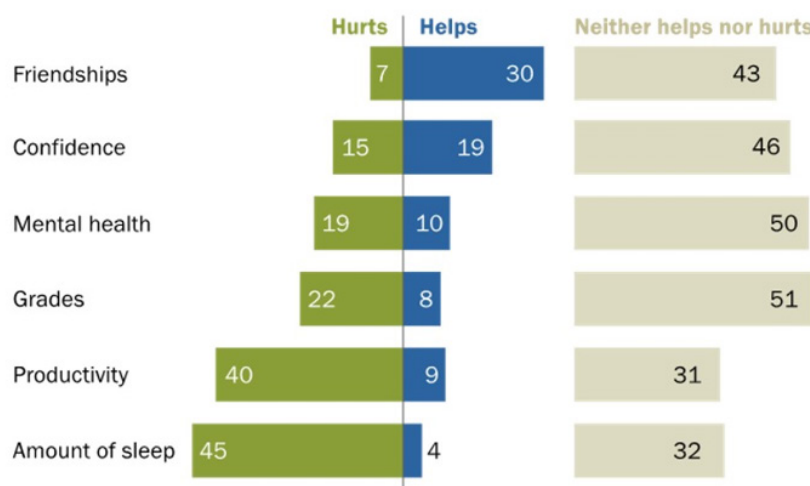
Marku and Kuneshka (2026) warn that excessive use of screen-based devices has been recognized as one of the major behavioral risk factors during childhood, as it promotes a sedentary lifestyle and contributes to the increasing prevalence of overweight and obesity. Therefore, the development and implementation of comprehensive public health strategies aimed at limiting screen time, while simultaneously encouraging the adoption of healthier lifestyle habits and balanced daily routines, are of paramount importance for improving children's physical health, as well as their educational outcomes and academic achievement.

When Faverio et al. (2025) from the Pew Research Center surveyed American adolescents regarding the potential effects of social media, they highlighted its bidirectional nature as both a source of benefits and risks. Certain aspects of life were perceived as enhanced through social media use, with

30% of teenagers reporting a positive impact on friendships, and 19% noting increased self-confidence, making these the only domains with a predominantly positive net effect. By contrast, negative effects are more frequently reported in the domains of academic work and daily functioning: 40% of adolescents believe that social media diminish their productivity (compared to 9% who perceive benefits), while 22% report adverse effects on academic performance, in contrast to only 8% who indicate improvement.

The most pronounced negative impact relates to sleep: as many as 45% of respondents report that social media reduce the amount of sleep they obtain, whereas only 4% believe they contribute to better rest. These findings underscore sleep as the domain most adversely affected, highlighting in particular the detrimental influence of late-night social media use on adolescents' rest patterns.

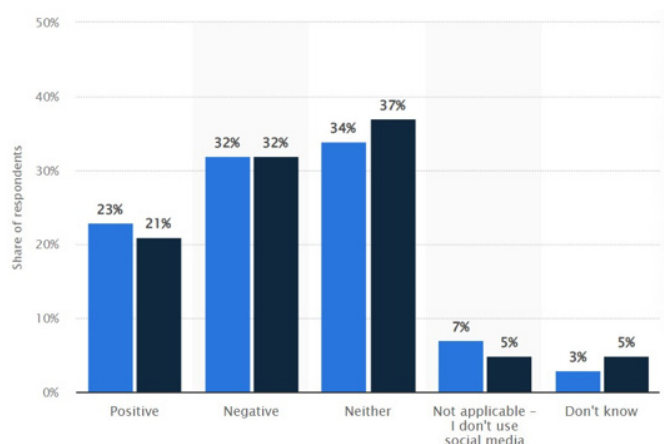
Figure 1. % of U.S. teens ages 13 to 17 who say using social media _ each of the following a lot/a little



Note: Survey conducted Sep. 18 – Oct. 10, 2024
Source: Pew Research Center, 2025

According to a study conducted in the United States in December 2025, modest gender differences were observed in the perception of the impact of social media on mental health: 23% of male respondents and 21% of female respondents evaluated this impact as positive. At the same time, an identical proportion of 32% of respondents from both genders reported that social media exert a negative effect on their mental health.

Graph 1. Mental health effects of social media for adults in the U.S. 2025, by gender



Source: Statista Research Department, 2025.

The use of social media is increasingly recognized as a potential risk factor for the development of mental health problems among adolescents. However, despite the growing interest of the scientific community in this topic, the number of longitudinal studies that systematically examine this association remains limited, and none of the existing studies has precisely quantified the proportion of adolescent

mental health problems that can be directly attributed to social media use.

In this context, Riehm et al. (2019) conducted a longitudinal cohort study involving a sample of 6,595 participants, followed across three waves of data collection: the first between September 12, 2013, and December 14, 2014; the second between October 23, 2014, and October 30, 2015; and the third between October 18, 2015, and October 23, 2016. The findings indicate that adolescents who spend more than three hours per day on social media may be at an elevated risk of developing mental health problems, particularly internalizing problems such as anxiety and depressive symptoms.

Based on these findings, the authors emphasize the need for further research aimed at systematically examining the effectiveness of various intervention strategies. Specifically, future studies should explore whether imposing limits on daily social media use, enhancing levels of media literacy, and the potential redesign of social media platforms themselves may constitute effective approaches to reducing the burden of mental health problems among adolescents.

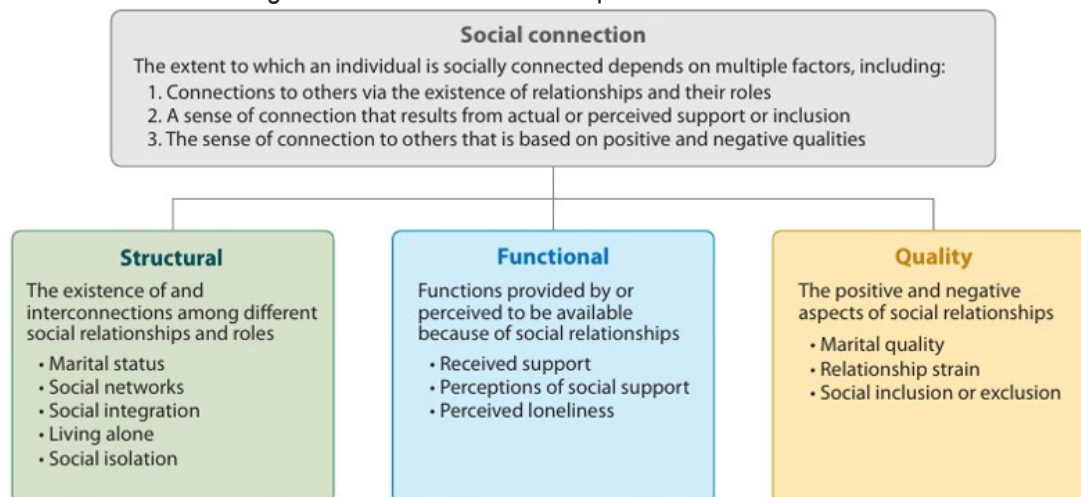
Table 1. The Impact of Social Media on the Mental Health of Youth: Evidence from Longitudinal Studies

Aspect	Positive Implications	Negative Implications	References
Depression and Anxiety	Moderate use may contribute to a sense of belonging and social support.	Increased prevalence of depressive and anxiety symptoms among adolescents with high levels of social media use.	Watson i sar., 2026 Tsomokos, 2025
Self-Esteem and Self-Image	The opportunity for identity expression and receiving positive feedback from peers.	Negative effects of social comparison, particularly among adolescent girls; increased risk of poor body image.	Tsomokos, 2025
Sleep	Moderate engagement may reduce feelings of isolation, thereby indirectly improving sleep quality.	Higher usage is associated with sleep disturbances and shorter sleep duration.	Tsomokos, 2025
Cognitive Functions	Moderate use may support cognitive engagement and access to information, potentially enhancing certain learning processes.	Excessive use is associated with reduced attention span, impaired concentration, and potential negative effects on executive functioning.	Watson i sar., 2026
Suicidal Ideation and Behaviors	There is no clear longitudinal evidence of a protective effect.	Elevated risk of suicidal ideation and attempts among adolescents with persistently high or rapidly increasing social media use.	Watson i sar., 2026

Source: Authors, based on data from multiple sources (see references), 2026.

According to the U.S. Surgeon General's Advisory (2023), a decline in social connectedness has been observed in the United States. Between 2003 and 2020, the time individuals spent socializing with friends decreased by approximately 20 hours per month, while overall social interaction with others declined by about 10 hours per month. Concurrently, individuals experiencing loneliness or dissatisfaction with the quality of their social relationships face an increased risk of premature mortality, as well as poorer health outcomes. Empirical evidence indicates that loneliness significantly contributes to an elevated risk of developing anxiety, depression, and dementia.

Figure 2. The Three Vital Components of Social Connection



Source: Holt-Lunstad, 2018

Based on a longitudinal study conducted on a nationally representative sample of adults in the Netherlands, collected across nine annual waves, Roberts et al. (2026) report that passive use of social media may contribute to increased levels of loneliness. At the same time, the authors emphasize that it remains premature to conclude that active social media use exerts a protective effect in terms of reducing loneliness. The findings further indicate the presence of a bidirectional relationship between the extent of social media use and loneliness.

4. CONCLUSION

The findings of this study contribute to a more nuanced understanding of the mechanisms that mediate the relationship between social media use and adverse mental health outcomes. In this regard, there is a clear need for sustained research attention directed toward the identification and analysis of specific processes emerging from complex interactions within the virtual environment that may pose risks to health. Concurrent with the growing number of social media users, there has been an increased prevalence of dissatisfaction with social interactions, diminished perceived connectedness with others, and heightened feelings of loneliness. Perceived loneliness, in turn, places individuals at elevated risk for anxiety, depression, and dementia, as well as for neurological and cardiovascular disorders.

Within a broader context, there is an imperative to develop and implement targeted interventions aimed at mitigating and reducing fatigue, psychological exhaustion, and distress associated with social media use. It is equally important to enhance users' competencies in recognizing misinformation, while strengthening trust in digital platforms through appropriate educational and regulatory frameworks. Future research should devote substantially greater attention to the phenomenon of negative social comparison in the context of social media use, given its documented association with increased depressive symptoms, as well as suicidal ideation and attempts among younger populations.

It is particularly concerning that the majority of assessments regarding the harmful effects of social media use on youth are predominantly based on self-report measures. In contrast, only a limited number of studies rely on more objective indicators, such as clinically relevant symptoms of mental disorders. This discrepancy points to a significant methodological limitation within the existing body of empirical literature.

REFERENCES

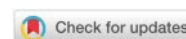
- Christodoulou, V., Konstantinou, P., Photiou, A., & Iordanou, K. (2026). Lost in the scroll: Emotional impacts of social media use among middle-aged adults. *Psychology of Popular Media*. <https://doi.org/10.1037/ppm0000671>
- Davila, J., Hershenberg, R., Feinstein, B. A., Gorman, K., Bhatia, V., & Starr, L. R. (2012). Frequency and quality of social networking among young adults: Associations with depressive symptoms, rumination, and corumination. *Psychology of Popular Media Culture*, 1(2), 72–86. <https://doi.org/10.1037/a0027512>
- Dimitrovska, M. (2026). The impact of ultra-processed foods on the global obesity epidemic, *Medis - Medical Science and Research*, 5(2), 93-97. <https://doi.org/10.35120/medisij0502093d>
- Di Napoli, W.A., Nollo, G., Pace, N. i Torri, E. (2015). Can the Clinical Use of Social Media Improve the Quality of Care in Mental Health? A Health Technology Assessment Approach in an Italian Mental Health Service. *Psichiatria Danubina*, 27 (1), 103-110.

- Faverio, M., Anderson, M., Park, E. (2025). Teens, Social Media and Mental Health. Available at: <https://www.pewresearch.org/internet/2025/04/22/teens-social-media-and-mental-health/#how-teens-see-social-media-s-impact-on-mental-health-friendships-sleep> (Accessed: May 22, 2026)
- Feinstein, B. A., Hershenberg, R., Bhatia, V., Latack, J. A., Meuwly, N., & Davila, J. (2013). Negative social comparison on Facebook and depressive symptoms: Rumination as a mechanism. *Psychology of Popular Media Culture*, 2(3), 161–170. <https://doi.org/10.1037/a0033111>
- Holt-Lunstad, J. (2018). Why Social Relationships Are Important for Physical Health: A Systems Approach to Understanding and Modifying Risk and Protection. *Annual Review Psychology*, 69, 437-458. <https://doi.org/10.1146/annurev-psych-122216-011902>
- Lloyd, A. (2014). Social Media: Help or Hindrance – What Role Does Social Media Play in Young People's Mental Health? *Psychiatria Danubina*, 26(1), 340–346.
- Marku, F., & Kuneshka, L. (2026). Association of Screen Time With BMI and Academic Performance Among Children Aged 6–17 Years in Tirana. *Medis – International Journal of Medical Sciences and Research*, 5(1), 27-32. <https://doi.org/10.35120/medisij0501027m>
- Okray, Z. (2022). Infodemic and Mental Health Consequences. *Collegium antropologicum*, 46(1), 69-76. <https://doi.org/10.5671/ca.46.1.10>
- Pew Research Center (2025). % of U.S. teens ages 13 to 17 who say using social media _ each of the following a lot/a little. Available at: https://www.pewresearch.org/internet/2025/04/22/teens-social-media-and-mental-health/pi_2025-04-22_teens-social-media-mental-health_0-10/ (Accessed: June 6, 2026)
- Richter, F. (2026). Social Media Is Keeping Teens from a Good Night's Sleep. Available at: <https://www.statista.com/chart/35970/self-reported-effects-of-social-media-use-on-teenagers/?lid=pp5gj2rnpdwl> (Accessed: June 27, 2026)
- Roberts, J. A., Young, P. D., & David, M. E. (2026). The Epidemic of Loneliness: A 9-Year Longitudinal Study of the Impact of Passive and Active Social Media Use on Loneliness. *Personality and Social Psychology Bulletin*, 52(5), 1111-1125.
- Statista Research Department, (2025). Mental health effects of social media for adults in the U.S. 2025, by gender. Available at: <https://www.statista.com/statistics/1457452/effect-of-social-media-on-mental-health-gender/> (Accessed: June 15, 2026)
- Tsomokos, D.I. (2025). Adolescent social media use and psychiatric outcomes: a longitudinal mediation analysis via interpersonal distrust, sleep, and self-image. *Social Psychiatry and Psychiatric Epidemiology*. <https://doi.org/10.1007/s00127-025-02999-w>
- Vogel, E. A., Rose, J. P., Roberts, L. R., & Eckles, K. (2014). Social comparison, social media, and self-esteem. *Psychology of Popular Media Culture*, 3(4), 206–222. <https://doi.org/10.1037/ppm0000047>
- Watson, C. S., Henrich, C. C., Long, D. M., & Fobian, A. D. (2026). Longitudinal Effects of Adolescent Digital Media Use on Mental Health in Young Adulthood. *Children*, 13(2), 215. <https://doi.org/10.3390/children13020215>
- U.S. Surgeon General's Advisory. (2023). Our epidemic of loneliness and isolation: The U.S. Surgeon General's Advisory on the healing effects of social connection and community. <https://www.hhs.gov/sites/default/files/surgeon-general-social-connection-advisory.pdf>

ELEVATED MATERNAL BMI AMONG WOMEN WITH SUCCESSFUL VAGINAL BIRTH AFTER CESAREAN: EXPERIENCE FROM A 9-YEAR SINGLE-CENTER SERIES

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Abstract: Maternal obesity is commonly associated with a reduced probability of vaginal birth after cesarean (VBAC), yet body mass index (BMI) alone does not determine the outcome of a trial of labor after cesarean (TOLAC). This study describes the BMI profile of women who achieved VBAC in a tertiary referral center, with particular attention to the representation of overweight and obesity among successful cases.

Objective: To describe the distribution of maternal BMI among successful VBAC cases and to assess the representation of elevated BMI, including severe obesity, within this group.

Materials and methods: A retrospective descriptive case series included 149 successful VBAC deliveries recorded between 2016 and 2025 at the University Hospital "Maichin Dom", Sofia. BMI was documented in 118 women. Patients were grouped as BMI <25 kg/m², 25.0–29.9 kg/m² and ≥30 kg/m². Obesity was additionally stratified into classes I, II and III. The study describes the characteristics of women who achieved VBAC and does not compare them with women who had a failed TOLAC.

Results: Mean BMI was 28.3 ± 6.6 kg/m² (range 19.0–64.0). Normal BMI was present in 43/118 women (36.4%), overweight in 37/118 (31.4%) and obesity in 38/118 (32.2%). Consequently, 75/118 successful VBAC cases (63.6%) occurred in women with BMI ≥25 kg/m². Among women with obesity, 26 (68.4%) had class I, 7 (18.4%) class II and 5 (13.2%) class III obesity.

Conclusion: Elevated BMI was common rather than exceptional among women who achieved VBAC in this series. Successful vaginal birth was observed across a wide BMI range, including BMI ≥40 kg/m². These findings should not be interpreted as BMI-specific TOLAC success rates, but they illustrate why BMI is better used as one component of individualized counseling than as a stand-alone exclusion criterion.

Keywords: TOLAC, VBAC, body mass index, obesity, overweight, cesarean delivery

Field: Medical Sciences and Health

1. INTRODUCTION

Counseling regarding mode of delivery after a previous cesarean section is often based on factors that alter the expected likelihood of vaginal delivery. Maternal BMI is one of these, but its clinical interpretation is not unambiguous. A lower likelihood of VBAC among obese women does not mean that vaginal delivery is unusual or unattainable for a particular woman with a high BMI. Current prognostic models continue to include BMI among the factors associated with the likelihood of successful VBAC. The updated model by Grobman et al. (2021) retains BMI as a prognostic factor, while excluding race and ethnicity from the assessment. The systematic review by Deng et al. (2022) also shows that BMI is among the commonly used predictors of successful VBAC. Lee et al., analyzing over four million deliveries after a previous cesarean section in the United States, found a progressive decrease in vaginal delivery rates with increasing BMI, while previous vaginal delivery significantly modified this relationship. Against this background, focusing only on women who achieved VBAC offers a different perspective. Rather than asking how often TOLAC is successful in each BMI category, the present study addressed a narrower question: how common is elevated BMI among women who have already achieved VBAC?

Objective: To characterize maternal BMI among women with successful VBAC at a tertiary center and to assess the representation of overweight and obesity, including severe obesity, in this cohort.

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2. MATERIALS AND METHODS

Clinical records of 149 women with successful vaginal birth after a previous cesarean delivery between 2016 and 2025 were reviewed. All deliveries occurred at the University Hospital of Obstetrics and Gynecology "Maichin Dom", Sofia, a tertiary obstetric referral center. The analysis presented here was restricted to maternal BMI and was designed as a descriptive case series.

BMI data were available for 118 women (79.2% of the cohort). For analysis, BMI was categorized as $<25 \text{ kg/m}^2$, $25.0\text{--}29.9 \text{ kg/m}^2$ and $\geq 30 \text{ kg/m}^2$. Women with BMI $\geq 30 \text{ kg/m}^2$ were further divided into class I ($30.0\text{--}34.9 \text{ kg/m}^2$), class II ($35.0\text{--}39.9 \text{ kg/m}^2$) and class III obesity ($\geq 40 \text{ kg/m}^2$). Continuous data are presented as mean $\pm$ standard deviation and range; categorical data as number and percentage.

This study includes only women with successful VBAC, not all women who attempted TOLAC. Women whose TOLAC ended in intrapartum cesarean delivery are therefore not represented. For this reason, TOLAC success rates were not compared between BMI groups, and the effect of BMI on TOLAC outcomes was not assessed.

3. RESULTS

Among the 118 women with documented BMI, the mean value was $28.3 \pm 6.6 \text{ kg/m}^2$, with a wide range from 19.0 to 64.0 kg/m^2 . Only 43 women (36.4%) were in the normal-weight category. Thirty-seven (31.4%) had overweight and 38 (32.2%) had obesity. Therefore, women with BMI $\geq 25 \text{ kg/m}^2$ accounted for 63.6% (75/118) of all successful VBAC cases with available BMI data.

Table 1. Distribution of successful VBAC cases according to maternal BMI

BMI category	n	%
Normal weight ($<25 \text{ kg/m}^2$)	43	36.4
Overweight ($25.0\text{--}29.9 \text{ kg/m}^2$)	37	31.4
Obesity ($\geq 30 \text{ kg/m}^2$)	38	32.2
Overweight + obesity ($\geq 25 \text{ kg/m}^2$)	75	63.6

Source: authors' research

The obese subgroup was not limited to mild obesity. Of the 38 women with BMI $\geq 30 \text{ kg/m}^2$, 26 (68.4%) had class I obesity, 7 (18.4%) had class II obesity and 5 (13.2%) had class III obesity. Thus, 12 women with BMI $\geq 35 \text{ kg/m}^2$ and five with BMI $\geq 40 \text{ kg/m}^2$ achieved vaginal birth after cesarean in the observed cohort.

Table 2. Distribution of obesity classes among successful VBAC cases with BMI $\geq 30 \text{ kg/m}^2$

Obesity class	n	% within obesity group
Class I ($30.0\text{--}34.9 \text{ kg/m}^2$)	26	68.4
Class II ($35.0\text{--}39.9 \text{ kg/m}^2$)	7	18.4
Class III ($\geq 40 \text{ kg/m}^2$)	5	13.2

Source: authors' research

The distribution is notable because the cohort was defined by outcome: every woman included had already achieved VBAC. Accordingly, the finding does not indicate equal success rates across BMI groups. It demonstrates instead that elevated BMI, including severe obesity, was substantially represented among successful vaginal births after cesarean in routine tertiary-care practice.

4. DISCUSSION

The main finding of this study was that elevated BMI was common among women who achieved successful VBAC. Most women with available BMI data had a BMI $\geq 25 \text{ kg/m}^2$, almost one third had obesity, and successful vaginal birth was observed even among women with severe obesity. These findings provide an important perspective, as obesity is usually considered a negative predictor of VBAC. The association between increasing BMI and a lower probability of successful VBAC is well established. Earlier studies by Durnwald et al. and Hibbard et al. showed that VBAC success decreased as BMI increased, and BMI was later included in several prediction models. However, our study could not confirm

or challenge this association because women with failed TOLAC were not included. Instead, our findings show that elevated BMI, including severe obesity, was not uncommon among women who achieved VBAC. Recent evidence also suggests that BMI should not be considered in isolation. In the large study by Lee et al., the rate of vaginal birth after TOLAC decreased from 66.7% in women with BMI <30 kg/m² to 48.1% in women with BMI 40–69.9 kg/m² among those without a previous vaginal delivery. However, among women with a previous vaginal delivery, the corresponding rates were considerably higher: 81.4%, 74.7%, and 67.3%. These findings suggest that the effect of BMI on the probability of VBAC is strongly influenced by the woman's obstetric history. A recent Canadian population-based study showed another important finding. Women with obesity were not only less likely to achieve VBAC, but also less likely to plan or attempt TOLAC. Thus, the lower VBAC rate among women with obesity may reflect both a lower chance of successful TOLAC and a lower likelihood of attempting it.

The negative effect of high BMI on labor and delivery appears to be multifactorial. Studies have shown slower cervical dilatation, a longer first stage of labor, and a greater need for oxytocin among women with obesity. Earlier studies suggested that these differences could be related to reduced myometrial contractility. However, more recent data did not demonstrate weaker uterine contractions and suggested that slower labor progress may also be related to differences in the structure and biomechanical properties of the cervix. The use and required dose of oxytocin also tend to increase with BMI. Other factors that are more common among women with obesity, including fetal macrosomia, gestational diabetes, hypertensive disorders, and the need for labor induction, may further reduce the probability of successful VBAC. Difficulties with intrapartum fetal monitoring may also contribute to a higher rate of intrapartum cesarean delivery.

Safety remains an important consideration when counseling women with obesity about TOLAC. Jude et al. reported a higher rate of composite adverse maternal outcomes among women with obesity undergoing TOLAC compared with planned repeat cesarean delivery. Recent expert reviews emphasize that the risks associated with unsuccessful TOLAC should be balanced against the risks of repeat cesarean delivery. The FIGO recommendations published in 2025 identify BMI <30 kg/m² as a favorable factor for VBAC success but do not consider obesity an absolute contraindication to TOLAC. Therefore, the decision should not be based on BMI alone, but on the overall obstetric profile and the availability of appropriate intrapartum monitoring and emergency cesarean delivery.

Our cohort illustrated this point particularly well. Five women with class III obesity achieved successful VBAC. This finding does not mean that TOLAC has a high success rate or is equally safe in all women with BMI ≥40 kg/m². However, it demonstrates the limitations of using a specific BMI threshold as a stand-alone criterion for patient selection. Previous vaginal birth, the indication for the previous cesarean delivery, cervical status, spontaneous onset of labor, fetal weight, maternal comorbidities, and the resources of the maternity unit may all influence the probability of successful VBAC.

The main limitation of this study was its design. The database included only women who achieved successful VBAC and did not include all women who attempted TOLAC. Therefore, BMI-specific success rates, the risk of failed TOLAC, and the association between BMI and uterine rupture could not be calculated. In addition, BMI data were unavailable for 31 of the 149 women. The results should therefore be interpreted as a description of the BMI distribution among women who achieved VBAC rather than as an assessment of the probability of successful TOLAC.

5. CONCLUSION

Women with elevated BMI constituted a substantial proportion of successful VBAC deliveries in this 9-year tertiary-center series. Almost two thirds of women with documented BMI had overweight or obesity, and successful VBAC occurred in all obesity classes, including class III. These findings do not contradict the lower probability of VBAC associated with increasing BMI, but show that successful VBAC can occur even in women with severe obesity. Therefore, BMI should be considered together with other obstetric factors when counseling women about TOLAC, rather than being used alone as a reason to exclude TOLAC.

REFERENCES

- Barnea, E. R., Ramasauskaite, D., Ubom, A. E., et al. (2025). FIGO good practice recommendations for vaginal birth after cesarean section. *International Journal of Gynecology & Obstetrics*, 171(1), 17–31.
- Bashirudin, S. B., Omar, S. Z., Gan, F., Hamdan, M., & Tan, P. C. (2023). Induction of labor after one previous cesarean: Predictors of vaginal birth. *European Journal of Obstetrics & Gynecology and Reproductive Biology*: X, 20, 100249. <https://doi.org/10.1016/j.eurox.2023.100249>
- Deng, B., Li, Y., Chen, J. Y., Guo, J., Tan, J., Yang, Y., & Liu, N. (2022). Prediction models of vaginal birth after cesarean delivery: A systematic review. *International Journal of Nursing Studies*, 135, 104359. <https://doi.org/10.1016/j.ijnurstu.2022.104359>
- Deshmukh, U., Denoble, A. E., & Son, M. (2024). Trial of labor after cesarean, vaginal birth after cesarean, and the risk of uterine rupture: An expert review. *American Journal of Obstetrics and Gynecology*, 230(3S), S783–S803.
- Durnwald, C. P., Ehrenberg, H. M., & Mercer, B. M. (2004). The impact of maternal obesity and weight gain on vaginal birth after cesarean section success. *American Journal of Obstetrics and Gynecology*, 191(3), 954–957. <https://doi.org/10.1016/j.ajog.2004.05.051>
- Gray, E., Brown, M. M., Woolcott, C. G., Fahey, J., Allen, V. M., Scott, H. M., Lisonkova, S., & Mehrabadi, A. (2026). Disparities in planned and successful vaginal delivery after a cesarean delivery by body mass index: A population-based cohort study. *AJOG Global Reports*, 6(1), 100595.
- Grobman, W. A., Sandoval, G., Rice, M. M., et al. (2021). Prediction of vaginal birth after cesarean delivery in term gestations: A calculator without race and ethnicity. *American Journal of Obstetrics and Gynecology*, 225(6), 664.e1–664.e7. <https://doi.org/10.1016/j.ajog.2021.05.021>
- Hautakangas, T., Uotila, J., Kontiainen, J., Huhtala, H., & Palomäki, O. (2022). Impact of obesity on uterine contractile activity during labour: A blinded analysis of a randomised controlled trial cohort. *BJOG: An International Journal of Obstetrics & Gynaecology*, 129(10), 1790–1797. <https://doi.org/10.1111/1471-0528.17128>
- Hibbard, J. U., Gilbert, S., Landon, M. B., et al. (2006). Trial of labor or repeat cesarean delivery in women with morbid obesity and previous cesarean delivery. *Obstetrics & Gynecology*, 108(1), 125–133. <https://doi.org/10.1097/01.AOG.0000223871.69852.31>
- Jévitt, C. M. (2020). Management of labor and delivery to reduce risk for cesarean birth in women with obesity. *Journal of Midwifery & Women's Health*, 65(3), 391–397.
- Jude, G., Fain, A., Raker, C., Rubenstein, S., Bicocca, M., Wagner, S., & Gupta, M. (2024). The association between trial of labor after cesarean in obese patients and adverse maternal outcomes. *Archives of Gynecology and Obstetrics*, 309(6), 2421–2426.
- Lee, M., Almeida, T. C., Saade, G., & Kawakita, T. (2024). Trial of labor versus repeat cesarean delivery in individuals with morbid obesity after previous cesarean delivery. *American Journal of Perinatology*, 41(14), 1980–1989.
- Norman, S. M., Tuuli, M. G., Odibo, A. O., Caughey, A. B., Roehl, K. A., & Cahill, A. G. (2012). The effects of obesity on the first stage of labor. *Obstetrics & Gynecology*, 120(1), 130–135.
- Vahratian, A., Zhang, J., Troendle, J. F., Savitz, D. A., & Siega-Riz, A. M. (2004). Maternal prepregnancy overweight and obesity and the pattern of labor progression in term nulliparous women. *Obstetrics & Gynecology*, 104(5 Pt 1), 943–951.
- Wu, Y., Kataria, Y., Wang, Z., Ming, W. K., & Ellervik, C. (2019). Factors associated with successful vaginal birth after a cesarean section: A systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, 19, 360.
- Zhang, J., Bricker, L., Wray, S., & Quenby, S. (2007). Poor uterine contractility in obese women. *BJOG: An International Journal of Obstetrics & Gynaecology*, 114(3), 343–348.

ANTIBACTERIAL ACTIVITY OF A NOVEL GREEN-SYNTHESIZED NANO-SILVER FLUORIDE AGAINST STREPTOCOCCUS MUTANS: A COMPARATIVE IN VITRO STUDY

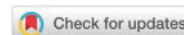
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Abstract: Background: Silver diamine fluoride is an effective non-invasive material for caries arrest, but its clinical use is limited due to the black discoloration it causes. Green synthesis of silver nanoparticles has emerged as a promising non-discoloring alternative with antimicrobial potential. Purpose: To evaluate the antibacterial activity of a novel green-synthesized nano-silver fluoride prepared with *Camellia sinensis* extract and compare its efficacy with silver diamine fluoride and silver diamine fluoride combined with potassium iodide against *Streptococcus mutans*. Methodology: Antibacterial activity was assessed using the agar well diffusion method. Three concentrations (100%, 10% and 1%) of each material were tested and inhibition zone diameters were measured. The data were analyzed using non-parametric statistical methods with a significance level of $p < 0.05$. Results: Silver diamine fluoride demonstrated the strongest antibacterial activity at all tested concentrations. The green-synthesized nano-silver fluoride exhibited concentration-dependent antimicrobial activity. No statistically significant differences were observed between the highest concentrations of nano-silver fluoride, silver diamine fluoride and silver diamine fluoride combined with potassium iodide. Potassium iodide alone showed no antibacterial effect. Conclusions: The green-synthesized nano-silver fluoride demonstrated significant concentration-dependent antibacterial activity against *Streptococcus mutans*. Although its inhibition zones were smaller than those of silver diamine fluoride, its activity at higher concentrations suggests promising potential as an alternative silver-based agent for non-operative caries management.

Keywords: silver diamine fluoride; nano-silver fluoride; green synthesis; *Streptococcus mutans*; antibacterial activity

Field: Medical Sciences and Health

1. INTRODUCTION

Silver diamine fluoride (SDF) is a well-established non-invasive material for arresting dental caries. First introduced in Japan by Nishino and Yamaga, it has regained considerable attention in recent years because of its proven clinical effectiveness. (Gao et al., 2021) Its therapeutic action is based on three principal mechanisms: remineralization, antiproteolytic and antibacterial effects. (Greenwall-Cohen et al., 2020) However, the permanent black discoloration associated with SDF remains its major clinical limitation. (Nguyen et al., 2017)

The application of potassium iodide (KI) following SDF has been proposed to reduce tooth discoloration. (Costa RO et al., 2013) Nevertheless, this effect is only temporary and the reduction of free silver ions may compromise the antibacterial efficacy of the material. (Sayed et al., 2018)

Silver nanoparticles have emerged as a promising alternative because of their high surface-area-to-volume ratio, enhanced antimicrobial activity and chemical stability. (Yin et al., 2020) Unlike SDF, materials that contain nanoparticles like nano-silver fluoride (NSF) do not cause tooth discoloration. (Liao et al., 2019)

Furthermore, green synthesis using plant extracts provides an environmentally friendly approach while avoiding toxic reducing agents. Therefore, the aim of the present study was to evaluate the antibacterial activity of a novel green-synthesized nano-silver fluoride against *Streptococcus mutans* and compare it with silver diamine fluoride and silver diamine fluoride combined with potassium iodide.

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2. MATERIALS AND METHODS

Bacterial strain

- *Streptococcus mutans* (reference strain ATCC® 35668™, Ridacom Ltd.). The strains were provided in the form of lyophilized cultures from a microbiological collection and stored at -20°C until the time of experimental work.

Culture media

- Modified LAPTg10 - broth

Composition (g/dm³): peptone - 15; yeast extract - 10; tryptone - 10; glucose - 10; Tween 80 - 1cm³/dm³; pH=6.6-6.8. The medium was sterilized for 20 min at 121°C.

- Modified LAPTg10 - agar

Composition (g/dm³): peptone - 15; yeast extract - 10; tryptone - 10; glucose - 10; Tween 80 - 1cm³/dm³; agar - 15; pH=6.6-6.8. The medium was sterilized for 20 min at 121°C.

- Brain Heart Infusion (BHI) - broth

Composition (g/dm³): Infusion from Brain Heart - 6.0; peptic digest of animal tissue (peptone a) - 6.0; Pancreatic Digest of Gelatin (Peptone G) - 14.5; NaCl - 5.0; glucose (dextrose) - 3.0; Na₂HPO₄ - 2.5. pH 7.4 ± 0.2. Sterilized for 15 min at 121°C.

Chemicals and solutions:

- Saline solution

Composition (g/dm³): NaCl - 5. Sterilized for 20min at 121°C.

- Ultrapure water - Ultrapure water - DNASE/RNASE - Free (Canvax Reagents SL)

Composition: water, deionized, reverse osmosis, ultraviolet light treatment, distillation and 0.1µm membrane filtration; pH - 5.4 - 7.0 at 25° C.

- Riva Star - capsules kit (SDI Dental Limited, Australia)

Composition: 38% silver diamine fluoride (SDF) - Ag - 253,870 ppm (25.3%), F - 44,800 ppm (4.48%), NH₃ - 8%, KI - 58.3%; pH - about 10.

- Nano-silver fluoride (NSF)

Composition: AgNO₃ - 0.01 mol/L, K₂CO₃, NaF - 0.01 g/mL, aqueous extract of *Camellia sinensis*; pH - 9.0. The NSF formulation was synthesized using a previously established green synthesis protocol. (Palankalieva et al., 2025)

Rehydration and cultivation of bacterial strain

The lyophilized *S. mutans* strain was rehydrated according to the manufacturer's instructions by adding 1 mL of sterile BHI broth to the ampoule. To achieve the required standardized cell concentration, an optimized cultivation protocol was applied. Briefly, 0.5 mL of the rehydrated suspension was transferred into 5 mL of modified LAPTg10 broth supplemented with 0.2 mL of 20% glucose. The cultures were incubated under anaerobic conditions using an anaerostat system (Anaerocult®, MERCK) at 37°C for at least 48 hours.

Preparation of bacterial inoculum

Bacterial suspensions were prepared to a concentration equivalent to 0.5 McFarland standard (approximately 1×10⁸ CFU/mL).

Determination of antimicrobial activity

The antimicrobial activity of the tested agents was evaluated using the agar well diffusion method. Petri dishes containing modified LAPTg10 agar were inoculated with the prepared bacterial suspensions. After agar solidification, wells with a diameter of 6 mm were aseptically created and evenly distributed to avoid overlapping inhibition zones.

Experimental groups and test solutions

The antimicrobial activity of the following agents was studied: silver diamine fluoride (SDF), silver diamine fluoride in combination with potassium iodide (SDF+KI), green-synthesized nano-silver fluoride with *Camellia sinensis* extract (NSF) and potassium iodide (KI). The test substances were diluted with ultrapure water in 3 decreasing concentrations - 100%, 10% and 1%. The created groups for each concentration of each compound are represented in Table 1.

Table 1. Experimental groups and concentrations of the tested silver compounds.

Group	Test agent	Concentration
Gr-NSF_100	Nano-silver fluoride (NSF)	100%
Gr-NSF_10	Nano-silver fluoride (NSF)	10%
Gr-NSF_1	Nano-silver fluoride (NSF)	1%
Gr-SDF_100	Silver diamine fluoride (SDF)	100%
Gr-SDF_10	Silver diamine fluoride (SDF)	10%
Gr-SDF_1	Silver diamine fluoride (SDF)	1%
Gr-RS_100	Silver diamine fluoride and potassium iodide (SDF+KI)	100%
Gr-RS_10	Silver diamine fluoride and potassium iodide (SDF+KI)	10%
Gr-RS_1	Silver diamine fluoride and potassium iodide (SDF+KI)	1%
Gr-KI_100	Potassium iodide (KI)	100%
Gr-KI_10	Potassium iodide (KI)	10%
Gr-KI_1	Potassium iodide (KI)	1%

Source: Authors' own research

The designation "100%" refers to the undiluted primary solution of the respective compound - 38% silver diamine fluoride and 5% nano-silver fluoride.

A volume of 0.06 mL from each test solution was introduced into the wells using a sterile micropipette. Ultrapure water was used as a negative control.

Incubation and measurement

The plates were incubated at 37°C under anaerobic conditions. Antimicrobial activity was assessed by measuring the diameter of the inhibition zones (in mm). All experiments were performed in quadruplicate.

Statistical methods

For data processing and graphical presentation, the IBM SPSS Statistics for Windows program (version 30.0, 2024) was used. The normality of the distribution of numerical variables (zones of inhibition in mm) was checked with the Shapiro-Wilk test. The variables were described with medians (Median) and interquartile ranges (IQR). For intergroup analysis Kruskal-Wallis test, followed by Mann-Whitney U test and Dunn test with Bonferroni correction were applied. All tests were performed at a significance level of $p < 0.05$.

3. RESULTS

After carrying out the agar-diffusion method for determining antibacterial activity, the zone of inhibition was observed. The measurement of its diameter in mm correlated with the antimicrobial activity of the tested solution.

The Shapiro-Wilk test for normality of distribution showed that the values of the studied groups were not normally distributed ($p < 0.05$). The Kruskal-Wallis test showed a statistically significant difference between the groups ($p < 0.05$). To determine between which groups a statistically significant difference was observed, Dunn's multiple comparisons test with Bonferroni correction was used.

Table 2 summarizes the medians (Median), interquartile ranges (IQR), as well as the results of the comparative statistical analysis.

The median values of the inhibition zones of *S. mutans* show that the highest antimicrobial activity is possessed by all concentrations of silver diamine fluoride - Gr-SDF_100 (Median - 40, IQR - 0), Gr-SDF_10 (Median - 40, IQR - 0), Gr-SDF_1 (Median - 40, IQR - 0), as well as the 100% solution of silver diamine fluoride with potassium iodide - Gr-RS_100 (Median - 40, IQR - 0). Laboratory-synthesized nano-silver fluoride demonstrated smaller diameter zones of inhibition at concentrations of 100% and 10% (Gr-NSF_100 - Median - 20, IQR - 0; Gr-NSF_10 - Median - 10, IQR - 0), but there was no statistically significant difference between these two groups and the groups of silver diamine fluoride and the 100- and 10-percent solutions of SDF+KI ($p > 0.05$). At 1% of the nano-silver fluoride solution, no bacterial inhibition was observed (Gr-NSF_1 - Median - 0, IQR - 0). All concentrations of potassium iodide also had no antibacterial effect against strains of *S. mutans* (Gr-KI_100 - Median - 0, IQR - 0; Gr-KI_10 - Median - 0, IQR - 0; Gr-KI_1 - Median - 0, IQR - 0).

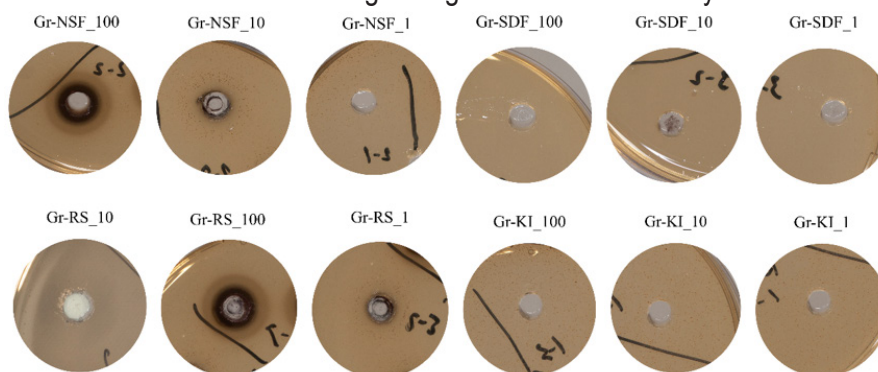
Table 2. Comparison of the inhibition zone diameters (mm) against *S. mutans* among the tested groups.

	Gr-NSF_100 (1) Median (IQR)	Gr-NSF_10 (2) Median (IQR)	Gr-NSF_1 (3) Median (IQR)	Gr-SDF_100 (4) Median (IQR)	Gr-SDF_10 (5) Median (IQR)	Gr-SDF_1 (6) Median (IQR)	Gr-RS_100 (7) Median (IQR)	Gr-RS_10 (8) Median (IQR)	Gr-RS_1 (9) Median (IQR)	Gr-KI_100 (10) Median (IQR)	Gr-KI_10 (11) Median (IQR)	Gr-KI_1 (12) Median (IQR)	Dunn's multiple comparisons test with Bonferroni correction
<i>S. mutans</i>	20 (0)	10 (0)	0 (0)	40 (0)	40 (0)	40 (0)	40 (0)	21,50 (5)	10,50 (1)	0 (0)	0 (0)	0 (0)	3↔4: $p < 0.05$ 3↔5: $p < 0.05$ 3↔6: $p < 0.05$ 4↔10: $p < 0.05$ 4↔11: $p < 0.05$ 4↔12: $p < 0.05$ 5↔10: $p < 0.05$ 5↔11: $p < 0.05$ 5↔12: $p < 0.05$ 6↔10: $p < 0.05$ 6↔11: $p < 0.05$ 6↔12: $p < 0.05$ 7↔10: $p < 0.05$ 7↔11: $p < 0.05$ 7↔12: $p < 0.05$

Source: Authors' own research

Figure 1 shows the inhibitory zones around each tested substance.

Figure 1. Representative inhibition zones produced by the tested silver compounds against *S. mutans* following the agar well diffusion assay



Source: Authors' own research

In Gr-NSF_100, a well-defined inhibitory zone with sharp and defined borders was observed. In Gr-NSF_10, such zone was also observed, but in a smaller size. This confirms the inhibitory effect of these two concentrations against *S. mutans*. In contrast, Gr-NSF_1 did not demonstrate an antibacterial effect, since there was no inhibitory halo around the well in the petri dish.

All groups of silver diamine fluoride - Gr-SDF_100, Gr-SDF_10 and Gr-SDF_1, showed wide homogeneous zones without bacterial growth, which is an indicator of the strong antibacterial effect at all concentrations of this compound.

In the commercial product Riva star, a decrease in the diameter of the inhibitory zone was observed with a decrease in the concentration of the solutions. Gr-RS_100 showed the widest halo, which decreased with Gr-RS_10 and was the smallest with Gr-RS_1. At all three concentrations, single streptococci were observed in the inhibitory halo.

At all concentrations of potassium iodide, no zone of inhibition was observed and bacterial growth was visible to the edge of all wells containing the different concentrations of this solution.

4. DISCUSSIONS

A dose-dependent antibacterial effect was observed for all tested silver compounds except SDF, with higher concentrations of SDF+KI and NSF producing larger inhibition zones. This suggests that the antimicrobial activity of SDF+KI and the laboratory-synthesized NSF is closely related to the availability of free silver ions in the solution. Silver ions are well known for their broad-spectrum antibacterial activity, while *S. mutans* is one of the primary microorganisms involved in dental caries development. (Lansdown, 2006) The consistently strong antibacterial activity of SDF observed in the present study is in agreement

with previous reports. (Wu et al., 2019)

The largest inhibition zones were produced by SDF, whereas lower concentrations of SDF+KI showed reduced antibacterial activity. Similar findings were reported by Alvarez-Marín et al. (2024), who also observed bacterial colonies within the inhibition zones of SDF+KI. This reduction is likely explained by the formation of insoluble silver iodide (AgI), which decreases the concentration of free silver ions responsible for the antibacterial effect. (Sayed et al., 2018)

Green-synthesized silver nanoparticles have attracted increasing attention because of their antimicrobial potential. Previous studies demonstrated that silver nanoparticles effectively inhibit *S. mutans* growth and biofilm formation. For example, Kumar et al. (2018) evaluated the antibacterial activity of green-synthesized silver nanoparticles prepared using *Viola serpens* leaf extract as a reducing and stabilizing agent. Using an agar diffusion assay, the authors demonstrated significant antibacterial activity against *S. mutans* and confirmed the potential of silver nanoparticles to inhibit biofilm formation.

However, to the best of our knowledge, there are no studies that have analyzed the antimicrobial effect of green-synthesized nano-silver fluoride prepared with *Camellia sinensis* (green tea) extract against *S. mutans*.

Silver nanoparticles tested alone and without the addition of other components, have been shown to successfully inhibit the growth of cariogenic bacteria. (Pérez-Díaz et al., 2015) The antimicrobial activity of fluoride is also well established. (Soleimani et al., 2021) Green tea possesses antibacterial properties against cariogenic bacteria that support its potential as an effective reducing and stabilizing agent in the synthesis of NSF. (Anita et al., 2015) In this context, the synergistic action of silver nanoparticles, fluoride and green tea extract could potentially enhance the antimicrobial efficacy and justify the application of such a combination for the prevention and stabilization of caries lesions.

According to the available literature, no comparative studies have been published comparing the antibacterial effect of SDF, SDF+KI and green-synthesized NSF against cariogenic bacteria.

The present findings are consistent with those of Karaduran et al. (2024), who reported greater antibacterial activity of SDF and SDF+KI than NSF. In contrast, Sharma et al. (2023) found NSF to be the most effective silver-based material. Such discrepancies are likely related to differences in NSF synthesis protocols, which can substantially influence the nanoparticle characteristics and biological activity. (Chahardoli et al., 2022)

The limitations of the study should be taken into consideration. Although the agar diffusion method is a standard approach for evaluating antibacterial activity, it cannot fully reproduce the complexity of oral biofilms and in vivo conditions. (Sissons CH et al., 1991) Therefore, these findings should be considered preliminary and further laboratory and clinical studies are required to confirm the antibacterial efficacy of green-synthesized nano-silver fluoride.

5. CONCLUSIONS

The novel nano-silver fluoride demonstrated promising antibacterial activity against *Streptococcus mutans* and may represent a sustainable alternative for non-operative caries management. Further in vitro and in vivo studies are needed to confirm its long-term antimicrobial performance and clinical applicability.

REFERENCES

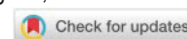
- Alvarez-Marín, C. A., Robles-Bermeo, N. L., Hassan Moustafa, W. H., & Medina-Solís, C. E. (2024). Antibacterial effects of silver diamine fluoride with and without potassium iodide against *Streptococcus mutans*. *Contemporary Clinical Dentistry*, 15(1), 22-26. https://doi.org/10.4103/ccd.ccd_393_23
- Anita, P., Balan, I. N., Ethiraj, S., Madan Kumar, P., & Sivasamy, S. (2015). In vitro antibacterial activity of *Camellia sinensis* extract against cariogenic microorganisms. *Journal of Basic and Clinical Pharmacy*, 6(1), 35-39. <https://doi.org/10.4103/0976-0105.145777>
- Chahardoli, A., Safaei, M., Mobarakeh, M. S., Fallahnia, N., Fatehi, B., Imani, M. M., & Golshah, A. (2022). Optimum green synthesis of silver nanoparticles with the highest antibacterial activity against *Streptococcus mutans* biofilm. *Journal of Nanomaterials*, 2022, Article 6261006. <https://doi.org/10.1155/2022/6261006>
- Costa, R. O., Macedo, P. M., Carvalhal, A., & Bernardes-Engemann, A. R. (2013). Use of potassium iodide in dermatology: Updates on an old drug. *Anais Brasileiros de Dermatologia*, 88(3), 396-402.
- Gao, S. S., Amarquaye, G., Arrow, P., Bansal, K., Bedi, R., Campus, G., Chen, K. J., Chibinski, A. C. R., Chinzorig, T., Crystal, Y. O., Duangthip, D., Ferri, M. L., Folayan, M. O., Garidkhuu, A., Hamama, H. H., Jirattanasopha, V., Kemoli, A., Leal, S. C., Leelataweewud, P., ... Chu, C. H. (2021). Global oral health policies and guidelines: Using silver diamine fluoride for caries control. *Frontiers in Oral Health*, 2, 685557. <https://doi.org/10.3389/froh.2021.685557>
- Greenwall-Cohen, J., Greenwall, L., & Barry, S. (2020). Silver diamine fluoride—An overview of the literature and current clinical techniques. *British Dental Journal*, 228(11), 831-838. <https://doi.org/10.1038/s41415-020-1641-4>
- Karaduran, B., Çelik, S., Uğuncü, M. Y., Topçuoğlu, N., Gök, M. K., & Koruyucu, M. (2024). Antibacterial effects of silver diamine

- fluoride, potassium iodide and nanosilver fluoride on dual-species biofilm. *Journal of Dentistry*, 147, 105097. <https://doi.org/10.1016/j.jdent.2024.105097>
- Kumar, A., Majumdar, R. S., & Dhewa, T. (2018). In vitro efficacy of biosynthesized AgNPs against *Streptococcus mutans* causing dental plaque formation. *Journal of Scientific & Industrial Research*, 77(4), 225-228.
- Lansdown, A. B. G. (2006). Silver in health care: Antimicrobial effects and safety in use. *Current Problems in Dermatology*, 33, 17-34. <https://doi.org/10.1159/000093928>
- Liao, C., Li, Y., & Tjong, S. C. (2019). Bactericidal and cytotoxic properties of silver nanoparticles. *International Journal of Molecular Sciences*, 20(2), 449. <https://doi.org/10.3390/ijms20020449>
- Nguyen, V., Neill, C., Felsenfeld, J., & Primus, C. (2017). Potassium iodide: The solution to silver diamine fluoride discoloration? *Advances in Dentistry & Oral Health*, 5(1), 555565. <https://doi.org/10.19080/ADOH.2017.05.555565>
- Palankaliev, A., Katsarov, P., & Belcheva, A. (2025). Green-synthesized nano-silver fluoride for remineralization of enamel lesions in primary teeth: A comparative in vitro study with SDF and SDF/KI. *Dentistry Journal*, 13(7), 331. <https://doi.org/10.3390/dj13070331>
- Pérez-Díaz, M. A., Boegli, L., James, G., Velasquillo, C., Sánchez-Sánchez, R., Martínez-Martínez, R.-E., Martínez-Castañón, G. A., & Martínez-Gutiérrez, F. (2015). Silver nanoparticles with antimicrobial activities against *Streptococcus mutans* and their cytotoxic effect. *Materials Science and Engineering: C*, 55, 360-366. <https://doi.org/10.1016/j.msec.2015.05.036>
- Sayed, M., Matsui, N., Hiraishi, N., Nikaido, T., Burrow, M. F., & Tagami, J. (2018). Effect of glutathione bio-molecule on tooth discoloration associated with silver diamine fluoride. *International Journal of Molecular Sciences*, 19(5), 1322. <https://doi.org/10.3390/ijms19051322>
- Sharma, P., Dhawan, P., Rajpal, S. K., & Sharma, R. (2023). A comparison of antimicrobial efficacy of silver-based preventive restorations (silver nitrate, silver diamine fluoride, and silver nanoparticles) against *Streptococcus mutans* monospecies biofilm model. *International Journal of Clinical Pediatric Dentistry*, 16(Suppl. 1), S13-S19. <https://doi.org/10.5005/jp-journals-10005-2575>
- Sissons, C. H., Cutress, T. W., Hoffman, M. P., & Wakefield, J. S. (1991). A multi-station dental plaque microcosm (artificial mouth) for the study of plaque growth, metabolism, pH, and mineralization. *Journal of Dental Research*, 70(11), 1409-1416.
- Soleimani, B., Goli, H., Naranjian, M., Mousavi, S. J., & Nahvi, A. (2021). Comparison of antimicrobial activity of fluoride varnishes against *Streptococcus mutans* and *Lactobacillus acidophilus*: An in vitro study. *Iranian Journal of Pediatrics*, 31(3), e111422. <https://doi.org/10.5812/ijp.111422>
- Wu, L., Gareiss, S. K., Morrow, B. R., Babu, J. P., Hottel, T., Garcia-Godoy, F., Li, F., & Hong, L. (2019). Antibacterial properties of silver-loaded gelatin sponges prepared with silver diamine fluoride. *American Journal of Dentistry*, 32(6), 276-280.
- Yin, I. X., Zhang, J., Zhao, I. S., Mei, M. L., Li, Q., & Chu, C. H. (2020). The antibacterial mechanism of silver nanoparticles and its application in dentistry. *International Journal of Nanomedicine*, 15, 2555-2562. <https://doi.org/10.2147/IJN.S246764>

CEPHALOMETRIC ASSESSMENT OF TRANSVERSE CHANGES IN FRONTO-ORBITAL AND ZYGOMATIC WIDTH BEFORE AND AFTER RAPID MAXILLARY EXPANSION IN PATIENTS WITH UNILATERAL POSTERIOR CROSSBITE

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Abstract: Rapid maxillary expansion (RME) is commonly used for the correction of transverse maxillary deficiency associated with posterior crossbite. Although its primary effect is directed toward the maxilla and the midpalatal suture, expansion forces may also induce measurable changes in the circummaxillary and zygomatic regions. The aim of the present study was to evaluate transverse changes in the zygomatic and frontozygomatic regions following RME in patients with unilateral posterior crossbite using posteroanterior cephalometric measurements. A three-year prospective clinical study included 47 patients with clinically diagnosed unilateral posterior crossbite and incomplete craniofacial growth, all treated with a tooth-borne Hyrax rapid maxillary expander. The sample consisted of 18 males (38.3%) and 29 females (61.7%), with a mean age of 16.59 ± 1.89 years. Digital posteroanterior cephalograms were obtained at the diagnostic stage and immediately before removal of the RME appliance. Zygomatic width was assessed as the linear distance between the bilateral Za landmarks (Za–Za), while the transverse dimension of the frontozygomatic region was evaluated as the distance between the bilateral Zmf landmarks (Zmf–Zmf). Pre- and post-treatment values were compared using a paired-samples t-test, and the relationship between the changes in the two parameters was assessed by Pearson correlation analysis. Mean Za–Za increased from 112.91 ± 12.52 mm before RME to 114.42 ± 12.43 mm after treatment, corresponding to a mean increase of 1.51 mm ($p < 0.001$). Mean Zmf–Zmf increased from 85.71 ± 10.73 mm to 86.62 ± 10.98 mm, with a mean change of 0.91 mm ($p < 0.001$). A significant positive correlation was found between the changes in Za–Za and Zmf–Zmf ($r = 0.582$, $p < 0.001$). The findings indicate that tooth-borne RME with a Hyrax appliance in patients with unilateral posterior crossbite is associated with statistically significant transverse changes not only in zygomatic width but also in the frontozygomatic region. These results suggest that the effects of conventional RME may extend beyond the immediate maxillary structures and may involve measurable, although limited, adaptation of more lateral and cranially located components of the midfacial complex.

Keywords: rapid maxillary expansion, unilateral posterior crossbite, posteroanterior cephalometry, zygomatic width, frontozygomatic region.

Field: Medical Sciences and Health

1. INTRODUCTION

Transverse maxillary deficiency is a common morphological basis of posterior crossbite and may be associated with a unilateral clinical presentation. In cases of skeletal maxillary constriction, rapid maxillary expansion (RME) aims to increase the transverse dimensions of the maxilla through an orthopedic effect on the midpalatal suture (Kumar, Gurunathan, Muruganandham, & Sharma, 2011).

Various appliances are used for RME, among which the Hyrax is one of the most widely used tooth-borne expanders. Upon activation, orthopedic forces are transmitted through the anchor teeth and alveolar structures to the maxillary complex; when a sufficient skeletal response is achieved, separation of the midpalatal suture and an increase in the basal width of the maxilla may occur (Kumar, Gurunathan, Muruganandham, & Sharma, 2011; Proffit et al., 2019). However, the skeletal and dentoalveolar components of expansion vary according to age, skeletal maturity, and type of anchorage. Data in older adolescents indicate that conventional tooth-borne RME may also produce measurable skeletal changes (Gokturk&Yavan, 2024). The classical concept of RME assumes that the application of high forces over a short period results not only in dental expansion but also in an orthopedic response of the maxilla and its associated structures (Leonardi et al., 2011; Ok, Kayalar & Sadry, 2023). CBCT studies show that the increase in transverse dimensions is greatest at the level of the dental arch and decreases toward the basal bone. The biological effect of RME is not limited to immediate separation of the midpalatal suture and may be accompanied by adaptation of other structures within the circummaxillary complex

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(Ahmida et al., 2023; Leonardi et al., 2011). Ghoneima et al. reported a significant increase in the widths of the intermaxillary, internasal, maxillonasal, frontomaxillary, and frontonasal sutures after RME, whereas changes in the frontozygomatic, zygomaticomaxillary, zygomaticotemporal, and pterygomaxillary sutures did not reach statistical significance (Ghoneima et al., 2011).

Of particular interest in this context is the zygomatic complex, which forms an important part of the lateral support of the midface. The three-dimensional study by Ok et al. showed that RME is followed by changes in the position of the zygomatic bone, including lateral displacement and external rotation, with the center of rotational change located near the superior part of the frontozygomatic region (Ok, Kayalar & Sadry, 2023). This suggests that the response of the zygomatic complex cannot be described solely by a change in the width of an individual suture, but should be considered a spatial skeletal adaptation. The literature regarding the magnitude and nature of changes in the frontozygomatic region after maxillary expansion is not entirely consistent. Differences among studies may be related to patient age and skeletal maturity, expander design and anchorage, as well as the methods and timing of imaging assessment (Ghoneima et al., 2011; Gokturk&Yavan, 2024; Sayar& Kılınc, 2019). Direct CBCT measurement of the width of the zygomaticofrontal suture is not equivalent to determining the transverse distance between bilaterally located frontozygomatic landmarks. The former characterizes a local sutural change, whereas the latter may reflect the combined effect of lateral displacement and rotation of the zygomatic complex (Ok, Kayalar & Sadry, 2023). Ahmida et al. reported immediate changes in some cranial and circummaxillary sutures after conventional RPE and MARPE; however, the response was not uniform across all investigated structures, and many of the differences outside the midpalatal suture were not maintained at long-term follow-up (Ahmida et al., 2023). In contrast, three-dimensional data on the zygomatic bone indicate that spatial changes of the complex may be measurable even when direct sutural expansion is limited (Ok, Kayalar & Sadry, 2023). Similar rotational and transverse changes of the midface have also been described with skeletal-borne expansion, although these findings are not directly equivalent to the effects of conventional tooth-borne RME (Alan, Kaya& Sancak, 2025).

Therefore, assessment of the interzygomatic and frontozygomatic transverse dimensions may provide additional information on the extent of the orthopedic effect beyond the immediate maxillary region. The aim of the present study was to assess, by means of posteroanterior cephalometry, changes in zygomatic and frontozygomatic width after rapid maxillary expansion using the Za-Za and Zmf-Zmf parameters.

2. MATERIALS AND METHODS

A three-year prospective clinical study was conducted using the results of posteroanterior (PA) cephalometric measurements in 47 patients with clinically confirmed unilateral posterior crossbite and incomplete growth (late adolescence). All patients were treated with a Hyrax appliance for maxillary expansion. The study sample comprised 18 males (38.3%) and 29 females (61.7%). The mean age was 16.59 ± 1.89 years, with a median age of 17 years.

Patients with craniofacial syndromes, cleft lip and/or palate, previous orthopedic or orthodontic expansion, previous orthognathic surgery, significant facial trauma, or radiographs with inadequate head positioning or insufficient landmark visibility were excluded.

The Hyrax rapid maxillary expander used in our study consisted of a 9–13 mm Leone expansion screw (Leone, Florence, Italy), with individually bent arms extending along the lingual surfaces of the posterior teeth and four bands on the anchor teeth (first premolars and first molars), with factory-soldered buccal tubes and free palatal surfaces. The bands were soldered to the rigid stainless-steel arms of the expansion screw. (Fig. 1)

Fig. 1: Hyrax appliance



Source: Created by the authors

During the initial 3–4 days, an intensive activation protocol was applied: $\frac{1}{4}$ turn = 0.25 mm every 6 hours, resulting in approximately 1 mm of expansion per day. After the appearance of clinical signs of midpalatal suture disjunction, activation was reduced to $\frac{1}{4}$ turn every 12 hours. The duration of active expansion was determined individually according to the required transverse correction and the achievement of adequate occlusal compensation (Stoilova- Todorova, 2018).

Digital posteroanterior cephalograms were obtained and analyzed for all patients at the diagnostic stage and immediately before removal of the RME appliance. PA cephalograms are an appropriate choice because they are sufficient for measuring the selected parameters and limit radiation exposure in accordance with the ALARA principle (Krasteva, 2019). Each patient and the patient's parents were informed about the purpose of the study and signed informed consent for the radiographic examination. The patients' legal guardians also provided consent for the use of RME as part of the orthodontic treatment and for the use of the resulting data for scientific purposes without disclosure of patient identity. Digital frontal cephalograms were obtained according to the established method of Ricketts R.M. (Ricketts, 1981). All cephalograms were traced twice by two operators in accordance with the described protocol for PA cephalometric analysis. After a period of 7 days, the measurements were repeated, and the arithmetic mean values of the investigated parameters were used to control for potential measurement errors. The initial and final PA cephalograms were traced using CorelDRAW Graphics Suite 2026 for digital tracing and graphic processing of the frontal cephalograms (Corel Corporation, 2026). The following landmarks were identified:

Zmf – zygomaticofrontal suture – its most medial aspect (left/right).

ZA – zygomatic arch – the point located at the most lateral aspect of the center of the zygomatic arch (left/right).

To assess changes in the fronto-orbital region and zygomatic width before and after RME, the following parameters were used:

Distance is in millimeters between the left and right Zmf landmarks (Zmf–Zmf).

Zygomatic width (Za–Za) – the left and right Za landmarks were connected and the linear distance was measured in millimeters (Ricketts, 1981). (Fig. 2)

Fig. 2: Measurement of zygomaticofrontal (Zmf-Zmf) and bizygomatic (ZA-ZA) width



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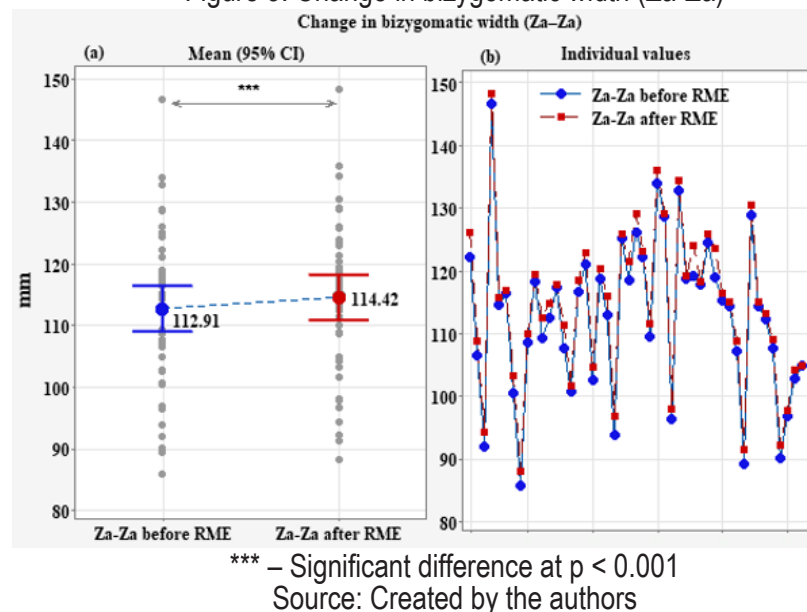
Data analysis was performed using IBM SPSS Statistics for Windows, version 28.0 (Armonk, NY: IBM Corp.).

3. RESULTS

Zygomatic width (Za–Za) and the zygomaticofrontal distance (Zmf–Zmf) showed normal distributions before and after RME. Changes in the values were analyzed using a paired-samples t-test. A significant increase was found for both measurements. Before RME, the mean zygomatic width (Za–Za) was 112.91 ± 12.52 mm and increased to 114.42 ± 12.43 mm after RME. The mean change was 1.51 mm and was statistically significant ($p < 0.001$). The mean distance between the left and right zygomaticofrontal landmarks (Zmf–Zmf) increased from 85.71 ± 10.73 mm to 86.62 ± 10.98 mm after RME, representing a significant change of 0.91 mm ($p < 0.001$).

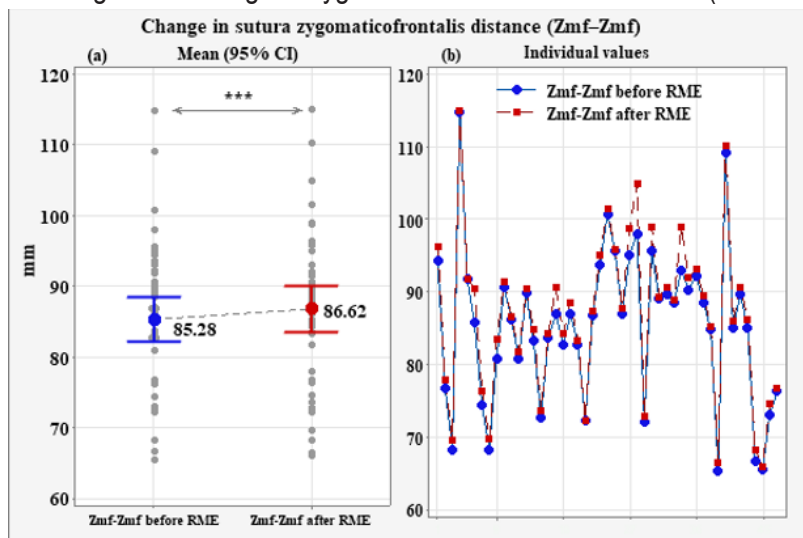
Figure 3(a) illustrates the mean values of zygomatic width (Za–Za) before and after RME. The changes in individual values show an increase in zygomatic width in all patients, with a minimum increase of 0.29 mm and a maximum increase of 2.84 mm (Figure 3b).

Figure 3: Change in bizygomatic width (Za–Za)



The mean values of the distance between the left and right zygomaticofrontal landmarks (Zmf–Zmf) before and after RME are presented in Figure 4(a). Changes in the individual values are shown in Figure 4(b). An increase was observed in all patients, with a minimum change of 0.03 mm and a maximum change of 1.80 mm.

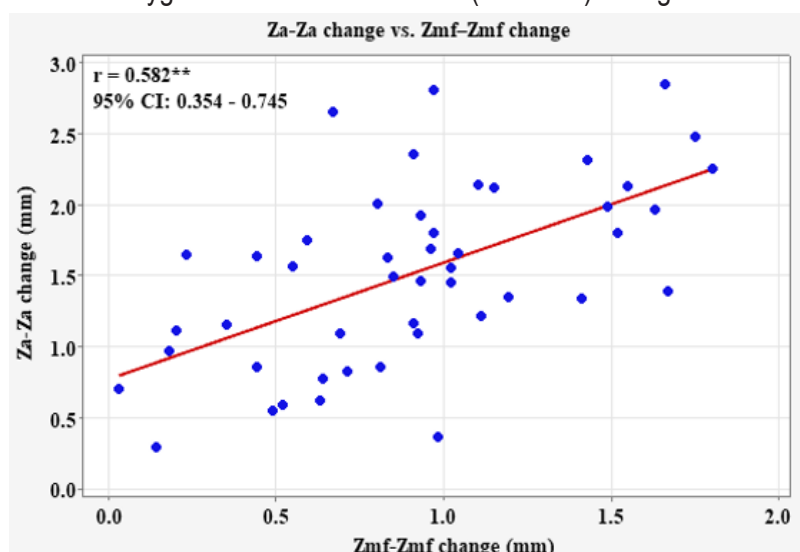
Figure 4: Change in zygomaticofrontal suture distance (Zmf-Zmf)



*** - Significant difference at $p < 0.001$
Source: Created by the authors

The relationship between the changes in the investigated transverse parameters after RME was assessed by correlation analysis using Pearson's test because the data were normally distributed. A strong positive correlation was found between the change in zygomatic width (Za-Za) and the change in the distance between the left and right zygomaticofrontal landmarks (Zmf-Zmf) ($r = 0.582$, $p < 0.001$) (Fig. 5).

Figure 5: Significant correlation between bizygomatic width change (Za-Za) and sutura zygomaticofrontalis distance (Zmf-Zmf) change



*** - Significant correlation at $p < 0.001$
Source: Created by the authors

4. DISCUSSION

In the present study, the transverse parameters Za–Za and Zmf–Zmf allow assessment of the possible involvement of the zygomatic and frontozygomatic complexes in the response to expansion. The results show that RME is followed by measurable changes not only in the maxillary region but also lateral to it, supporting the concept of RME as an intervention with a potential orthopedic effect on the circummaxillary complex (Ahmida et al., 2023; Ok, Kayalar & Sadry, 2023).

Following expansion, the Za–Za width increased by 1.51 mm. The increase in this parameter may be regarded as an indirect indicator of transverse adaptation of the zygomatic complex. This interpretation is consistent with the three-dimensional observations of Ok et al., who found changes in both maxillary width and the frontozygomatic and zygomaticomaxillary regions after RME in growing patients. According to their findings, the interzygomatic distance increased by approximately 2.00 mm (Ok, Kayalar & Sadry, 2023). In addition to linear changes, the authors described lateral displacement and external rotation of the zygomatic bone. Although the 3D measurements used in that study are not directly comparable with the PA cephalometric Za–Za parameter, the similar magnitude of the observed changes supports the presence of a moderate skeletal response beyond the immediate region of the midpalatal suture.

Patient age is an important factor in the interpretation of these results. With advancing skeletal maturation, resistance of the circummaxillary sutures increases, and a more limited orthopedic component may be expected compared with the early mixed dentition. Nevertheless, the data of Gokturk and Yavan show that conventional tooth-borne RME can produce measurable skeletal changes even in older adolescents (Gokturk & Yavan, 2024). The mean age in their conventional RME group was 16.74 years, which is close to the mean age of 16.59 years in the present study. Their findings demonstrate that a skeletal effect is possible even in late adolescence. This concept is also supported by a 2026 CBCT study including patients aged 10–17 years and comparing tooth-borne Hyrax, hybrid, and bone-borne expansion (Yazdan Ozen & Ceylan, 2026). Significant skeletal and dental maxillary expansion was observed with all three appliance types, although the bone-borne approach produced a greater skeletal component. In the context of the present study, these findings indicate that a conventional Hyrax appliance may produce a skeletal response even during adolescence, although the expected magnitude of this effect is smaller than with bone-borne designs.

A statistically significant increase was also found for the Zmf–Zmf parameter, with a mean post-expansion change of 0.91 mm. In interpreting this result, it is important to emphasize that Zmf–Zmf represents a linear transverse distance between the left and right Zmf cephalometric landmarks and does not directly measure the width of the zygomaticofrontal suture. Therefore, the observed change should not be regarded as direct evidence of disjunction of the zygomaticofrontal suture. It more likely reflects spatial adaptation of the zygomatic complex involving a combination of lateral displacement and rotational changes. This distinction is also essential when comparing the present findings with the CBCT literature. Ahmida et al. directly assessed changes in several cranial and circummaxillary sutures after conventional RPE and MARPE (Ahmida et al., 2023). The authors reported immediate changes in some of the investigated sutures but did not identify a uniform directional response across all analyzed structures, and at long-term follow-up most changes outside the midpalatal suture were not maintained. Therefore, the increase in Zmf–Zmf in the present study should be interpreted more conservatively—as an indicator of a change in the position of the frontozygomatic region rather than as evidence of direct opening of the suture itself (Ahmida et al., 2023).

In summary, the observed changes in Za–Za and Zmf–Zmf suggest that the effect of RME in the investigated patients is not entirely limited to the maxilla. The transverse response of the zygomatic and frontozygomatic complexes was moderate in magnitude and most likely reflects the combined effects of lateral displacement and rotational adaptation of the adjacent structures.

5. CONCLUSION

Rapid maxillary expansion with a Hyrax appliance in patients with unilateral posterior crossbite results in a statistically significant increase in zygomatic width (Za–Za) and in the transverse distance between the frontozygomatic landmarks (Zmf–Zmf). The findings show that the effect of RME is not limited to the maxilla but also involves more lateral and cranially located structures of the midface. These results support the concept that, even in late adolescence, conventional rapid maxillary expansion may be associated with limited but measurable circummaxillary skeletal changes.

REFERENCES

- Ahmida, A., Mehta, S., Amelemah, E., Bashir, R., Vich, M. L., Tadinada, A., Allareddy, V., & Yadav, S. (2023). Short-term and long-term effects of miniscrew-assisted and conventional rapid palatal expansion on the cranial and circummaxillary sutures. *American Journal of Orthodontics and Dentofacial Orthopedics*, 163(4), e115–e126. <https://doi.org/10.1016/j.ajodo.2023.01.007>
- Alan, A., Kaya, Y., & Sancak, K. (2025). Mid-facial skeletal and soft tissue changes after maxillary skeletal expander application: A retrospective CBCT study. *BMC Oral Health*, 25(1), 1168. <https://doi.org/10.1186/s12903-025-06569-z>
- Cobourne, M. T., & DiBiase, A. T. (2025). *Handbook of orthodontics* (3rd ed.). Elsevier.
- Corel Corporation. (2026). CorelDRAW® Graphics Suite 2026. <https://www.coreldraw.com/en/product/coreldraw/>
- Ghoneima, A., Abdel-Fattah, E., Hartsfield, J., El-Bedwehi, A., Kamel, A., & Kula, K. (2011). Effects of rapid maxillary expansion on the cranial and circummaxillary sutures. *Am J Orthod Dentofacial Orthop.*, 140(4), 510–519. doi:10.1016/j.ajodo.2010.10.024
- Gokturk, M., & Yavan, M. A. (2024). Comparison of the short-term effects of tooth–bone-borne and tooth-borne rapid maxillary expansion in older adolescents. *Journal of Orofacial Orthopedics / Fortschritte der Kieferorthopädie*, 85, 43–55. <https://doi.org/10.1007/s00056-022-00401-x>
- Krasteva, S. (2019). Graphical and analytical analysis of transverse deviations during movement of the lower jaw (2nd expanded ed.). MU-Plovdiv.
- Kumar, S. A., Gurunathan, D., Muruganandham, & Sharma, S. (2011). Rapid maxillary expansion: A unique treatment modality in dentistry. *Journal of Clinical and Diagnostic Research*, 5(4), 906–911. <https://doi.org/10.7860/JCDR/2011/1449>
- Leonardi, R., Sicurezza, E., Cutrera, A., & Barbato, E. (2011). Early post-treatment changes of circummaxillary sutures in young patients treated with rapid maxillary expansion. *The Angle Orthodontist*, 81(1), 36–41. doi: 10.2319/050910-250.1
- Ok, U., Kayalar, E., & Sadry, S. (2023). Three-dimensional zygomatic changes after rapid maxillary expansion in growing patients. *Journal of Orofacial Orthopedics / Fortschritte der Kieferorthopädie*, 84(3), 147–156. <https://doi.org/10.1007/s00056-021-00348-5>
- Proffit, W. R., Fields, H. W., Larson, B. E., & Sarver, D. M. (2019). *Contemporary orthodontics* (6th ed.). Elsevier.- 208-240;430
- Ricketts, R. M. (1981). Perspectives in the clinical application of cephalometrics. *Angle Orthod.*, 51(2), 115–150. doi: 10.1043/0003-3219(1981)051<0115:PITCAO>2.0.CO;2.
- Sayar, G., & Kiliç, D. D. (2019). Rapid maxillary expansion outcomes according to midpalatal suture maturation levels. *Prog Orthod.*, 20, 27. doi: 10.1186/s40510-019-0278-9.
- Stoilova-Todorova, M. (2018). Rapid maxillary expansion for correction of maxillary transverse insufficiency [Candidate dissertation]. Plovdiv.
- Yazdan Özen, G., & Ceylan, İ. (2026). Investigation of the effects of tooth-borne, tooth-bone-borne and bone-borne rapid maxillary expansion appliances on the nasomaxillary complex using CBCT. *Turkish Journal of Orthodontics*, 39(1), 17–25. <https://doi.org/10.4274/TurkOrthod.2026.2025.25>

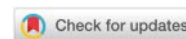
AGE-RELATED DIFFERENCES IN THE SELECTION AND EVALUATION OF DENTAL CARE

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Abstract: Dental care is a multifactorial process that is determined by the individual characteristics of the patient, the professional qualities of the dentist and his team, the accessibility of the dental clinic, the patient's previous experience and awareness of dental treatment. As part of the demographic characteristics of patients, age is an important factor when choosing a dentist. In the scientific literature, the authors study the relationship between the age of patients and the way they search for dental specific information, with the criteria that they consider important when making their choice of a dentist - recommendations from relatives and acquaintances, good reviews on social networks and the Internet, the location of the dental practice near the patient's home, random selection of a dentist and clinic, preference for visiting the same dentist for years. The demographic factor - patient's age also has an impact on assessing the quality of dental care provided. In recent decades, there has been a rapid development of new tendencies in the management and assessment of the quality of dental services worldwide. The aim of this scientific study is to investigate the influence of patients' age as a factor influencing the choice of a dentist and clinic for dental treatment, and the subsequent assessment of the quality of the dental care provided. A cross-sectional study was conducted between September 2025 and May 2026. 529 patients from different ages participated in the scientific study, with the youngest patient participating in the study being 18 years old and the oldest 89. The average age of the patients participating in the study is 53 years old. For the purposes of the study, the patients filled out a questionnaire. The questionnaire provided for patients to fill out is anonymous, and participation in the scientific study is voluntary. The information from the questionnaire was used and presented only in summary form. The data from the scientific study was processed using the SPSS v.31.0 statistical software. The results of the scientific study show that younger patients more often choose a dentist through reviews from social networks, which are the main source of information for them. For older patients, the first choice is the dental office closest to home. The location of the dental clinic and its team gains importance due to differences in patient mobility, transport accessibility and the need for more frequent visits. 30.6% of all patients participating in the study choose the dentist they want to visit through a recommendation from acquaintances and friends. In the scientific literature, personal recommendation is considered a form of social trust, where the decision is based on the real experience of family members, friends and acquaintances. The analysis of the age of patients in relation to the individual criteria for choosing a dentist can help to better adapt dental services to the needs and preferences by patients' different age groups.

Keywords: patient age, dental care quality, dental care utilization, patient preferences

Field: Medical Sciences and Health

1. INTRODUCTION

Dental care is a multifactorial process that is determined by the individual characteristics of the patient, the professional qualities of the dentist and his team, the accessibility of the dental clinic, the patient's previous experience and awareness of dental treatment. (Crocker et al., 2024) As part of the demographic characteristics of patients, age is an important factor when choosing a dentist. In the scientific literature, the authors study the relationship between the age of patients and the way they search for dental specific information, with the criteria that they consider important when making their choice of a dentist - recommendations from relatives and acquaintances, good reviews on social networks and the Internet, the location of the dental practice near the patient's home, random selection of a dentist and clinic, preference for visiting the same dentist for years. (Reda et al., 2018) The demographic factor - patient's age also has an impact on assessing the quality of dental care provided. In recent decades, there has been a rapid development of new tendencies in the management and assessment of the quality of dental services worldwide. Since ancient times, products and services have been evaluated based on their quality. This is evidenced by the works of the ancient Greek scientist and philosopher Aristotle. (Jonkisz et al., 2021)

The aim of this scientific study is to investigate the influence of patients' age as a factor influencing the choice of a dentist and clinic for dental treatment, and the subsequent assessment of the quality of

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the dental care provided.

2. MATERIALS AND METHODS

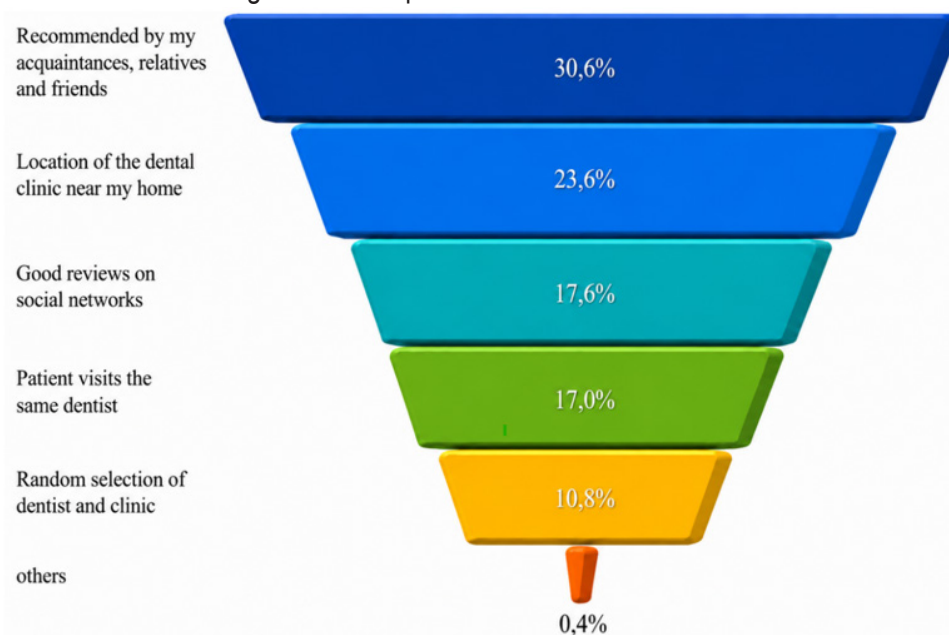
A cross-sectional study was conducted between September 2025 and May 2026. Written permission was obtained from KENI before the start of the research. For the purposes of the research, patients completed a questionnaire including fourteen socio-demographic questions, thirty-three questions related to the assessment of the quality of the dental services provided, six questions related to the assessment of patient satisfaction, five questions regarding patient trust, and six questions assessing patient loyalty to the clinic, the dentist, and his team. The questionnaire provided for patients to fill out is anonymous, and participation in the scientific study is voluntary. The information from the questionnaire was used and presented only in summary form. The data from the scientific study was processed using the SPSS v.31.0 statistical software.

3. RESULTS

529 patients from different ages participated in the scientific study, with the youngest patient participating in the study being 18 years old and the oldest 89. The average age of the patients participating in the study is 53 years old.

The choice of a dentist is determined most by recommendations from acquaintances, followed by the location of the dental office and in third place are reviews from social networks. (Fig.1)

Fig 1. Patients' preference based on various factors

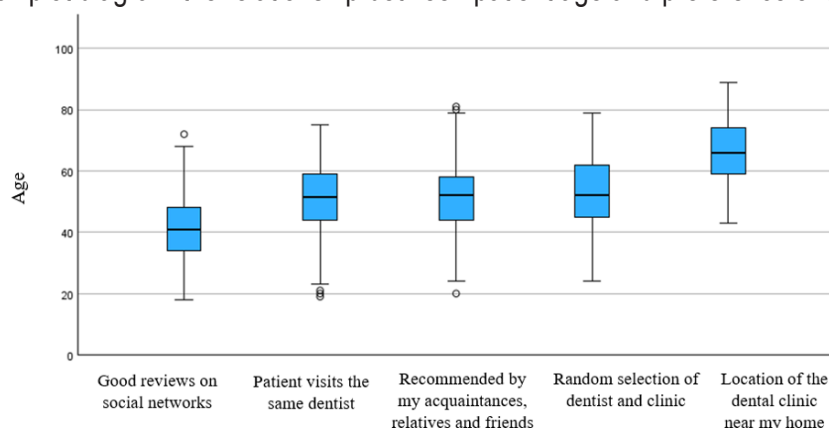


Source: Authors' research

To the question from the survey "When you need dental care, how do you choose the dentist to visit?" 162 (30.6%) patients answered that they choose a dentist who was recommended to them by acquaintances and friends. For 125 (23.6%) respondents out of all those who took part, the location of the dental clinic near home is an important factor in choosing a dentist and clinic. 17.6% of all those participating in the scientific study choose a dentist who has good reviews on social networks and the Internet from other patients. 90 (17.0%) patients indicated that they visit the same dentist for many years. Only 10.8% of all patients indicated that they make a random choice of dentist and clinic to visit.

In recent decades, the reason for choosing a dentist and the relationship with the socio-demographic factor age have been of interest. Since only two respondents, which is less than half of all respondents, answered that their choice was dictated by another unspecified reason, these other reasons will not be considered in the analysis. The relationship between age and the reason for choosing a dentist can be presented by a box plot diagram. (Fig.2)

Fig 2. Box plot diagram-the relationship between patient age and preference of clinic and dentist



Source: Authors' research

The results of the scientific study show that younger patients more often choose a dentist through reviews from social networks, which are the main source of information for them. Young patients pay more attention to the online reputation of the clinic and dentists, look at photos of clinical cases “before-after”, reviews and the digital presence of the dentist. Young patients do not have long-term contact with a dentist and this is also one of the reasons for looking for information online. The box plot diagram shows that patients around 50 years of age responded that they visit the same dentist because they have already built trust in a specific doctor and clinic, have a positive personal experience, prefer continuity in treatment or have a more complex dental history, which makes changing doctors less desirable for them. For older patients, the first choice is the dental office closest to home. The location of the dental clinic and its team gains importance due to differences in patient mobility, transport accessibility and the need for more frequent visits.

4. DISCUSSIONS

In their scientific studies, the authors found age-related differences in the criteria for choosing a dentist and clinic. The results of the study by Tâncu et al. (2019) show that age can be considered a significant factor related to the different prioritization of the characteristics of dental services when making a decision to choose a dental practice. The results of our study confirm the conclusions of the scientific study by Tâncu et al. (2019) that the choice of a dentist is influenced by the location of the dental clinic, the reputation of the dentist and the socio-demographic characteristics of the patient.

Similar to the research of Nitschke, I., Ulbrich, T. et al. (2022), in which the authors found that personal recommendation is the most important way in which patients learn about and choose a dentist, the results of our study show that the majority 30.6% of all patients participating in the study choose the dentist they want to visit through a recommendation from acquaintances and friends. In the scientific literature, personal recommendation is considered a form of social trust, where the decision is based on the real experience of family members, friends and acquaintances. (Jung et al., 2018) In their scientific work Nitschke, I., von Chlingensperg, R. et al. (2022), describe that for younger patients, online reviews and the presence of dentists in social networks and the Internet are becoming increasingly important when choosing a clinic and dental care provider. Similar results are reported in the studies of Al-Khalifa (2024), Gušić et al. (2024) and Freire et al. (2023). These studies confirm that good online reviews and recommendations have a greater relative weight in the choice of clinic and dentist by younger patients.

Nyyssönen et al. (1984) studied continuity of dental visits. The authors found age differences in the frequency of changing dentists and clinics – younger patients changed their dentists more often than older patients.

5. CONCLUSIONS

The analysis of the age of patients in relation to the individual criteria for choosing a dentist can help to better adapt dental services to the needs and preferences by patients' different age groups. From the research conducted, the selection criteria and the results of the scientific study show a strong relationship with the patient's age factor. Patient selection reflects generational differences in the way they seek and evaluate health information.

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The present study was conducted as part of the research undertaken for a doctoral dissertation. The author would like to express sincere gratitude to the academic board of directors of the Faculty of Dental Medicine and the Medical University of Varna.

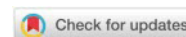
REFERENCES

- Al-Khalifa, K. S. (2024). The use of Instagram among dental patients in Saudi Arabia. *Acta Informatica Medica*, 32(1), 54–60. <https://doi.org/10.5455/aim.2024.32.54-60>
- Crocker, T. F., Ensor, J., Lam, N., Jordão, M., Bajpai, R., Bond, M., Forster, A., Riley, R. D., Andre, D., Brundle, C., Ellwood, A., Green, J., Hale, M., Mirza, L., Morgan, J., Patel, I., Patetsini, E., Prescott, M., Ramiz, R., Todd, O., ... Clegg, A. (2024). Community based complex interventions to sustain independence in older people: systematic review and network meta-analysis. *BMJ (Clinical research ed.)*, 384, e077764. <https://doi.org/10.1136/bmj-2023-077764>
- Freire, Y., Sánchez, M. G., Suárez, A., Joves, G., Nowak, M., & Díaz-Flores García, V. (2023). Influence of the use of social media on patients changing dental practice: a web-based questionnaire study. *BMC oral health*, 23(1), 365. <https://doi.org/10.1186/s12903-023-03078-9>
- Georgieva, G. (2025). Quality in terms of dental health services. *MEDIS – International Journal of Medical Sciences and Research*, 4(3), 41-45. <https://doi.org/10.35120/medisij0403041g>
- Gušić, I., Stojilković, M., Alija, S., Prodanović, D., Mirnić, J., & Veljović, T. (2024). The impact of social media on the selection of dentists based on their social media presence among residents of Vojvodina, Serbia: a cross-sectional study. *BMC public health*, 24(1), 3348. <https://doi.org/10.1186/s12889-024-20884-0>
- Jonkisz, A., Karniej, P., & Krasowska, D. (2021). SERVQUAL Method as an "Old New" Tool for Improving the Quality of Medical Services: A Literature Review. *International journal of environmental research and public health*, 18(20), 10758. <https://doi.org/10.3390/ijerph182010758>
- Jung, Y. S., Yang, H. Y., Choi, Y. H., Kim, E. K., Jeong, S. H., Cho, M. J., Nam, S. H., & Song, K. B. (2018). Factors affecting use of word-of-mouth by dental patients. *International dental journal*, 68(5), 314–319. <https://doi.org/10.1111/idj.12387>
- Nitschke, I., von Chlingensperg, R., Schrock, A., Hopfenmüller, W., & Jockusch, J. (2022). What Counts for the Old and Oldest Old?—An Analysis of Patient Criteria for Choosing a Dentist—Part I: Awareness and Selection Criteria, Infrastructure, and Dental Office Equipment. *International journal of environmental research and public health*, 19(14), 8307. <https://doi.org/10.3390/ijerph19148307>
- Nitschke, I., Ulbrich, T., Schrock, A., Hopfenmüller, W., & Jockusch, J. (2022). What Counts for the Old and Oldest Old?—An Analysis of Patient Criteria for Choosing a Dentist—Part II: Personal Characteristics and Soft Skills. *International journal of environmental research and public health*, 19(14), 8621. <https://doi.org/10.3390/ijerph19148621>
- Nyyssönen, V., Herranen, K., & Rimpelä, M. (1984). Attendance pattern and continuity of dental care of Finnish adults over a 5 year period. *Social Science & Medicine*, 19(7), 677–681. [https://doi.org/10.1016/0277-9536\(84\)90239-9](https://doi.org/10.1016/0277-9536(84)90239-9)
- Reda, S. M., Krois, J., Reda, S. F., Thomson, W. M., & Schwendicke, F. (2018). The impact of demographic, health-related and social factors on dental services utilization: Systematic review and meta-analysis. *Journal of dentistry*, 75, 1–6. <https://doi.org/10.1016/j.jdent.2018.04.010>
- Tâncu, A. M. C., Purcărea, V. L., Pantea, M., & Imre, M. (2019). Key Factors Correlations in Selecting Dental Services. *Journal of medicine and life*, 12(1), 83–89. <https://doi.org/10.25122/jml-2019-0023>

PATIENT'S AWARENESS, UNDERSTANDING AND PERCEPTION OF CONVENTIONAL CONSTRUCTIONS AND IMPLANT SUPPORTED PROSTHESES

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Abstract: Tooth loss could be due to many reasons and it would ultimately affect the patient's well-being and self-esteem. With increasing age and depending on the patient's oral hygiene as well as possibly being involved in different traumatic experiences and injuries, increasing level of prosthetic treatment is also established. Before undergoing any kind of prosthetic treatment when mouth rehabilitation dental patients need to make an informed decision on the way the treatment plan would be carried out the best possible way for them according to their expectations. The aim of the present study is to assess the awareness, understanding and perception of tooth supported and implant supported prostheses among dental patients when making their selection. A systematic review of the scientific literature on the topic published in the period from 2015 to 2025 was conducted, including articles from the databases PubMed, Web of Science (WoS), Scopus, Wiley. Keywords which were used for the purposes of scientific research are: "patient awareness", "dental implants", "prosthetic constructions", "conventional methods". The results of this scientific study show that one of the major factors influencing the choice between tooth-supported and implant-supported prosthetic treatment is financial constraint. A solid percentage of dental patients would turn to implant supported constructions after understanding the benefits from this kind of therapy. Education towards the direction of patient's awareness and understanding the divergence between implant and conventional treatment needs to be carried out in order for them to make the right informed decision.

Keywords: patient awareness, dental implants, prosthetic constructions, conventional methods

Field: Medical Sciences and Health

1. INTRODUCTION

Tooth loss could be due to many reasons and it would ultimately affect the patient's well-being and self-esteem. It is usually caused by severe caries lesions, localized or generalized periodontitis, periapical diseases, fractures, orthodontic problems, impacted teeth. (Broers DLM et al. 2021) (Suzuki S et al. 2022) In time depending on the case different patient discomforts such as reduced alveolar ridge as well as shortened prosthesis-bearing area, diminished masticatory efficiency and facial profile alteration can occur. This is going to have a negative impact on patient's self-image and enjoying social activities. With increasing age and depending on the patient's oral hygiene as well as possibly being involved in different traumatic experiences and injuries, increasing level of prosthetic treatment is also established. (Warreth et al. 2013) Having a long lasting dental problem and thinking of making a dental appointment when this issue becomes even more severe or just postponing the dental visit is something the dentist need to consider when constructing the treatment plan for the patient. (Nevins et al. 2009) The patients usually have higher expectations when the area of interest is in the esthetic zone or is related to smile function and satisfaction. If the clinician presents different treatment options the patients knowledge and awareness on these issues plays an important role on the final treatment decision. (Shenoy et al. 2023) The aim of the scientific research is to investigate the awareness, understanding and perception on the topic of tooth supported and implant supported prostheses among dental patients when making their selection.

2. MATERIALS AND METHODS

A systematic review of the scientific literature on the topic published in the period from 2015 to 2025 was conducted, including articles from the databases PubMed, Web of Science (WoS), Scopus, Wiley. Keywords which were used for the purposes of scientific research are: "patient awareness", "dental implants", "prosthetic constructions", "conventional methods".

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3. RESULTS

Dental implants have become an established treatment modality for the rehabilitation of partially and completely edentulous patients, providing enhanced prosthetic retention, stability, and masticatory function. These benefits can contribute to improved oral health-related quality of life and favorable long-term clinical outcomes. The implants are osseointegrated in the bone (mandibula or maxilla) for set period of time after being placed. The duration usually depends on the surface of the implant and the state of the extraction or placement site. The construction on top of the implants could be fixed right after.

The patients can also choose the conventional methods option where a fixed partial dentures such as crowns and bridges could be used or removable dentures where they better fit the purpose. Some patients tend to understand that choosing implants as an option has the advantage of adjacent teeth not needing to be prepared, even though most have concerns about the financial part, not willing to undergo the surgery and then waiting during healing time, leading to prolonged treatment time. (Shenoy et al. 2023) (Rustemeyer et al. 2007)

Before undergoing any kind of prosthetic treatment when mouth rehabilitation dental patients need to make an informed decision on the way the treatment plan would be carried out the best possible way for them according to their expectations.

4. DISCUSSIONS

Al-Fareh et al. (2023) in their scientific research describes a face to face interview questionnaire and clinical examination to better understand the patient's perception and awareness about the topic. More than half of their participants are in unison with one another that missing teeth examined clinically should be replaced by one form or another. Nearly 80% of their participants pointed out dental caries as a primary reason for already missing teeth. Trauma and periodontitis as secondary and tertiary reasons respectively. More than 2/3 of the participants have shown no knowledge of implant supported prosthesis and the ones that did weren't exactly sure of the procedure. More than half of the participants expressed concerns that cost would be very high. Less than 10% though were of the mindset that the procedure of implant placement would be complicated and difficult to perform. Almost all the individuals agreed that implant supported prostheses are useful. More than 80% were willing to learn more about constructions over implants. Most of females in comparison to males considered the implant insertion and the healing period as painful. 65% of all the participants already had a fixed construction in their oral cavity, but around that same number of participants hoped to receive an implant fixed prosthesis after learning the benefits of it. Only a few numbers of participants showed the willingness to accept removable construction.

Al-Haj Husain et al. (2023) have conducted another similar scientific study in a Swiss University based on patient's knowledge, awareness and attitudes towards dental implants. The dentists were appointed as a primary source of information on the topic. A self-explanatory online questionnaire was used in this particular study. Around 42% of the participants had one dental appointment per year, while 38 % only visited dentist when emergencies. In this study around 78% of participants demonstrated awareness of dental implants as treatment solution, with 64% reporting a high level of perceived knowledge, considering themselves to be well informed about the topic. Dental implants were primarily preferred option with bridges and crowns following right after. 45% of the participants were willing to be charged with higher cost in order to have the implants placed by certified professionals. Around half of the participants had high esthetic expectations and were of the mindset that the implants would last around 10-20 years.

According to scientific research that Krupińska AM et al. (2023) made at Wroclaw Medical University, Poland 75% of the participants were aware of dental implants as a treatment option but only 40% understood the mechanics and the procedures behind it. Internet was the primary source of information but the high cost were very concerning for the patients.

In another scientific study that Ho K et al. (2022) have conducted in Japan patients believed that the purpose of dental implants was to avoid dentures and improve chewing function. Cost and longevity were primary concerns. They also expressed limited knowledge about bone grafts.

5. CONCLUSIONS

The results of this scientific study show that one of the major factors influencing the choice between tooth-supported and implant-supported prosthetic treatment is financial constraint. A solid percentage of dental patients would turn to implant supported constructions after understanding the benefits from this kind of therapy. Education towards the direction of patient's awareness and understanding the divergence between implant and conventional treatment needs to be carried out in order for them to make the right informed decision.

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REFERENCES

- Al-Fareh, A., Dubais, M., Smran, A., El Bahra, S., & Samran, A. (2023). Awareness, knowledge, and perception of tooth-supported and implant-supported prostheses among adults in Sana'a City: A survey-based study. *Oral*, 3(3), 337–352. <https://doi.org/10.3390/oral3030028>
- Al-Haj Husain, A., De Cicco, O., Stadlinger, B., Bosshard, F. A., Schmidt, V., Özcan, M., & Valdec, S. (2023). A survey on attitude, awareness, and knowledge of patients regarding the use of dental implants at a Swiss university clinic. *Dentistry Journal*, 11(7), 165. <https://doi.org/10.3390/dj11070165>
- Broers, D. L. M., Dubois, L., de Lange, J., Su, N., & de Jongh, A. (2022). Reasons for tooth removal in adults: A systematic review. *International Dental Journal*, 72(1), 52–57. <https://doi.org/10.1016/j.identj.2021.01.011>
- Ho, K., Bahammam, S., Chen, C. Y., Hojo, Y., Kim, D., Kondo, H., Da Silva, J., & Nagai, S. (2022). A cross-sectional survey of patient's perception and knowledge of dental implants in Japan. *International Journal of Implant Dentistry*, 8(1), 14. <https://doi.org/10.1186/s40729-022-00410-w>
- Krupińska, A. M., & Bogucki, Z. (2023). Evaluation of patients' awareness and knowledge regarding dental implants among patients of the Department of Prosthetic Dentistry at Wrocław Medical University in Poland. *Advances in Clinical and Experimental Medicine*, 32(11), 1319–1325. <https://doi.org/10.17219/acem/174032>
- Nevins, M., Uzel, N. G., & Kim, D. M. (2009). The safety and efficacy of dental implants for periodontally compromised patients: A review of current knowledge. *Dental Implantology Update*, 20(11), 81–87.
- Papakoca, K., & Petrovski, M. (2022). Aesthetics of dental implants - periodontal and surgical aspects. *KNOWLEDGE - International Journal*, 52(4), 505–510. Retrieved from <https://ojs.ikm.mk/index.php/kij/article/view/5260>
- Rustemeyer, J., & Bremerich, A. (2007). Patients' knowledge and expectations regarding dental implants: Assessment by questionnaire. *International Journal of Oral and Maxillofacial Surgery*, 36(9), 814–817. <https://doi.org/10.1016/j.ijom.2007.05.003>
- Shenoy, A., Ganapathy, D. M., Maiti, S., & Sivaswamy, V. (2023). Knowledge, attitude, and perception regarding the financial aspects of prosthetic rehabilitation using dental implants: A double-questionnaire-based study. *Journal of Long-Term Effects of Medical Implants*, 33(3), 21–29. <https://doi.org/10.1615/JLongTermEffMedImplants.2022042615>
- Suzuki, S., Sugihara, N., Kamijo, H., Morita, M., Kawato, T., Tsuneishi, M., Kobayashi, K., Hasuike, Y., & Sato, T. (2022). Reasons for tooth extractions in Japan: The second nationwide survey. *International Dental Journal*, 72(3), 366–372. <https://doi.org/10.1016/j.identj.2021.05.008>
- Warreth, A., McAleese, E., McDonnell, P., Slami, R., & Guray, S. M. (2013). Dental implants and single implant-supported restorations. *Journal of the Irish Dental Association*, 59(1), 32–43.

HEMATOLOGIC INDICES AS POTENTIAL BIOMARKERS IN URTICARIA: A COMPARATIVE CASE-CONTROL STUDY IN ALBANIAN POPULATION

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Abstract: Urticaria is primarily a mast cell-mediated inflammatory disorder in which basophils, eosinophils, platelets, and multiple inflammatory mediators contribute to its pathophysiology. Routinely available hemogram-derived inflammatory indices may provide inexpensive and objective measures of systemic inflammatory alterations and may have potential value as biomarkers of disease activity, particularly in chronic urticaria, where disease assessment relies substantially on subjective patient-reported outcomes. Although several hematological ratios and indices have been investigated in urticaria, data from the Albanian population remain limited. This study evaluated selected hematological parameters in hospitalized patients with high disease activity urticaria compared with controls and assessed their associations with C-reactive protein (CRP). This cross-sectional retrospective case-control study included 113 patients hospitalized with diagnosis urticaria at the main tertiary hospital center in Tirana and 398 controls who underwent hemogram testing as part of routine health examinations in private practice. The median age was 50 (32–57) years in the urticaria group and 42 (32–54) years in controls with no statistical difference between groups, while females comprised 83 (73.45%) and 269 (67.59%), respectively. Acute urticaria was diagnosed in 55 (48.67%) patients and chronic urticaria in 58 (51.33). All evaluated hematological parameters differed significantly between patients with urticaria and controls ($p < 0.001$). Patients with urticaria had statistically significant lower absolute eosinophil, basophil, and lymphocyte counts and PDW (platelet distribution width), while MPV (mean platelet volume) and NLR (neutrophil to lymphocyte ratio) were higher. Undetectable eosinophil and basophil counts were observed in 79 (69.91%) and 99 (87.61%) urticaria patients, respectively. Spearman's rank correlation analysis showed that NLR was positively correlated with CRP ($p = 0.233$, $p = 0.013$) and inversely correlated with eosinophils ($p = -0.487$, $p < 0.001$) and basophils ($p = -0.276$, $p = 0.003$). Eosinophils and basophils were moderately positively correlated ($p = 0.430$, $p < 0.001$), while basophils were inversely correlated with CRP ($p = -0.230$, $p = 0.014$) and eosinophils with MPV ($p = -0.1919$, $p = 0.042$). No significant correlations were observed between CRP and eosinophils, MPV, or PDW, or between NLR and MPV or PDW. No significant changes were found between groups of chronic and acute urticaria for studied variables. Hospitalized patients with urticaria demonstrated a distinct hematological profile, particularly increased NLR and MPV and decreased eosinophil, basophil, lymphocyte, and PDW values. The association between NLR and CRP suggests potential relevance as a low-cost marker of systemic inflammation. Further prospective studies are needed to validate these findings in the Albanian population and to determine the potential utility of these hematological indices as markers of urticaria disease activity.

Keywords: Urticaria; Hematological indices; Neutrophil-to-lymphocyte ratio; Systemic inflammation; Biomarkers

Field: Medical Sciences and Health

1. INTRODUCTION

Urticaria is a skin disorder characterized by the presence of wheals, angioedema, or both. It encompasses a broad range of clinical presentations, and different urticaria subtypes may occur co-exist in the same patient. (Zuberbier et al., 2026) It is reported that urticaria affects up to 20% of people worldwide (Kolkhir et al., 2022) and its global burden has increased, reaching 66.48 million cases in 2021, with higher rates among females and younger individuals and a projected continued rise. (Tan et al., 2025)

Urticaria is considered acute when symptoms last ≤ 6 weeks and chronic when they persist for > 6 weeks and may be further categorized as inducible or spontaneous depending on the presence of identifiable triggers. (Zuberbier et al., 2026) Mast cell activation leads to the release of mediators, including histamine and platelet-activating factor (PAF), which contribute to itching, vasodilation, erythema, and recruitment of inflammatory cells. (Zuberbier et al., 2026) However, the inflammatory response in urticaria is not restricted to mast cells. Basophils, eosinophils, platelets, and components of both the innate and adaptive immune systems may contribute to the development and persistence of the disease. Assessment of urticaria severity remains challenging, as clinical evaluation largely depends on subjective patient-reported measures. Therefore, there is growing interest in accessible laboratory biomarkers that may complement clinical assessment. Complete blood count parameters and derived inflammatory indices,

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have gained attention as inexpensive and readily available markers of systemic inflammation.

Eosinopenia and basopenia in CSU(chronic spontaneous urticaria) has been related to CSU subtypes (Su Küçük & Yücel, 2026) According a recent publication, the combination of eosinopenia and basopenia may better predict poor response to second-generation H1-antihistamines than eosinopenia alone (OR 9.5 vs. 4.8). Eosinopenia is associated with type IIb autoimmunity, higher disease activity, and poorer treatment response, supporting its potential role as a biomarker in CSU (Kolkhir et al., 2020).

Recent studies report that CRP(c-reactive protein) may serve as potential biomarkers for distinguishing patients with CSU from healthy controls (Plavsic et al., 2021) with serum CRP concentrations significantly higher in CSU patients as compared with the healthy subjects and significantly correlated with the platelet count in CSU patients. (Kasperska-Zajac et al., 2014). Elevated C-reactive protein (CRP) levels have been associated with greater urticaria activity, impaired quality of life, and poorer response to antihistamine treatment. (Kolkhir et al., 2018)

Increased platelet count and MPV in CSU may reflect the inflammatory state of the disease, suggesting an ongoing but compensated platelet destruction-production process(Di Pino et al., 2022). A positive correlation between CRP and NLR (neutrophil to lymphocyte ratio) was reported in the CSU group. (Temizel et al., 2026) High NLR and low eosinophil and basophil counts have been associated with a poor response to second-generation H1-antihistamines, whereas normal or high eosinophil counts were associated with a better treatment response (Calzari et al., 2025)

However, findings remain inconsistent and sometimes controversial across studies while data on these hematological biomarkers in Albanian patients with urticaria are currently lacking.

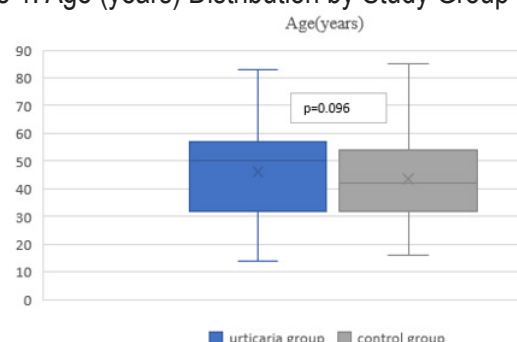
2. MATERIALS AND METHODS

This retrospective, cross-sectional case-control study was conducted at the main tertiary hospital center in Tirana, Albania, and included patients hospitalized with a diagnosis of urticaria and a control group comprising individuals undergoing routine health examinations in private medical practice. Clinical, demographic, and laboratory data were retrospectively extracted from available medical records, with the first complete blood count obtained at hospital admission used for patients with urticaria. The analyzed variables included age, absolute neutrophil, lymphocyte, eosinophil, and basophil counts, mean platelet volume (MPV), platelet distribution width (PDW), and serum C-reactive protein (CRP), expressed in mg/dL. The neutrophil-to-lymphocyte ratio (NLR) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. The study database and anaysis was performed using Ms Excel 2016 and SPSS. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Differences between the urticaria and control groups were assessed using the Mann–Whitney U test. Associations among hematological parameters, NLR, and CRP were evaluated using Spearman's rank correlation coefficient (ρ). All statistical tests were two-sided, and statistically significance was set 0.05. The study was approved by Ethics Committee of University of Medicine, Tirana.

3. RESULTS

A total of 113 hospitalized patients with urticaria were included in the analysis, comprising 55 (48.7%) patients with acute urticaria and 58 (51.3%) with chronic urticaria. The median age of patients with urticaria was 50 years (IQR, 32–57), and 83 (73.45%) were female. The control group consisted of 398 individuals, with a median age of 42 years (IQR, 32–54), of whom 269 (67.59%) were female.

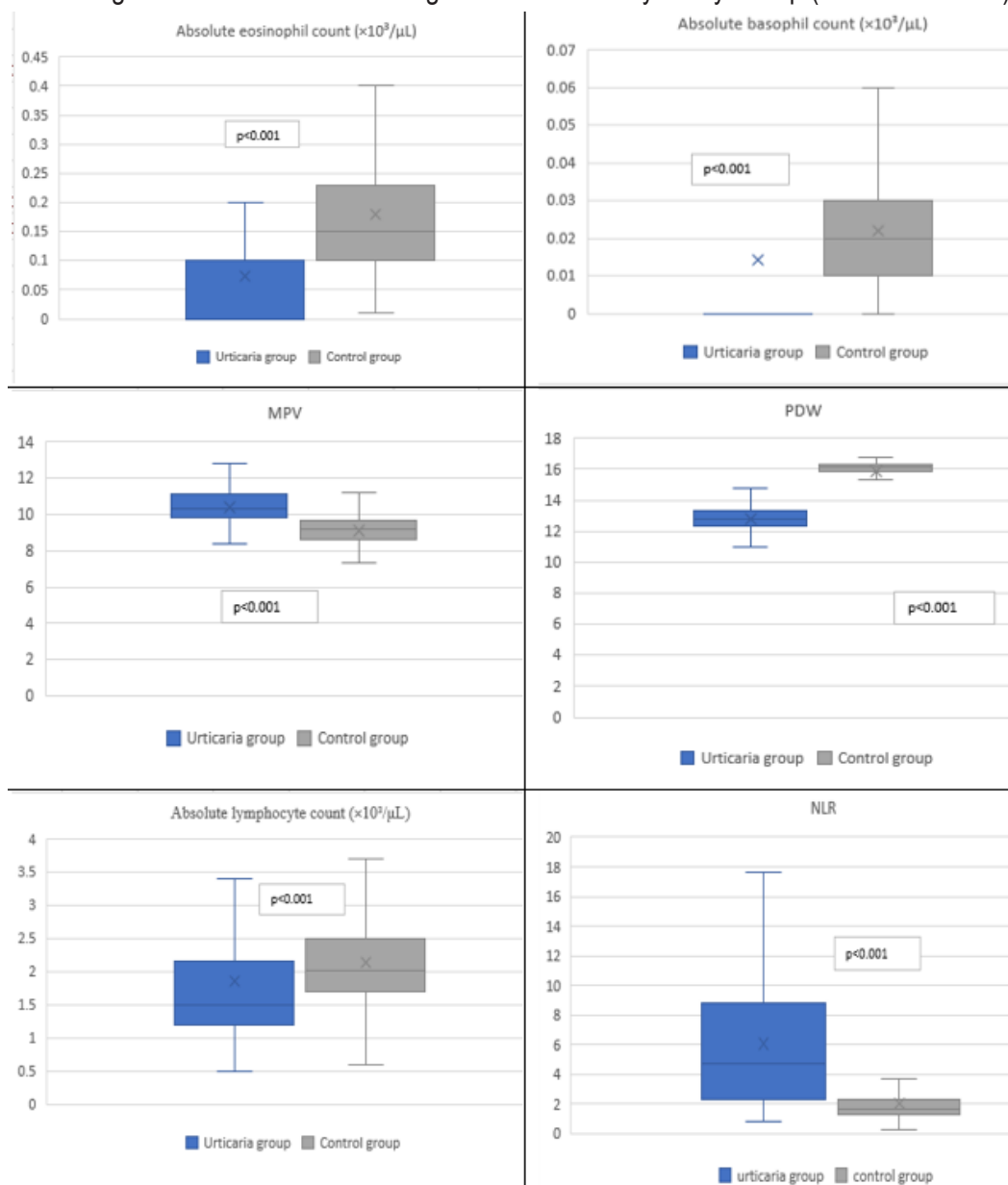
Figure 1. Age (years) Distribution by Study Group Median (IQR).



Source: Authors' research

Absolute eosinophil, basophil, and lymphocyte counts, mean platelet volume (MPV), platelet distribution width (PDW), and neutrophil-to-lymphocyte ratio (NLR) were compared using the Mann-Whitney U test. All evaluated hematological parameters differed significantly between patients with urticaria and controls ($p < 0.001$). Median eosinophil count was significantly lower in patients with urticaria than in controls, $0.00 (0.00-0.10) \times 10^3/\mu\text{L}$ versus $0.15 (0.10-0.23) \times 10^3/\mu\text{L}$, respectively ($U = 7760.00$, $p < 0.001$), as was basophil count, $0.00 (0.00-0.00) \times 10^3/\mu\text{L}$ versus $0.02 (0.01-0.03) \times 10^3/\mu\text{L}$ ($U = 9284.50$, $p < 0.001$). Undetectable eosinophil and basophil counts were observed in 79 (69.91%) and 99 (87.61%) patients, respectively.

Figure 2. Distribution of Hemogram Parameters by Study Group (Median and IQR)



Source: Authors' research

MPV was significantly higher in patients with urticaria, $10.30 (9.80-11.10)$ fL versus $9.20 (8.60-9.70)$ fL ($U = 7888.00$, $p < 0.001$), whereas PDW was lower, $7.60 (4.60-11.30)$ fL versus $16.10 (15.90-16.30)$ fL ($U = 2456.00$, $p < 0.001$). The absolute lymphocyte count was also lower, $1.50 (1.20-2.10) \times 10^3/\mu\text{L}$ versus $2.01 (1.69-2.51) \times 10^3/\mu\text{L}$ ($U = 14151.00$, $p < 0.001$), while NLR was substantially higher, $4.75 (2.29-8.62)$ versus $1.66 (1.28-2.28)$ ($U = 8095.00$, $p < 0.001$).

CRP resulted $0.30(0.11-0.97)$ mg/dL and was elevated (> 0.5 mg/dL) in 41(36.28%) of urticaria patients.

Spearman's rank correlation analysis demonstrated a weak inverse correlation between basophils and CRP ($\rho = -0.230$, $p = 0.014$), whereas eosinophils were not significantly correlated with CRP ($\rho = -0.1286$, $p = 0.175$). Eosinophils and basophils demonstrated a positive correlation ($\rho = 0.430$, $p < 0.001$). Neither PDW nor MPV was significantly correlated with CRP ($\rho = -0.009$, $p = 0.925$ and $\rho = -0.076$, $p = 0.427$, respectively). Eosinophils showed a weak inverse correlation with MPV ($\rho = -0.1919$, $p = 0.042$), while basophils were not correlated with MPV ($\rho = -0.007$, $p = 0.944$). NLR demonstrated a weak positive correlation with CRP ($\rho = 0.233$, $p = 0.013$), but no significant correlations with MPV ($\rho = 0.017$, $p = 0.859$) or PDW ($\rho = -0.029$, $p = 0.756$). NLR demonstrated an inverse correlation with eosinophils ($\rho = -0.487$, $p < 0.001$) and an inverse correlation with basophils ($\rho = -0.276$, $p = 0.003$).

No statistically significant changes were found between groups of chronic and acute urticaria for hemogram parameters and CRP levels.

4. DISCUSSION

Our finding of increased MPV is consistent with previous study, which suggested that these changes may reflect increased platelet turnover and an ongoing, compensated platelet destruction-production process associated with inflammation in CSU (Di Pino et al., 2022). Results are controversial with other studies reports where MPV was significantly lower in CU patients compared with the controls (7.45 ± 0.69 vs. 7.96 ± 0.58 fl, $p = 0.000$) in adults (Yim et al., 2019) and also in children with CU, MPV (fL) levels were significantly lower when compared to healthy children (7.42 ± 0.77 and 7.89 ± 0.65 , respectively; $p = 0.004$) (Akelma et al., 2015). Another study found no significant differences in MPV and PDW between CSU group and the healthy subjects. (Kasperska-Zajac et al., 2014)

Disease activity and disease duration may influence MPV and PDW values and could partly explain differences between our findings and those of previous studies. Notably, our study included patients with both acute and chronic urticaria, whereas most previous studies have focused predominantly on chronic spontaneous urticaria, which may contribute to differences in platelet indices. However, no significant differences in MPV or PDW were observed between the acute and chronic urticaria groups in our study.

Kolkhir et al. reported eosinopenia in 10% of patients with CSU, which was associated with higher disease activity, type IIb autoimmunity, elevated CRP levels, and poorer response to antihistamines and omalizumab. Eosinophil counts also correlated positively with basophil counts, and 81% of patients with CSU with undetectable eosinophils had basopenia. (Kolkhir et al., 2020) In our study of hospitalized patients with urticaria, who may represent a subgroup with higher disease activity, eosinopenia and basopenia were frequently observed. Undetectable eosinophil and basophil counts were present in 69.91% and 87.61% of patients, respectively. Serum CRP concentrations were significantly higher in CSU patients as compared with the healthy subjects in adults (Kasperska-Zajac et al., 2014) and children. (Akelma et al., 2015) Elevated CRP levels were reported in approximately one-third of patients with CSU and were associated with ASST (Autologous Serum Skin Test) positivity and arterial hypertension (Kolkhir et al., 2018) and not correlated with disease activity. (Plavsic et al., 2021) In our study CRP was elevated in 36.28% of patients without significant differences between acute and chronic urticaria group.

5. CONCLUSIONS

Hospitalized patients with urticaria demonstrated a distinct peripheral hematological profile, characterized by increased NLR and MPV and reduced eosinophil, basophil, lymphocyte, and PDW values compared with controls. The positive association between NLR and CRP supports its relationship with systemic inflammatory activity, while the inverse association between NLR and eosinophil count may reflect coordinated alterations in circulating leukocyte profiles. The concomitant increase in MPV and reduction in PDW may indicate altered platelet size distribution, activation, and turnover, supporting a potential contribution of platelet-mediated mechanisms to the inflammatory processes underlying urticaria. These findings suggest that routinely available hemogram-derived parameters, particularly NLR, MPV, and PDW, may provide accessible and cost-effective complementary markers of systemic inflammatory alterations. Nevertheless, their clinical and prognostic significance requires further investigation in larger, prospective, and well-characterized cohorts, with appropriate adjustment for potential confounders, including comorbidities, concomitant medications, and other clinical factors, particularly in the Albanian population.

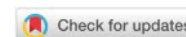
REFERENCES

- Akelma, A. Z., Mete, E., Cizmeci, M. N., Kanburoglu, M. K., Malli, D. D., & Bozkaya, D. (2015). The role of mean platelet volume as an inflammatory marker in children with chronic spontaneous urticaria. *Allergologia Et Immunopathologia*, 43(1), 10–13. <https://doi.org/10.1016/j.aller.2013.06.002>
- Calzari, P., Favale, E. M., Cugno, M., Asero, R., Marzano, A. V., & Ferrucci, S. M. (2025). Predictors of early treatment response to antihistamines and omalizumab in chronic spontaneous urticaria. *Frontiers in Allergy*, 6, 1728559. <https://doi.org/10.3389/falgy.2025.1728559>
- Di Pino, M., Ruberto, M. F., Costanzo, G., Firinu, D., Piras, M. S., Mura, M. N., Del Giacco, S., Coghe, F., Marongiu, F., & Barcellona, D. (2022). Chronic spontaneous urticaria: A low-grade disseminated intravascular coagulation only partially reversed by Omalizumab. *Clinical and Experimental Medicine*, 23(2), 495–502. <https://doi.org/10.1007/s10238-022-00838-9>
- Kasperska-Zajac, A., Grzanka, A., Jarzab, J., Misiolek, M., Wyszynska-Chlap, M., Kasperski, J., & Machura, E. (2014). The association between platelet count and acute phase response in chronic spontaneous urticaria. *BioMed Research International*, 2014, 650913. <https://doi.org/10.1155/2014/650913>
- Kolkhir, P., Altrichter, S., Hawro, T., & Maurer, M. (2018). C-reactive protein is linked to disease activity, impact, and response to treatment in patients with chronic spontaneous urticaria. *Allergy*, 73(4), 940–948. <https://doi.org/10.1111/all.13352>
- Kolkhir, P., Church, M. K., Altrichter, S., Skov, P. S., Hawro, T., Frischbutter, S., Metz, M., & Maurer, M. (2020). Eosinopenia, in Chronic Spontaneous Urticaria, Is Associated with High Disease Activity, Autoimmunity, and Poor Response to Treatment. *The Journal of Allergy and Clinical Immunology. In Practice*, 8(1), 318-325.e5. <https://doi.org/10.1016/j.jaip.2019.08.025>
- Kolkhir, P., Giménez-Arnau, A. M., Kulthanan, K., Peter, J., Metz, M., & Maurer, M. (2022). Urticaria. *Nature Reviews Disease Primers*, 8(1), 61. <https://doi.org/10.1038/s41572-022-00389-z>
- Plavsic, A., Tomic-Spiric, V., Arandjelovic, S., Miskovic, R., Dimitrijevic, M., & Peric-Popadic, A. (2021). Biomarkers of disease activity in patients with chronic spontaneous urticaria. *Advances in Dermatology and Allergology*, 38(6), 1017–1022. <https://doi.org/10.5114/ada.2021.112276>
- Su Küçük, Ö., & Yücel, M. B. (2026). Clinical and molecular aspects of managing chronic spontaneous urticaria: Identifying endotypes, phenotypes, and determinants of treatment response and resistance. *Frontiers in Allergy*, 6, 1706705. <https://doi.org/10.3389/falgy.2025.1706705>
- Tan, S., Chen, Z., & Lin, T. (2025). Global, regional, and National burden of urticaria (1990–2021), its potential risk factors, and projections to 2046. *BMC Public Health*, 25(1), 2709. <https://doi.org/10.1186/s12889-025-23321-y>
- Temizel, K. A., Dursun, P., & Ikizoglu, G. (2026). The effect of omalizumab treatment on inflammatory parameters in urticarial diseases: A retrospective study. *Postepy Dermatologii I Alergologii*, 43(2), 138–143. <https://doi.org/10.5114/ada.2026.161026>
- Trajkova, V. & Velickova, N. (2022). Association of autoimmune status with ASST, autoimmune and atopic diseases in CSU patients. *MEDIS – International Journal of Medical Sciences and Research*, 1(3), 1-5. <https://doi.org/10.35120/medisij010355t>
- Yim, J. H., Park, H. J., Cho, S. Y., & Shin, M. K. (2019). Mean Platelet Volume and Mean Platelet Volume/Platelet Count Ratio in Chronic Urticaria. *Annals of Dermatology*, 31(4), 467. <https://doi.org/10.5021/ad.2019.31.4.467>
- Zuberbier, T., Ansari, Z. A., Abdul Latiff, A. H., Abuzakouk, M. M., Agcaoili-De Jesus, M. S., Agondi, R. C., Al-Ahmad, M., Alangari, A. A., Alhameli, H., Alonso Bello, C. D., Alshareef, S., Al-Tamemi, S., Altrichter, S., Al Wahshi, H., Aquilina, S., Araújo, M., Arnaout, R., Asero, R., Ballmer-Weber, B., ... Giménez-Arnau, A. M. (2026). The International Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. *Allergy*, 81(8), 2582–2632. <https://doi.org/10.1111/all.70210>

MOTOR DEVELOPMENT AND MOTOR DEFICITS IN CHILDREN WITH AUTISM SPECTRUM DISORDER

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Abstract: Motor development represents an essential component of childhood development and is closely associated with functional independence, participation, and performance in everyday activities. Children with Autism Spectrum Disorder (ASD) frequently present with difficulties in motor coordination, balance, postural control, muscle strength, and fine motor performance, which may affect their overall functional abilities. The aim of the present study was to investigate motor development and identify the predominant motor deficits in children with ASD aged 4 to 7 years. The study included 60 children diagnosed with ASD, who were divided into an experimental group ($n = 30$) and a control group ($n = 30$). A comprehensive assessment of motor functioning was performed using a battery of standardized motor tests evaluating static and dynamic balance, postural control, lower-limb explosive power, hand grip strength, fine motor coordination, spatial orientation, and motor speed. The assessment included the Pediatric Berg Balance Scale, standing long jump, hand dynamometry, fine motor performance assessed through a graphic dictation task, spatial orientation speed, and tapping. The findings demonstrated varying degrees of motor difficulties across several functional domains. The most pronounced impairments were observed in balance and postural control, muscle strength, fine motor coordination, and motor speed. Difficulties in maintaining stable body positions and performing coordinated movements were particularly evident, suggesting reduced efficiency of postural and motor control mechanisms. Reduced grip strength and lower performance in tasks requiring rapid and precise motor responses were also observed. These findings indicate that motor difficulties in children with ASD are multidimensional, involving both gross and fine motor functions. The identified deficits may negatively affect participation in age-appropriate activities and limit functional independence. The results emphasize the importance of comprehensive motor assessment as an essential component of the therapeutic evaluation of children with ASD. Identification of specific motor impairments can provide a basis for individualized intervention planning and support the integration of targeted physiotherapy and occupational therapy strategies aimed at improving balance, strength, coordination, motor planning, and functional performance.

Keywords: autism spectrum disorder, motor development, motor deficits, balance, postural control, muscle strength, motor coordination, physiotherapy, occupational therapy.

Field: Medical Sciences and Health

1. INTRODUCTION

Motor development is a fundamental component of child development and plays an essential role in the acquisition of functional independence, participation in everyday activities, and adaptation to environmental demands. In children with Autism Spectrum Disorder (ASD), motor functioning is increasingly recognized as an important aspect of the overall developmental profile, as motor difficulties may occur alongside the core characteristics of the disorder and may substantially affect participation in daily life. A systematic review and meta-analysis reported a high prevalence of motor impairments among children with ASD, with difficulties affecting multiple components of motor functioning (Kangarani-Farahani et al., 2024). The motor profile of children with ASD is highly heterogeneous and may involve impairments in balance, coordination, postural control, motor planning, muscle strength, and fine motor performance. Recent comparative studies have demonstrated significant differences between children with ASD and their typically developing peers in balance, postural control, and overall motor skills, highlighting the need for systematic and multidimensional assessment of motor functioning (Martín-Díaz et al., 2024). Postural control is particularly important for effective motor functioning, as it enables the body to maintain stability in different positions and during purposeful movement. In children with ASD, difficulties in postural regulation may be associated with reduced balance capacity and less efficient strategies for maintaining body stability. In our previous study, a structured program combining sensory integration with physiotherapy-based balance training resulted in significant improvements in static and dynamic balance, postural stability, and coordination in children with ASD (Mihaylov, 2026). These findings emphasize the importance of postural control as a key component of motor functioning and support the need for a broader assessment of motor abilities encompassing both gross and fine motor skills. In addition to balance and postural control,

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children with ASD may experience difficulties in performing fundamental motor skills. Evidence from a systematic review and meta-analysis indicates that exercise-based interventions can positively influence locomotor skills, object control, and stability, emphasizing the clinical relevance of targeted motor training (Ji et al., 2023). At the same time, these findings highlight the importance of identifying specific areas of motor impairment before intervention in order to tailor therapeutic programs to the individual functional needs of each child. Fine motor skills represent another essential component of motor development, as they are required for the successful performance of numerous daily and educational activities. A large-scale study involving young children demonstrated differences in fine motor performance according to diagnostic profile, with children with ASD exhibiting specific characteristics in manual and visual-motor functioning (Lin et al., 2024). These findings suggest that the assessment of motor development should not be limited to gross motor abilities and balance but should also encompass skills related to movement precision, speed, and coordination. Within this context, comprehensive assessment of motor functioning is particularly relevant to physiotherapy and occupational therapy practice. The combined evaluation of balance, postural control, lower-limb explosive power, hand muscle strength, fine motor skills, spatial orientation, and motor response speed allows for the development of a more comprehensive individual motor profile. Such an assessment may facilitate the identification of specific motor deficits and provide a foundation for planning targeted physiotherapy and occupational therapy interventions. Therefore, the aim of the present study is to assess motor development and identify the predominant motor deficits in children with ASD aged 4–7 years using a comprehensive battery of standardized motor tests evaluating balance, postural control, muscle strength, fine motor skills, spatial orientation, and motor speed.

2. MATERIALS AND METHODS

The present study employed a cross-sectional descriptive-analytical design to investigate motor development and identify the predominant motor deficits in children with Autism Spectrum Disorder (ASD). The analysis was based exclusively on baseline assessment data obtained prior to the implementation of the therapeutic intervention. A total of 60 children diagnosed with ASD, aged 4–7 years, participated in the study. The diagnosis had been previously established according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) by qualified clinical specialists. The participants were subsequently allocated into an experimental group (EG; $n = 30$) and a control group (CG; $n = 30$) as part of a broader intervention study. However, the present analysis includes only the baseline motor assessment performed before the intervention. Therefore, the primary focus of the current study is the motor profile and motor deficits of the total sample ($n = 60$), rather than the effects of the therapeutic intervention. Motor performance was evaluated using a comprehensive battery of standardized motor tests assessing both gross and fine motor abilities. The assessment covered six major functional domains:

- Pediatric Berg Balance Scale (PBBBS) – assessment of static and dynamic balance and functional postural control;
- Standing Long Jump Test – assessment of lower-limb explosive power;
- Hand Dynamometry – measurement of maximal hand grip strength;
- Graphic Dictation Test – assessment of fine motor coordination and visuomotor integration;
- Spatial Orientation Speed Test – assessment of spatial orientation and motor organization;
- Tapping Test – assessment of motor speed and upper-limb movement frequency.

All assessments were administered individually under standardized conditions. The same assessment procedures were applied to all participants in order to ensure consistency and minimize measurement variability.

Statistical analyses were performed primarily for the total sample ($n = 60$) in order to characterize the overall motor profile of children with ASD. Continuous variables were summarized using mean values and standard deviations (Mean $\pm$ SD), while categorical variables were presented as absolute frequencies and percentages. Baseline results were additionally examined separately for the experimental and control groups to assess group comparability prior to intervention. Between-group differences in continuous variables were analyzed using appropriate parametric or non-parametric tests according to the distribution of the data. Differences in categorical variables were examined using the chi-square (χ^2) test. Statistical significance was set at $p < 0.05$.

3. RESULTS

A total of 60 children with Autism Spectrum Disorder (ASD), aged 4–7 years, were included in the baseline assessment. Of all participants, 37 (61.67%) were boys and 23 (38.33%) were girls. The control group consisted of 18 boys (60.00%) and 12 girls (40.00%), while the experimental group included 19 boys (63.33%) and 11 girls (36.67%). No statistically significant difference in sex distribution was observed between the groups ($\chi^2(1) = 0.071$, $p = 0.790$). The baseline assessment revealed motor difficulties across multiple functional domains. The most pronounced impairments were observed in balance and postural control. The mean score on the Pediatric Balance Scale was 27.0 ± 6.4 points out of a maximum of 56, indicating substantially reduced balance performance in the examined sample. Difficulties were particularly evident during tasks requiring the maintenance of a stable body position, changes in the base of support, weight transfer, and the controlled execution of functional movements. Performance on the Standing Long Jump Test also indicated limitations in gross motor functioning. The children achieved a mean jumping distance of approximately 63.5 ± 18.7 cm. In addition to reduced lower-limb explosive power, difficulties in coordinating the preparatory phase, take-off, and landing were observed. Some participants demonstrated insufficient arm–leg coordination and reduced postural stability during landing, suggesting that performance was influenced by both strength and motor coordination. Hand dynamometry demonstrated reduced grip strength, with a mean value of approximately 7.2 ± 2.1 kg for the dominant hand and 6.5 ± 2.0 kg for the non-dominant hand. The difference between the two hands indicated functional asymmetry, while the overall performance suggested limitations in upper-limb muscle strength in a proportion of the assessed children. Fine motor performance assessed using the Graphic Dictation Test was also affected. The mean score for the total sample was approximately 5.4 ± 2.6 points out of 12. Based on the established scoring criteria, 8 children (13.33%) demonstrated a high level of performance, 15 (25.00%) a medium level, 24 (40.00%) a low level, and 13 (21.67%) a very low level. Thus, 61.67% of the participants were classified within the low or very low performance categories. The most frequent difficulties involved inaccurate reproduction of graphic elements, errors in movement direction and sequence, and reduced visuomotor coordination. Difficulties were additionally observed in spatial orientation and motor organization. The children required more time and demonstrated a greater number of errors during tasks involving rapid spatial orientation and organization of an appropriate motor response. These findings suggest reduced efficiency in the integration of spatial information with purposeful motor performance. The Tapping Test revealed limitations in motor speed and the frequency of repetitive movements. During the 10-second testing interval, the children produced a mean of approximately 31.8 ± 7.4 dots with the dominant hand and 27.6 ± 6.9 dots with the non-dominant hand, corresponding to approximately 3.18 and 2.76 movements per second, respectively. Differences between the two hands indicated functional asymmetry, while the relatively reduced movement frequency reflected difficulties in rapid repetitive motor performance. Overall, the baseline assessment demonstrated a multidimensional pattern of motor deficits in the examined children with ASD. The most prominent difficulties involved balance and postural control, lower-limb explosive power, hand grip strength, fine motor coordination, spatial organization, and motor speed. The simultaneous involvement of several motor domains indicates that motor difficulties in ASD extend beyond isolated deficits and may affect the overall efficiency and organization of functional movement.

4. DISCUSSION

The present study identified a multidimensional pattern of motor difficulties in children with Autism Spectrum Disorder (ASD), involving balance and postural control, muscle strength, fine motor coordination, spatial organization, and motor speed. The findings support the growing evidence that motor impairments in ASD are not limited to an isolated motor domain but may affect several components of motor functioning simultaneously. This is consistent with the systematic review and meta-analysis by Kangarani-Farahani et al. (2024), which demonstrated that motor difficulties are highly prevalent among children with ASD and may involve both gross and fine motor abilities. Balance and postural control emerged as particularly affected areas in the present sample. The mean Pediatric Balance Scale score of 27.0 ± 6.4 points suggests substantial difficulties in maintaining postural stability during functional motor tasks. Similar findings were reported by Martín-Díaz et al. (2024), who observed significantly poorer performance in static and dynamic balance and overall motor skills in children with ASD compared with neurotypically developing peers. More recent evidence from the systematic review and meta-analysis by Xu et al. (2025) further indicates that children and adolescents with ASD experience difficulties across several dimensions of balance control, particularly sensory orientation, verticality, and anticipatory postural adjustments.

These findings suggest that impaired balance in ASD may reflect broader difficulties in the organization and integration of sensory information required for efficient postural regulation. The relationship between sensory processing and postural control appears particularly relevant during early childhood. Ferreiro-Pérez et al. (2024) demonstrated alterations in the use of sensory information for postural control in preschool children with ASD, emphasizing the importance of sensory processing for maintaining stability during functional activities. This relationship is also consistent with our previous findings, in which a structured program combining sensory integration and physiotherapy-based balance training was associated with improvements in static and dynamic balance, postural stability, and coordination in children with ASD (Mihaylov, 2026). Taken together, these observations support the inclusion of postural control and sensory-motor integration as important components of motor assessment and intervention planning in children with ASD. The observed limitations in lower-limb explosive power and hand grip strength further demonstrate that the motor profile of children with ASD extends beyond balance deficits. Reduced muscle performance may influence the execution of activities requiring jumping, propulsion, stabilization, object manipulation, and sustained physical effort. Martín-Díaz et al. (2024) similarly identified strength as one of the motor domains showing pronounced differences between children with ASD and neurotypically developing participants. These deficits may have functional implications for participation in play, physical activity, self-care, and other age-appropriate daily activities. Fine motor difficulties represented another important component of the motor profile. Reduced performance in the Graphic Dictation Test indicated difficulties in precise movement control, visuomotor integration, and the organization of sequential hand movements. Lin et al. (2024) also identified distinctive patterns of fine motor performance among young children with ASD, supporting the need to include fine motor assessment as part of a comprehensive evaluation. Such difficulties may be particularly relevant during the preschool and early school years, when drawing, writing preparation, object manipulation, dressing, and other activities increasingly require accurate and coordinated hand movements. The findings related to spatial orientation and the Tapping Test additionally suggest difficulties in the speed and organization of motor responses. Reduced frequency of repetitive movements and differences between the dominant and non-dominant hands may reflect limitations in rapid motor execution and functional asymmetry. When considered together with deficits in balance, strength, and fine motor coordination, these findings reinforce the view that motor difficulties in ASD should be approached as a complex functional profile rather than as isolated impairments. From a clinical perspective, comprehensive motor assessment may therefore provide valuable information for individualized intervention planning. Physiotherapy interventions may target postural control, balance, muscle strength, coordination, and gross motor performance, whereas occupational therapy can further address fine motor abilities, visuomotor integration, motor planning, and the transfer of acquired skills to meaningful everyday activities. A systematic review by Date et al. (2024) indicates that different sensorimotor interventions may improve aspects of postural balance control in individuals with ASD, although heterogeneity across intervention protocols and outcome measures limits the generalizability of current evidence. This highlights the importance of individualized assessment and clearly defined therapeutic objectives. Overall, the present findings support the inclusion of systematic motor assessment in the clinical evaluation of children with ASD. Early identification of deficits in balance, postural control, strength, coordination, and motor speed may facilitate the development of more targeted physiotherapy and occupational therapy programs aimed not only at improving isolated motor abilities but also at promoting functional independence and participation in everyday activities.

5. CONCLUSION

Children with Autism Spectrum Disorder demonstrate a multidimensional pattern of motor deficits affecting both gross and fine motor functioning. The most prominent difficulties involve balance and postural control, muscle strength, fine motor coordination, spatial organization, and motor speed. These findings highlight the importance of comprehensive motor assessment for the early identification of functional limitations. Individualized physiotherapy and occupational therapy interventions targeting the identified deficits may contribute to improved motor performance, functional independence, and participation in everyday activities.

REFERENCES

- Date, S., Munn, E., & Frey, G. C. (2024). Postural balance control interventions in autism spectrum disorder (ASD): A systematic review. *Gait & Posture*, 109, 170–182. <https://doi.org/10.1016/j.gaitpost.2024.01.034>.
- Ferreiro-Pérez, M., Abuín-Porras, V., Martín-Casas, P., & Ortiz-Gutiérrez, R. M. (2024). Postural control and sensory processing in preschool children with autistic spectrum disorder: A cross-sectional study. *Children*, 11(3), 303. <https://doi.org/10.3390/children11030303>.
- Ji, Y.-Q., Tian, H., Zheng, Z.-Y., Ye, Z.-Y., & Ye, Q. (2023). Effectiveness of exercise intervention on improving fundamental motor skills in children with autism spectrum disorder: A systematic review and meta-analysis. *Frontiers in Psychiatry*, 14, 1132074. <https://doi.org/10.3389/fpsy.2023.1132074>.
- Kangarani-Farahani, M., Malik, M. A., & Zwicker, J. G. (2024). Motor impairments in children with autism spectrum disorder: A systematic review and meta-analysis. *Journal of Autism and Developmental Disorders*, 54(5), 1977–1997. <https://doi.org/10.1007/s10803-023-05948-1>.
- Lin, L.-Y., Hwang, I.-T., Hsu, C.-F., Yu, W.-H., Lai, P.-C., Chen, Y.-W., & Tu, Y.-F. (2024). Comparing fine motor performance among young children with autism spectrum disorder, intellectual disability, attention-deficit/hyperactivity disorder, and specific developmental disorder of motor function. *Frontiers in Pediatrics*, 12, 1372980. <https://doi.org/10.3389/fped.2024.1372980>.
- Magdalini Vasilakaki, E., & Simonska, M. (2025). Language development of children with autism spectrum disorder: relationship to the ratio of hand fingers length (2D:4D). *KNOWLEDGE - International Journal*, 73(1), 371–375. Retrieved from <https://ojs.ikm.mk/index.php/kij/article/view/7924>
- Martín-Díaz, P., Cuesta-Gómez, A., Fernández-González, P., & Carratlá-Tejada, M. (2024). Balance and motor skills differences between children and teenagers with autism spectrum disorder and neurotypically developing. *Autism Research*, 17(8), 1545–1555. <https://doi.org/10.1002/aur.3181>.
- Mihaylov, I. (2026). Assessment of sensory processing in children with autism spectrum disorder using the short sensory profile: a study of 60 participants. *MEDIS – International Journal of Medical Sciences and Research*, 5(2), 87-91. <https://doi.org/10.35120/medisij0502087m>
- Mihaylov, I. (2026). Effectiveness of sensory integration interventions on postural control development in children with autism spectrum disorder: An experimental study. *Knowledge – International Journal*, 75(4), 403–408.
- Xu, W., Li, N., & Qi, J. (2025). Balance control in children and youth with autism spectrum disorder: A systematic review and meta-analysis. *Alpha Psychiatry*, 26(3), 42869. <https://doi.org/10.31083/AP42869>.

BLOOD DONATION IN DONORS WITH ARTERIAL HYPERTENSION: CURRENT ELIGIBILITY CRITERIA AND CHALLENGES

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Abstract: Blood donation occupies a central place in modern transfusion medicine and is essential for ensuring timely and safe transfusion therapy. The effective functioning of transfusion systems depends directly on maintaining a stable pool of voluntary and regular blood donors, which requires optimization of donor selection while strictly adhering to medical and ethical principles for protecting donor health.

Over recent decades, chronic non-communicable diseases have tended to occur at younger ages worldwide, changing the health profile of potential donors and creating new challenges for transfusion medicine. Conditions traditionally associated with older age are increasingly being seen in younger people, resulting in a growing proportion of individuals with chronic conditions who are willing to participate in blood donation programs. In this context, arterial hypertension has become one of the most common chronic conditions and affects a substantial proportion of working-age adults, including potential blood donors. Its increasing prevalence poses challenges for transfusion practice, particularly with regard to reconsidering traditional eligibility criteria, individual risk assessment, and ensuring donor safety during and after donation.

Historically, arterial hypertension was often regarded as a relative or absolute contraindication to blood donation because of concerns about adverse hemodynamic reactions. Current scientific evidence and international guidelines support a more differentiated approach in which the degree of blood pressure control, the stability of antihypertensive therapy, and the absence of clinically significant complications are the key considerations. Accordingly, the presence of arterial hypertension alone is increasingly recognized as not constituting an automatic contraindication to blood donation.

1. INTRODUCTION

Arterial hypertension is one of the most prevalent chronic diseases among working-age adults and is a leading modifiable risk factor for cardiovascular morbidity and mortality. Its increasing prevalence, including among potential blood donors, challenges transfusion medicine to reconcile donor safety with the need to maintain a sustainable donor pool. In this context, European recommendations for the management of arterial hypertension are highly relevant to the development of contemporary donor selection criteria.

2. AIM

This review aims to systematize and analyze current scientific publications, recommendations, and good practices related to blood donation in individuals with arterial hypertension, with emphasis on donor selection criteria, potential risks, the significance of antihypertensive therapy, and the role of healthcare professionals in assessing, monitoring, and ensuring donor safety.

3. METHODOLOGY

This publication is a narrative literature review intended to summarize and analyze current scientific evidence on blood donation in donors with arterial hypertension. Medical and organizational aspects of donor selection were examined, with a particular focus on donor safety.

The literature search was conducted in PubMed/MEDLINE, Scopus, and Web of Science, as well as in official guidelines and recommendations issued by international and national health and transfusion organizations. The keywords blood donation, arterial hypertension, donor eligibility, and donor safety were used in combination with the Boolean operators AND and OR.

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Peer-reviewed scientific publications and relevant regulatory documents addressing eligibility criteria for donors with arterial hypertension, physiological responses, and risks associated with blood donation were included. The data were analyzed and synthesized thematically in the context of contemporary transfusion practice.

3.1. Arterial hypertension: definition, classification, and clinical context

According to the 2018 recommendations of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH), arterial hypertension is a chronic condition characterized by a persistent elevation in arterial blood pressure that exceeds the physiological regulatory capacity of the cardiovascular system and is associated with an increased risk of cardiovascular, cerebrovascular, and renal complications (Williams et al., 2018). In clinical practice, it is defined as office blood pressure with systolic values ≥ 140 mmHg and/or diastolic values ≥ 90 mmHg, confirmed by repeated measurements performed under standardized conditions (Williams et al., 2018).

According to the updated 2024 European classification of blood pressure, values in adults are divided into the following categories:

- Normal blood pressure – systolic < 120 mmHg and diastolic < 70 mmHg;
- Elevated blood pressure – systolic $120\text{--}139$ mmHg and/or diastolic $70\text{--}89$ mmHg;
- **Arterial hypertension – systolic ≥ 140 mmHg and/or diastolic ≥ 90 mmHg** (McEvoy et al., 2024).

Within arterial hypertension, degrees of severity are also distinguished, which are relevant both to clinical management and to assessing eligibility for blood donation:

- Grade I – $140\text{--}159 / 90\text{--}99$ mmHg;
- Grade II – $160\text{--}179 / 100\text{--}109$ mmHg;
- Grade III – ≥ 180 mmHg / ≥ 110 mmHg.

In transfusion medicine, it is essential to distinguish clearly between the diagnostic classification of arterial hypertension and the assessment of the donor's current hemodynamic stability required for safe blood donation. Blood pressure values therefore need to be interpreted in relation to the donor's overall condition, the degree of hypertension control, the stability of antihypertensive therapy, and the absence of clinically significant complications (World Health Organization, 2012).

3.2. Antihypertensive therapy and its relevance to donor safety

According to current ESC clinical recommendations, antihypertensive therapy is based on several major drug classes, used either alone or in combination to achieve sustained blood pressure control and reduce cardiovascular risk. The principal therapeutic classes include angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, calcium channel blockers, diuretics, and beta-adrenergic blockers for selected clinical indications. In resistant hypertension and specific clinical situations, other drug classes may also be used, including mineralocorticoid receptor antagonists and centrally acting agents.

Contemporary treatment increasingly relies on combination therapy, which allows lower doses to be used, improves tolerability, and provides more effective blood pressure control. In transfusion practice, knowledge of antihypertensive therapy is important because treatment may influence hemodynamic stability and the risk of adverse reactions during blood donation. Careful assessment of the therapeutic regimen and its stability supports accurate evaluation of donor eligibility and effective preventive monitoring.

3.3. European guidelines from 2018 and 2024: aspects relevant to donor selection

The 2024 European guidelines on arterial hypertension reflect an evolution in the assessment and management of elevated blood pressure compared with the 2018 ESC/ESH guidelines, placing greater emphasis on early intervention and prevention of cardiovascular risk. The diagnostic threshold for arterial hypertension remains $\geq 140/90$ mmHg, while an expanded classification introduces the category of "elevated blood pressure" ($120\text{--}139/70\text{--}89$ mmHg), which is considered clinically relevant because of its association with increased cardiovascular risk (McEvoy et al., 2024; Williams et al., 2018).

A substantial change is also evident in therapeutic targets. Whereas the 2018 guidelines recommended a stepwise reduction in blood pressure, initially targeting $< 140/90$ mmHg with further reduction if treatment was well tolerated, the 2024 guidelines define lower target values, with a preferred systolic blood pressure target of $120\text{--}129$ mmHg for most patients. This approach is supported by evidence of a greater reduction in cardiovascular morbidity and mortality with more intensive blood pressure control, provided that treatment is individualized and well tolerated.

The 2024 guidelines also strengthen the role of out-of-office blood pressure measurement, recommending 24-hour ambulatory and home monitoring as standard approaches for confirming the diagnosis, refining risk stratification, and reducing the influence of phenomena such as white-coat hypertension. Pharmacological management has likewise shifted from a conservative model based on

initial monotherapy toward earlier use of dual combination therapy to achieve and maintain target values more rapidly.

Despite the potential clinical benefits, applying stricter target values may result in a smaller proportion of patients being classified as adequately controlled in real-world populations. This highlights the need to optimize treatment strategies, improve adherence, and actively involve healthcare professionals in long-term follow-up. In blood donation practice, this context is important because the assessment of blood pressure control influences eligibility decisions and the frequency of donor deferrals.

3.4. Eligibility criteria for blood donors with arterial hypertension – literature synthesis

Current transfusion guidelines and scientific publications consistently treat arterial hypertension as a condition in which eligibility for blood donation is determined by current blood pressure values, the degree of disease control, the stability of antihypertensive therapy, and the absence of clinical complications, rather than by the diagnosis itself (AABB, America's Blood Centers, & American Red Cross, 2022; Eder et al., 2009; Newman, 2013b; World Health Organization, 2012).

In the United States, the selection of donors with arterial hypertension is regulated through clearly defined numerical thresholds. Under federal regulations, donors should have a systolic blood pressure between 90 and 180 mmHg and a diastolic blood pressure of no more than 100 mmHg on the day of donation. Values outside these limits may be accepted only after an individual medical assessment and documented determination that donation is safe (U.S. Food and Drug Administration, 2026). Practical guidance from the American Red Cross is consistent with this regulatory model and explicitly states that well-controlled hypertension and the use of antihypertensive medication do not constitute contraindications, whereas a measured blood pressure above 180/100 mmHg results in temporary deferral.

In contrast to this threshold-based model, the United Kingdom and Ireland use a more clinically oriented approach in which publicly fixed numerical blood pressure limits are not the primary criterion. The Donor Selection Guidelines of the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services state that donors with arterial hypertension should not donate in the presence of symptoms such as dizziness or syncope, heart failure, significant renal impairment, or when antihypertensive treatment has been changed within the previous four weeks (Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee, 2022).

Similar criteria are applied by the Irish Blood Transfusion Service, where blood donation is acceptable when blood pressure is well controlled, orthostatic hypotension is absent, and therapy is stable without recent adjustments (Irish Blood Transfusion Service, 2023).

A similar clinically based approach is found in the New Zealand Blood Service guidelines, where hypertension and antihypertensive treatment are considered compatible with blood donation when control is adequate and symptoms are absent. Additional restrictions apply to donors taking beta-blockers, including a minimum period of stable therapy and an adequate heart rate, to reduce the risk of adverse hemodynamic reactions (New Zealand Blood Service, 2021).

Canadian Blood Services provides an organizational example of a more liberalized, risk-adapted model. In this system, routine blood pressure measurement is not performed at every subsequent donation, and in first-time donors isolated values outside predefined ranges do not automatically result in deferral (Canadian Blood Services, 2022). This approach is supported by empirical studies showing that automatically deferring donors solely because of transient deviations in blood pressure does not significantly reduce adverse reactions but can substantially reduce the available donor pool (Clement et al., 2021; Goldman et al., 2013).

European practices for accepting blood donors with arterial hypertension are characterized by the absence of a single, legally fixed "European threshold" for blood pressure; instead, selection criteria are shaped within national regulatory and organizational frameworks. Despite this variability, a value of approximately 180/100 mmHg is commonly used as a practical reference, particularly in systems where blood pressure measurement is part of mandatory pre-donation screening (Ringdal et al., 2022b). At the same time, major European guidance documents, including the Guide to the Preparation, Use and Quality Assurance of Blood Components issued by the European Directorate for the Quality of Medicines & HealthCare (EDQM), emphasize that systematic measurement of blood pressure and pulse is not a mandatory requirement for determining donor eligibility. This allows for a more flexible, clinically oriented approach based on individual risk assessment (European Directorate for the Quality of Medicines & HealthCare, 2025).

In continental Europe, several countries use threshold-based models with clearly defined numerical limits. Germany and Italy are representative examples, where eligibility for blood donation is generally determined at systolic blood pressure values up to 180 mmHg and diastolic values up to 100 mmHg, with medical judgment applied in borderline cases. National transfusion and health authorities in these

countries use these values as reference points for donor safety, resulting in a hybrid model that combines numerical thresholds with clinical discretion (Bundeszentrale für gesundheitliche Aufklärung, 2023; Ministero della Salute, 2023).

In addition, some European countries use a more restrictive or “intermediate” selective approach in which values above a given level do not automatically lead to definitive exclusion but require mandatory medical assessment. Such an approach is formally described in France, where temporary non-acceptance on the day of donation is provided for resting blood pressure >180 mmHg systolic and/or >100 mmHg diastolic, while at values >160/90 mmHg donation may be permitted at the discretion of the physician in the transfusion service (République Française, 2016).

The Scandinavian countries illustrate a more dynamic and evolving approach. In Norway, policies have gradually shifted from more restrictive rules for donors with arterial hypertension and those receiving antihypertensive treatment toward a more liberal, risk-adapted model. This development is based on accumulating empirical evidence showing no increased risk of adverse reactions in donors with well-controlled hypertension and demonstrates how national practice can evolve in response to scientific evidence and the needs of the donor system (Ringdal et al., 2022b).

3.5. Summary of the literature synthesis

The literature identifies two predominant models for selecting blood donors with arterial hypertension:

(1) a regulatory threshold-based framework based on specific numerical blood pressure values;

(2) a clinically oriented framework in which disease and treatment stability, absence of symptoms, and absence of hypertensive complications are the principal considerations.

Both approaches broadly share the view that controlled arterial hypertension is not a contraindication to blood donation when an adequate individual assessment of donor risk is performed.

3.6. Bulgaria – regulatory framework and position within European models

Against the background of European variability, national systems determine the specific thresholds and mechanisms used for pre-donation assessment. In the Republic of Bulgaria, eligibility for blood donation in individuals with arterial hypertension is governed by a clearly formalized regulatory framework set out in the medical standard “Transfusion Hematology,” approved by Ordinance No. 9 of 25 April 2006 of the Ministry of Health, as subsequently amended. Under this standard, assessment of a prospective donor’s health status includes a mandatory pre-donation medical examination in which blood pressure measurement is an obligatory component.

The regulation states that individuals with systolic blood pressure up to 180 mmHg and diastolic blood pressure up to 100 mmHg are eligible to donate. Values above these limits are grounds for temporary deferral unless an individual medical assessment documents that donation does not pose a risk to the donor’s health (Ministry of Health of the Republic of Bulgaria, 2006). The Bulgarian system therefore applies a regulatory threshold-based framework in which numerical blood pressure values play a central role in donor selection.

From a practical perspective, this model provides a high degree of uniformity in eligibility criteria across blood centers and mobile teams throughout the country. Clearly defined thresholds facilitate the work of healthcare professionals involved in donor screening and reduce subjective differences in assessment between individual services. This is particularly important in a decentralized blood donation system and when large numbers of donors are being assessed. At the same time, the Bulgarian regulatory framework does not formally define an intermediate threshold (for example, around 160/90 mmHg) that would serve as a warning zone requiring greater caution and more detailed clinical assessment, as is provided in some other European countries such as France. Consequently, the model can be described as more strictly threshold based, with limited flexibility in borderline or situationally elevated blood pressure, for example in white-coat hypertension or stress before donation.

Within the spectrum of European practice, Bulgaria is positioned close to continental European countries that use similar numerical thresholds, such as Italy and Germany, and determine eligibility largely on the basis of blood pressure values measured at the time of donation. In contrast to the clinically oriented models used in the United Kingdom and Ireland, where disease stability, symptoms, and changes in therapy play a leading role, Bulgarian practice places greater emphasis on objectively measurable indicators defined at regulatory level.

In summary, the Bulgarian system for selecting blood donors with arterial hypertension is characterized by clear regulatory provisions, a high degree of standardization, and a threshold-based model using a limit of 180/100 mmHg. This approach provides predictability and organizational consistency but raises the question of whether more flexible mechanisms for

individual clinical assessment should be introduced for donors with well-controlled hypertension, in line with trends in contemporary European transfusion practice.

4. DISCUSSION

4.1. Clinical safety and control of arterial hypertension in blood donation

Epidemiological, clinical, and observational evidence accumulated over the past decade consistently supports the view that controlled arterial hypertension is not an independent risk factor for serious adverse reactions to blood donation when the donor is clinically stable and antihypertensive therapy has remained unchanged (J. M. Johnsen et al., 2023; Newman, 2013a). Contemporary cohort and observational studies, including Scandinavian population analyses, do not show an increased frequency of severe hemodynamic complications in hypertensive donors compared with normotensive donors, provided that blood pressure is adequately controlled and there is no target-organ damage (K. M. N. Johnsen et al., 2023; Nissen-Meyer & Seghatchian, 2019; Stainsby et al., 2010). Physiological adaptation to moderate acute volume loss during blood donation further supports this conclusion. Current experimental and clinical data indicate that, in healthy and compensated individuals, whole-blood donation produces moderate and transient changes in peripheral blood pressure without substantial impairment of central hemodynamics, aortic pressure, or vascular stiffness (Thibeault et al., 2025). This is directly relevant to donors with well-controlled hypertension, in whom compensatory mechanisms are generally preserved and allow the donation procedure to be completed safely.

Accumulating evidence does not support a causal relationship between blood donation and the development or worsening of arterial hypertension. Instead, the main risk profiles are associated predominantly with vasovagal reactions rather than elevated blood pressure. Particularly informative in this context is the large national retrospective case-control study by Wang et al., which included 1,253,678 blood donations between 2010 and 2013. The authors reported an extremely low rate of adverse reactions (0.1%); in multivariable analysis, lower pre-donation systolic blood pressure (<124 mmHg), rather than elevated values, was identified as an independent risk factor for adverse events. In contrast, pre-donation diastolic blood pressure ≥ 75 mmHg was not associated with increased risk, calling into question traditionally restrictive approaches to donors with controlled hypertension (Wang et al., 2019).

These objective clinical findings are complemented by the donor perspective examined in the national survey by Makowicz et al., which included 2,387 voluntary blood donors. The authors reported that 89.7% of respondents did not consider regular blood donation likely to increase arterial blood pressure, and confidence in this view increased significantly with greater donation experience ($p < 0.001$). Although the study was based on subjective self-assessment and did not include direct clinical measurements, its findings are consistent with observational and clinical data indicating no adverse effect of blood donation on blood pressure in clinically stable individuals (Makowicz et al., 2022).

In this context, equating the diagnosis of arterial hypertension with increased donor risk without sufficient clinical justification may lead to overly cautious decisions and unnecessary restriction of the donor pool. The contemporary evidence-based model supports a shift from a diagnosis-oriented to a function-oriented approach, in which current hemodynamic stability, symptoms, and changes in therapy are more important than the formal diagnostic label (Newman, 2013a).

Epidemiological data from a large donor study in the United States further highlight the importance of definitional and organizational factors in assessing arterial hypertension in transfusion practice. An analysis of more than 116,000 blood donors showed that application of the updated 2017 ACC/AHA (American College of Cardiology/American Heart Association) criteria would classify more than half of donors as hypertensive, including approximately 47% of individuals aged 20–44 years (Housekeeper et al., 2020). This clearly demonstrates the need to distinguish between the diagnostic classification of arterial hypertension and blood donor eligibility criteria, which should be based on actual functional risk. At the same time, the high frequency with which elevated blood pressure is detected positions blood donation centers as an effective platform for public health screening and health promotion without necessarily requiring unjustified restriction of the donor pool.

4.2. Role of antihypertensive therapy in donor risk assessment

Analysis of the current literature indicates that antihypertensive therapy itself does not increase the risk of adverse reactions when it is stable and well tolerated (Joint Professional Advisory Committee, 2022; K. M. N. Johnsen et al., 2023). On the contrary, effective pharmacological blood pressure control may be considered a factor contributing to donor safety by reducing blood pressure variability and the risk of extreme hemodynamic responses (European Directorate for the Quality of Medicines & HealthCare,

2023). In practice, however, different drug classes may have different implications for donor selection. For example, beta-blockers may limit compensatory tachycardia during acute volume loss, warranting closer assessment of heart rate and symptoms, whereas diuretics require attention to hydration status (McEvoy et al., 2024). These considerations support the need for a careful clinical interview and professional interpretation rather than formal application of universal exclusion criteria.

Contemporary transfusion guidelines increasingly position antihypertensive treatment as part of the overall clinical assessment rather than as an independent reason for deferral, consistent with the concept of risk-adapted donor selection (European Directorate for the Quality of Medicines & HealthCare, 2023; Joint Professional Advisory Committee, 2022).

4.3. Organizational consequences of threshold-based models and donor deferral

From an organizational perspective, arterial hypertension is among the leading causes of temporary deferral from blood donation in many national transfusion systems, particularly where blood pressure is routinely measured before donation and fixed numerical thresholds are applied. Available empirical evidence suggests that automatic deferral based on a single measurement outside a predefined range does not substantially reduce the frequency of adverse reactions, while it may have a clear negative effect on donor retention and repeat donation (D. S. Lamba et al., 2023; Maghsudlu et al., 2024; R. Lamba et al., 2023; Thibeault et al., 2025).

This effect is particularly relevant in individuals with labile or situationally elevated blood pressure, including white-coat hypertension, increased emotional stress before donation, or physical exertion immediately before assessment (McEvoy et al., 2024). In transfusion systems with limited clinical flexibility, such donors may be deferred repeatedly, which can ultimately result in the loss of potential regular donors and additional pressure on blood supplies. In this context, the regulatory and conceptual analysis by Debecho and Hailu further supports reconsideration of strictly threshold-based models. The authors emphasize that treated, clinically stable arterial hypertension is not a contraindication to blood donation provided that blood pressure is within acceptable limits at the time of donation and does not show marked fluctuations. Particular attention is drawn to the risk of unjustified deferral based on a single measurement in situations characteristic of the donor setting, such as white-coat hypertension, supporting the need for individualized, clinically oriented assessment rather than formal application of fixed numerical thresholds (Debecho & Hailu, 2019).

In response to these organizational and clinical challenges, some transfusion systems have introduced more flexible models of pre-donation assessment, including repeat measurement after a short period of rest, clinical triage, or selective measurement. Available data suggest that these approaches may achieve a better balance between donor safety and the availability of blood components without compromising safety (Canadian Blood Services, n.d.). Blood pressure is therefore retained as an important risk indicator but interpreted as part of a broader clinical and organizational assessment tailored to the donor's individual functional profile.

4.4. Clinically oriented versus regulatory threshold-based models – comparative analysis

Comparison of international practice identifies two conceptually different but partly overlapping models. Regulatory threshold-based models provide a high degree of standardization, legal clarity, and operational predictability, which is particularly important in large and decentralized systems, but they limit individualized clinical assessment in borderline cases (Bundesärztekammer, 2023; U.S. Food and Drug Administration, 2026). Clinically oriented models, used in the United Kingdom, Ireland, and some Scandinavian countries, provide greater flexibility and allow more precise differentiation between actual and potential risk, but they require a higher level of clinical competence and organizational resources (Irish Blood Transfusion Service, n.d.; Joint Professional Advisory Committee, 2026).

Current scientific evidence does not demonstrate the clear superiority of either model in terms of safety, but it does indicate that excessive restrictiveness does not produce proportional benefits, while risk-adapted approaches can optimize donor selection without compromising safety.

4.5. Professional aspects and the role of healthcare professionals

In risk-adapted donor selection, healthcare professionals play a key role. Accurate blood pressure measurement, recognition of symptoms associated with hemodynamic instability, assessment of treatment stability, and appropriate donor information are critical elements in evidence-based decision-making (European Directorate for the Quality of Medicines & HealthCare, 2025). A review of the literature indicates that the quality of pre-donation screening depends not only on fixed numerical limits but also on clinical competence and consistency in the application of assessment algorithms, underscoring the need for targeted training and standardized yet flexible protocols.

In the Bulgarian context, the regulatory threshold-based model using a limit of 180/100

mmHg provides clarity and uniformity but also restricts opportunities for individualized clinical judgment in donors with well-controlled hypertension and situationally elevated values. In light of international evidence, this raises the possibility of introducing intermediate clinical mechanisms—such as repeat measurement after a short rest, assessment of symptoms, and evaluation of treatment stability—which could improve the effectiveness of donor selection without compromising safety.

5. CONCLUSION

Comparison of international practices indicates that well-controlled arterial hypertension is not, in itself, a contraindication to blood donation. Eligibility should be determined by blood pressure at the time of assessment, hemodynamic stability, stability of antihypertensive therapy, and the absence of clinical complications rather than by the formal presence of the diagnosis.

International practice broadly follows two approaches: a regulatory threshold-based model using clearly defined numerical limits and a clinically oriented model based on symptoms, stability, and changes in treatment. Both seek to balance safety with preservation of the donor pool, although excessive restrictiveness may result in unnecessary deferral when blood pressure is situationally elevated.

In conclusion, optimization of blood donation criteria for donors with arterial hypertension should be based on individualized risk assessment and an evidence-based balance between protecting donor health and maintaining a sustainable donor pool—an essential condition for the reliable functioning of modern transfusion systems.

REFERENCES

- AABB, America's Blood Centers, & American Red Cross. (2022). Joint comments to the U.S. Food and Drug Administration on blood pressure and pulse donor eligibility requirements.
- Bundesärztekammer. (2023). Richtlinie zur Gewinnung von Blut und Blutbestandteilen und zur Anwendung von Blutprodukten (Richtlinie Hämotherapie): Gesamtnovelle 2023. Bundesärztekammer.
- Bundeszentrale für gesundheitliche Aufklärung. (2023). Blutspende – Voraussetzungen und Ausschlusskriterien. Bundeszentrale für gesundheitliche Aufklärung.
- Canadian Blood Services. (n.d.). Eligibility: Medical conditions and treatments. Canadian Blood Services.
- Canadian Blood Services. (2022). Donor eligibility and wellness guidelines. Canadian Blood Services.
- Clement, M., Shehu, E., & Chandler, T. (2021). The impact of temporary deferrals on future blood donation behavior across the donor life cycle. *Transfusion*, 61(6), 1799–1808. <https://doi.org/10.1111/trf.16387>
- Debecho, D. A., & Hailu, A. (2019). Assessment of blood donation safety by people diagnosed with diabetes, hypertension, malaria and cancer. *Journal of Advances in Medicine and Medical Research*, 29(10), 1–8. <https://doi.org/10.9734/JAMMR/2019/v29i1030136>
- Eder, A. F., Hillyer, C. D., Dy, B. A., Notari, E. P., & Benjamin, R. J. (2009). Adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds. *JAMA*, 301(22), 2279–2286.
- European Directorate for the Quality of Medicines & HealthCare. (2025). Guide to the preparation, use and quality assurance of blood components (22nd ed.). Council of Europe.
- European Directorate for the Quality of Medicines & HealthCare. (2023). Guide to the preparation, use and quality assurance of blood components (21st ed.). Council of Europe.
- Goldman, M., Osmond, L., Yi, Q.-L., Cameron-Choi, K., & O'Brien, S. F. (2013). Frequency and risk factors for donor reactions in an anonymous blood donor survey. *Transfusion*, 53(9), 1979–1984. <https://doi.org/10.1111/trf.12011>
- Housekeeper, J. R., Adams, S. A., Patel, R. R., & Shaz, B. H. (2020). Large number of blood donors have hypertension based on the updated 2017 ACC/AHA hypertension guidelines. *Annals of Blood*, 5, Article 21. <https://doi.org/10.21037/aob.2020.03.02>
- Irish Blood Transfusion Service. (n.d.). Blood pressure: High or low. Irish Blood Transfusion Service.
- Irish Blood Transfusion Service. (2023). Donor eligibility guidelines. Irish Blood Transfusion Service.
- Johnsen, J. M., Ullum, H., Petersen, M. S., et al. (2023). Risk factors for vasovagal reactions in blood donors: A large cohort study. *Transfusion*, 63(1), 45–54. <https://doi.org/10.1111/trf.17223>
- Johnsen, K. M. N., Magnussen, K., Erstad, C., Bhatti, S. N., & Nissen-Meyer, L. S. H. (2023). Safe blood donation from donors using antihypertensive medication: A multi-center retrospective quality study from South-East Norway. *Journal of Blood Medicine*, 14, 337–343. <https://doi.org/10.2147/JBM.S390609>
- Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. (2022). Donor selection guidelines. UK Blood Transfusion and Tissue Transplantation Services.
- Joint Professional Advisory Committee. (2022). Guidelines for the Blood Transfusion Services in the United Kingdom (8th ed.). Joint Professional Advisory Committee.
- Joint Professional Advisory Committee. (2026). Whole blood and component donor selection guidelines (Edition 203, Release 79). UK Blood Transfusion and Tissue Transplantation Services.
- Lamba, R., Kaur, P., Sharma, S., et al. (2023). Causes of donor deferral and their impact on donor return: A systematic review. *Transfusion Medicine Reviews*, 37(1), 15–24. <https://doi.org/10.1016/j.tmr.2022.10.002>
- Lamba, D. S., Sachdev, S., Hans, R., Krishan Dhawan, H., Sharma, R. R., & Marwaha, N. (2023). Review of blood donor deferral with emphasis on donor and patient safety. *Transfusion Clinique et Biologique*, 30(1), 56–62. <https://doi.org/10.1016/j.transcli.2022.10.002>

- org/10.1016/j.traccli.2022.07.002
- Maghsudlu, M., Teimourpour, A., Amini-Kafiabad, S., Nazemi, A. M., O'Brien, S. F., & Sarem, F. (2024). The return rate of deferred blood donors in Iran. *Transfusion Clinique et Biologique*, 31(3), 135–140. <https://doi.org/10.1016/j.traccli.2024.04.002>
- Makowicz, D., Dziubaszewska, R., Lisowicz, K., & Makowicz, N. (2022). Impact of regular blood donation on the human body: Donors' perspective. *Journal of Transfusion Medicine*, 15(2), 133–140. <https://doi.org/10.5603/JTM.2022.0011>
- McEvoy, J. W., McCarthy, C. P., Bruno, R. M., Elliott, W. J., Hayward, C., Laurent, S., et al. (2024). 2024 ESC guidelines for the management of elevated blood pressure and hypertension. *European Heart Journal*, 45(38), 3912–4018. <https://doi.org/10.1093/eurheartj/ehae178>
- Ministero della Salute. (2023). Chi può donare il sangue. Ministero della Salute.
- Ministry of Health of the Republic of Bulgaria. (2006). Ordinance No. 9 of 25 April 2006 approving the medical standard "Transfusion Hematology." *State Gazette*, No. 41 of 19 May 2006, as subsequently amended and supplemented. [in Bulgarian].
- New Zealand Blood Service. (2021). Blood donor eligibility criteria. New Zealand Blood Service.
- Newman, B. H. (2013a). Blood donor complications after whole-blood donation. *Current Opinion in Hematology*, 20(6), 533–537. <https://doi.org/10.1097/MOH.0b013e328365a90b>
- Newman, B. H. (2013b). Donor suitability and hypertension. *Transfusion*, 53(6), 1149–1153. <https://doi.org/10.1111/trf.12008>
- Nissen-Meyer, L. S. H., & Seghatchian, J. (2019). Donor health assessment—When is blood donation safe? *Transfusion and Apheresis Science*, 58(1), 113–116. <https://doi.org/10.1016/j.transci.2018.12.016>
- Penjišević, A., & Sančanin, B. (2023). Key factors for safe and rational security of blood and blood components. *MEDIS – International Journal of Medical Sciences and Research*, 2(3), 19-24. <https://doi.org/10.35120/medisij020319p>
- République Française. (2016). Arrêté du 5 avril 2016 fixant les critères de sélection des donneurs de sang: Annexe II (version updated September 2, 2025). *Légifrance*.
- Ringdal, K. G., Lappegård, J., Wiersum-Osselton, J., et al. (2022). Blood donor selection and deferral in Europe: Past, present and future. *Vox Sanguinis*, 117(6), 729–738.
- Ringdal, K. G., Kjaergaard, J., Ullum, H., et al. (2022). Blood pressure and adverse donor reactions: A population-based cohort study. *Transfusion*, 62(4), 789–798. <https://doi.org/10.1111/trf.16851>
- Stainsby, D., Brunskill, S., Chapman, C. E., Dorée, C., & Stanworth, S. (2010). Safety of blood donation from individuals with treated hypertension or non-insulin dependent type 2 diabetes: A systematic review. *Vox Sanguinis*, 98(3), 431–440. <https://doi.org/10.1111/j.1423-0410.2009.01275.x>
- Thibeault, C., Lewin, A., Rabusseau, I., & Germain, M. (2025). Deferring blood donors with out-of-range blood pressure: Does it decrease the risk of adverse reactions? *Transfusion*, 65(6), 1083–1091. <https://doi.org/10.1111/trf.18264>
- U.S. Food and Drug Administration. (2026). Code of Federal Regulations, Title 21, Part 630: Requirements for blood and blood components. U.S. Government Publishing Office.
- Wang, H.-H., Chen, P.-M., Lin, C.-L., Jau, R.-C., Hsiao, S.-M., & Ko, J.-L. (2019). Joint effects of risk factors on adverse events associated with adult blood donations. *Medicine*, 98(44), e17758. <https://doi.org/10.1097/MD.00000000000017758>
- Williams, B., Mancia, G., Spiering, W., Agabiti Rosei, E., Azizi, M., Burnier, M., et al. (2018). 2018 ESC/ESH guidelines for the management of arterial hypertension. *European Heart Journal*, 39(33), 3021–3104. <https://doi.org/10.1093/eurheartj/ehy339>
- World Health Organization. (2012). Blood donor selection: Guidelines on assessing donor suitability for blood donation. World Health Organization.

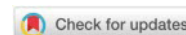
NEURAL COMPENSATION DURING INFORMATION PROCESSING IN NORMAL COGNITIVE AGING: A FOCUSED TASK-BASED FMRI REVIEW

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Abstract: Normal cognitive aging is heterogeneous. Processing speed, working memory, cognitive flexibility, and executive control often decline with age. Semantic knowledge is usually better preserved. Task-based functional magnetic resonance imaging (fMRI) can show how neural recruitment changes before overt cognitive impairment. This focused review examines task-based fMRI studies in cognitively healthy middle-aged and older adults. The main domains are semantic retrieval, working memory, interference control, response inhibition, and set shifting. Evidence was identified through PubMed/MEDLINE searches through 22 July 2026, targeted searches for recent task-fMRI studies, and backward and forward citation tracking. Across domains, older adults show changes in prefrontal lateralization, earlier recruitment of dorsolateral prefrontal and frontoparietal regions, and lower segregation between control and default-mode systems. These findings do not always indicate compensation. Working-memory studies support load-dependent compensation under some conditions. Stroop, Trail Making, and cognitive-control studies also show reduced task responsiveness and dedifferentiation. Semantic tasks provide a useful contrast because core semantic regions are often preserved while control-network recruitment changes with task demand. Vascular aging is a particular constraint, because age-related changes in cerebrovascular reactivity and in the hemodynamic response can produce apparent over-recruitment in the absence of any change in neuronal computation. In line with established frameworks, compensation is treated as a task-specific and demand-sensitive fMRI change associated with preserved or better performance. Hyperactivation without behavioral benefit may reflect effort, neural inefficiency, dedifferentiation, or altered neurovascular coupling. Current evidence supports a performance-based, network-level model of compensation. Longitudinal studies, vascular calibration, standardized tasks, and better test-retest reliability are needed before task-fMRI measures can be used as individual biomarkers of successful cognitive aging.

Keywords: normal cognitive aging, neural compensation, semantic processing, task-based fMRI, cognitive control.

Field: Medical Sciences and Health

1. INTRODUCTION

Normal cognitive aging is not a uniform decline. Its course varies markedly between individuals. Processing speed, working memory, divided attention, and executive control are more vulnerable than accumulated semantic knowledge. Older adults may therefore remain clinically and neuropsychologically normal while the neural systems that support performance are already changing (Cabeza et al., 2018; Stern et al., 2019).

Here, information processing refers to the selection, maintenance, manipulation, retrieval, and control of task-relevant information. These operations are examined with paradigms that probe semantic retrieval, working memory, interference control, response inhibition, and task switching. Commonly used tests include the Stroop task and the Trail Making Test (TMT). Task-based fMRI measures BOLD responses during defined cognitive tasks and can show how regional activation and network coupling vary with task demand. Several models have been proposed to explain age-related changes in task-evoked activation and recruitment. HAROLD refers to reduced hemispheric asymmetry. PASA describes a posterior-to-anterior shift. CRUNCH proposes earlier recruitment followed by a capacity limit. STAC/STAC-r describes compensatory scaffolding influenced by reserve and life-course factors (Cabeza, 2002; Davis et al., 2008; Reuter-Lorenz & Cappell, 2008; Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014). None of these patterns proves compensation by itself. Increased blood-oxygen-level-dependent (BOLD) activity can also reflect greater effort, lower neural efficiency, reduced functional specificity, or vascular effects (Morcom & Henson, 2018).

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The main question is whether additional neural recruitment helps an older person maintain performance. This review summarizes task-based fMRI findings across several information-processing domains. It applies established operational criteria for compensation and separates it from brain maintenance, dedifferentiation, and inefficient recruitment.

2. METHODS

PubMed/MEDLINE was searched through 22 July 2026. We also used targeted searches for recent task-fMRI studies, backward and forward citation tracking, and checks of primary reports in PubMed or publisher records. Search terms covered normal cognitive aging, healthy older adults, semantic processing, task-based fMRI, BOLD, compensation, cognitive control, working memory, semantic processing, Stroop, inhibition, task switching, Trail Making, processing speed, lateralization, and functional connectivity.

Eligible studies were peer-reviewed human studies of cognitively healthy middle-aged or older adults. Adult-lifespan studies were included when older-age effects could be interpreted separately. Studies had to use task-based BOLD fMRI and a defined cognitive task. We excluded resting-state-only studies, structural imaging, electrophysiology, conference abstracts, and studies limited to mild cognitive impairment, dementia, stroke, or major psychiatric disease. Seminal theoretical papers, reviews, and methodological studies were included when they directly informed the interpretation of compensation. This was a focused review. No meta-analysis or formal risk-of-bias tool was used. An fMRI finding was considered supportive of compensation only if recruitment was task-relevant, changed with cognitive demand within functional capacity, and was associated with preserved or better performance (Cabeza et al., 2018; Mauti et al., 2024).

3. RESULTS AND DISCUSSION

3.1. DEMAND-DEPENDENT PREFRONTAL RECRUITMENT

Working-memory studies show why task load matters when interpreting over-recruitment. In a verbal maintenance task, Cappell et al. (2010) found greater right dorsolateral prefrontal cortex (DLPFC) activity in older adults at lower memory loads, with similar accuracy between groups. At the highest load, older adults were less accurate and showed less DLPFC recruitment than younger adults. This pattern is consistent with the CRUNCH model. Additional resources may be recruited earlier with age, but recruitment reaches a limit when task demand exceeds available capacity. The relevant finding is the relation between activation, load, and behavior, not hyperactivation alone.

Age-related lateralization is also context-dependent. Hennessee et al. (2022) studied 461 adults aged 20-89 years. The relation between prefrontal laterality and cognition changed with age. Greater left lateralization was associated with better cognition in middle age. Less lateralized activation was associated with better cognition in older age. Bilateral recruitment may therefore be adaptive in some older adults, but it is not a universal marker of compensation. A recent task-fMRI review reached a similar conclusion. Cognitive reserve was more consistently linked to neural efficiency, while evidence for additional recruitment was mixed and more apparent at higher task demands (Mauti et al., 2024).

Eight studies are summarized in Table 1. They were selected because each links a defined task-fMRI pattern to behavior and, together, they cover the main domains reviewed here: working memory, cognitive control and set shifting, and semantic processing. The table is illustrative rather than exhaustive. It shows how similar activation patterns have been interpreted differently depending on whether a brain-behavior association was demonstrated.

Table 1. Representative task-based fMRI studies relevant to neural compensation in normal cognitive aging

Study	Task/domain	Principal task-fMRI finding	Interpretation
Cappell et al., 2010	Verbal working memory	Right DLPFC over-recruitment at lower loads; under-recruitment at the highest load	Supports load-dependent CRUNCH when performance is preserved at lower load
Talwar et al., 2020	Trail Making Test	TMT-B>A recruited left frontal-parietal/insular regions; increasing age related to lower posterior activity and worse performance	Age-related change, but not clear compensation
Rieck et al., 2021	Inhibition, shifting, working memory	Control-network connectivity became less domain-specific; frontal/default/dorsal-attention integration increased with age	More consistent with reconfiguration and dedifferentiation
Hennessee et al., 2022	Semantic judgment	Prefrontal activation became less lateralized with age; lower laterality related to better cognition in older age	Age-contingent evidence for adaptive bilateral recruitment
Wu & Hoffman, 2023	Semantic control	Core semantic responses were preserved; older adults showed altered DMN and multiple-demand engagement	Partial support; behavioral benefit not uniform
Haitas et al., 2024	Semantic distance manipulation	Task demand increased behavioral cost, but the predicted age-by-demand CRUNCH interaction was not confirmed	Does not support a universal CRUNCH response in semantic processing
Garcia et al., 2024	Semantic association	Canonical semantic regions remained robustly engaged; activation varied with association strength and abstractness	Supports maintenance/selective demand effects more than direct compensation
Langer et al., 2025	Semantic vs rhyme decisions	Semantic-network coherence increased during semantic decisions; age related to greater DMN-control coupling	Network reconfiguration; compensatory value remains inferential

Source: Compiled by the authors from the studies cited in the table

3.2. COGNITIVE CONTROL, SET SHIFTING, AND DEDIFFERENTIATION

Interference and set-shifting studies show that increased recruitment is not always beneficial. In the color-word Stroop task, Milham et al. (2002) found lower responsiveness of DLPFC and parietal control regions in older adults. Older adults also showed broader ventral visual and anterior inferior prefrontal activity and greater anterior cingulate sensitivity to competing information. The pattern was interpreted as less efficient attentional control rather than successful compensation.

The fMRI adaptation of the TMT illustrates how set-shifting demands can be examined while partly controlling for visual-motor processing through the TMT-B > TMT-A contrast. Talwar et al. (2020) studied 36 cognitively healthy adults aged 52-85 years with an fMRI version of the test. TMT performance engaged bilateral frontal, parietal, temporal, occipital, and motor regions. The TMT-B > TMT-A contrast recruited the left inferior frontal and inferior parietal regions, insula, and cingulate cortex. Older age was associated with slower and less accurate performance and lower task-related activity in posterior cortical regions. These findings describe the neural demands of set shifting in healthy aging. They do not, by themselves, show compensation.

Network analyses lead to the same caution. Rieck et al. (2021) studied inhibition, response initiation, shifting, and working memory in 144 adults aged 20-86 years. Functional-connectivity patterns across control domains became more similar with age, especially in control and default-mode systems. Frontal, default-mode, and dorsal-attention networks also became more integrated. This pattern shows age-related reconfiguration, but the loss of domain specificity also indicates dedifferentiation. Consistent with established compensation frameworks, broader integration is interpreted as adaptive only when it is associated with preserved or better performance (Cabeza et al., 2018; Stern et al., 2019).

3.3. SEMANTIC PROCESSING AND PRESERVED PERFORMANCE

Within the broader information-processing framework, semantic tasks are useful for studying compensation because conceptual knowledge is often preserved while controlled retrieval and selection become more demanding. This allows neural changes to be studied before a clear semantic deficit appears. Hoffman and Morcom (2018) found broadly similar left-lateralized semantic recruitment in younger and older adults. Older adults also showed more right frontal and parietal activity. However, greater extra-network activity was not consistently linked to better performance. Peelle et al. (2013) found greater bilateral premotor and left lateral occipital recruitment in better-performing than in poorer-performing older adults, providing a direct brain-behavior link.

Recent studies give a more detailed picture. Wu and Hoffman (2023) found preserved responses in the core semantic network, with age-related differences in default-mode and multiple-demand systems. Alves et al. (2023) found greater recruitment of temporal representational regions and medial orbitofrontal cortex when older adults named atypical concepts. This suggests greater reorganization when concepts are less prototypical. Garcia et al. (2024) found robust angular, temporal, and inferior frontal activation in healthy older adults. Activation varied with association strength and abstractness. The pattern supports demand-sensitive recruitment rather than a global age effect.

Garcia et al. (2022) found distributed task-related connectivity among anterior middle temporal, angular, and inferior frontal regions in older adults. Wu and Hoffman (2024) found stronger bilateral inferior frontal coupling during semantic tasks. In contrast, the left inferior frontal-ventral anterior temporal

interaction was stronger in younger adults. Langer et al. (2025) found increased within-semantic-network connectivity during semantic decisions and greater coupling of the default-mode network with frontoparietal and cingulo-opercular systems with age. These patterns may support performance, but a behavioral benefit was not shown in every study. Haitas et al. (2024) also did not confirm the predicted age-by-demand CRUNCH interaction when semantic distance was manipulated. Compensation during semantic processing is therefore not a uniform response to task difficulty.

3.4. WHEN DOES TASK-RELATED REORGANIZATION REPRESENT COMPENSATION?

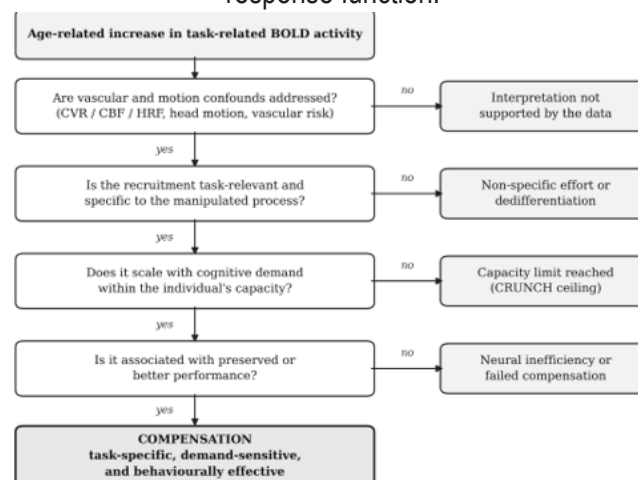
Established frameworks support three operational criteria when a task-fMRI finding is interpreted as compensatory (Cabeza et al., 2018; Stern et al., 2019).

First, the change should relate to preserved accuracy, a smaller reaction-time cost, or better performance within the older group.

Second, it should be specific to the task or to a manipulated level of demand. Diffuse hyperactivation is more consistent with nonspecific effort or lower efficiency.

Third, recruitment should occur while performance remains within the individual's functional range. Increased activation with declining performance may indicate failed compensation or resource exhaustion.

Figure 1. A decision framework for interpreting an age-related increase in task-related BOLD activity. A finding is labeled compensatory only when vascular and motion confounds have been addressed and all three criteria are satisfied. CBF, cerebral blood flow; CVR, cerebrovascular reactivity; HRF, hemodynamic response function.



Source: Authors' own elaboration

Compensation should also be separated from brain maintenance. Maintenance refers to preservation of a relatively youth-like neural pattern. Compensation requires a change in neural processing that helps sustain performance under age-related challenge. Morcom and Henson (2018) showed why this distinction matters. Standard analyses showed greater prefrontal activity with age, but multivariate analyses indicated that the extra activity carried little task-specific information. This favored reduced specificity rather than compensation. Stiernman et al. (2023) later found widespread BOLD overactivation during cognitive control in older adults without a matching increase in task-related glucose metabolism. A larger BOLD response is therefore not direct evidence of greater neuronal computation.

3.5. VASCULAR AND CARDIOMETABOLIC MODIFIERS OF THE BOLD RESPONSE

Neurovascular aging further complicates interpretation. BOLD amplitude depends on cerebral blood flow, vascular reactivity, and the hemodynamic response. In 335 adults, Tsvetanov et al. (2015) showed that vascular correction changed apparent age effects on task-related BOLD activity. Head motion, sensory impairment, vascular risk, medication, and reaction-time differences can add further bias. These factors should be measured and modeled when possible.

The vascular contribution deserves separate consideration in a clinical context, because the older adults seen in everyday practice are rarely free of cardiovascular risk. The BOLD signal is a hemodynamic proxy for neuronal activity, and the neurovascular coupling on which it depends may itself be altered by aging and by disease (D'Esposito et al., 2003). Arterial stiffening, endothelial dysfunction, reduced cerebrovascular reactivity, and cerebral small-vessel disease can all change the amplitude, shape, and

latency of the hemodynamic response function without any change in the underlying neuronal computation. Two findings discussed above point in the same direction. Vascular correction altered the apparent age effect on task-related BOLD in 335 adults (Tsvetanov et al., 2015), and widespread BOLD overactivation during cognitive control was not matched by a corresponding increase in glucose metabolism (Stiernman et al., 2023).

Vascular effects are also not uniform across the brain. In 541 middle-aged adults, cerebrovascular reactivity was lower in regions underlying the default-mode network than in comparison regions among participants with prehypertension or hypertension (Haight et al., 2015). A regionally selective vascular effect of this kind can mimic, exaggerate, or mask precisely the network-level patterns that are then interpreted as compensation or dedifferentiation. Despite this, only a small minority of the many thousands of published BOLD aging studies have applied any form of vascular correction (Tsvetanov et al., 2021). For studies of normal cognitive aging, we therefore regard it as good practice to report blood pressure, diabetes, smoking status, and white-matter hyperintensity burden among the sample characteristics and, where feasible, to acquire a vascular calibration measure such as breath-hold or hypercapnic cerebrovascular reactivity, arterial spin labeling, or resting-state fluctuation amplitude. In the absence of such information, a compensatory interpretation of hyperactivation in an older sample cannot be distinguished from a vascular one.

3.6. METHODOLOGICAL AND CLINICAL IMPLICATIONS

Most studies are cross-sectional and use different tasks and relatively modest samples. Cross-sectional differences cannot show that a compensatory pattern developed before later cognitive decline in the same person. Longitudinal studies are needed to test whether task-specific recruitment predicts preserved cognition, later decompensation, or stable individual variation. Task difficulty should be calibrated or modeled so that age groups are compared at a similar effective load. Accuracy, reaction time, and error rate can be used to quantify this load. The same nominal task may be more demanding for an older adult; without this control, hyperactivation may reflect task difficulty rather than compensation.

Reliability also limits clinical use. Elliott et al. (2020) reported poor mean test-retest reliability across common task-fMRI measures, with a meta-analytic mean intraclass correlation of 0.397. Task-fMRI remains useful for group-level research, but a single activation contrast should not be treated as an individual biomarker. A stronger candidate marker would combine preserved neuropsychological performance, reproducible task-specific recruitment, a positive brain-behavior relation, and persistence after control of vascular and motion-related confounders.

Using several paradigms may strengthen interpretation because each task stresses a different part of information processing. Semantic tasks test the interaction between stored knowledge and control. Working-memory tasks test load-dependent capacity. Stroop and response-inhibition tasks assess conflict and suppression of competing responses. TMT-B relative to TMT-A adds switching and visual-motor demands. If the same frontoparietal or cingulo-opercular recruitment appears across tasks and is linked to preserved performance, the evidence for a broader compensatory mechanism is stronger than hyperactivation in a single task.

For the practising clinician the immediate message is a cautionary one. Task-based fMRI is at present a group-level research tool. It should not be requested in order to establish whether an individual older patient is aging normally, and a single activation contrast should not be read as evidence of preserved cognition in that person. The assessment of cognition in older adults remains neuropsychological, and clinical imaging retains its established role in excluding structural, vascular, and neurodegenerative pathology. The value of the evidence reviewed here is explanatory: it shows why a seemingly more active brain in an older patient is not reassuring in itself, and why vascular health, task effort, and measured performance have to be interpreted together rather than separately.

4. LIMITATIONS OF THIS REVIEW

This was a focused rather than a systematic review. Studies were identified mainly through PubMed/MEDLINE with citation tracking, so relevant work indexed only in other databases or published in languages other than English may have been missed. No protocol was registered, study selection and data extraction were not performed in duplicate, no formal risk-of-bias instrument was applied, and no meta-analysis was undertaken; the studies in Table 1 are illustrative rather than exhaustive. The available samples are also predominantly Western, highly educated, and cross-sectional, which limits generalization to older populations with lower educational attainment or a greater burden of untreated vascular risk. These constraints should be kept in mind when weighing the conclusions below.

5. CONCLUSION

Task-based fMRI shows both preservation and reorganization during normal cognitive aging. Older adults may recruit bilateral prefrontal, frontoparietal, cingulo-opercular, and domain-specific regions as task demand rises. These changes are not always compensatory. A compensatory interpretation requires task specificity, sensitivity to demand, and a measurable behavioral benefit. Without this convergence, the finding is better described as reorganization, inefficiency, dedifferentiation, or possible failed compensation. Semantic, working-memory, Stroop, and set-shifting tasks provide complementary views of this process. Longitudinal validation, standardized behavioral criteria, vascular calibration, and better reliability are needed before task-fMRI patterns can serve as individual markers of successful cognitive aging.

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REFERENCES

- Alves, M., Figueiredo, P., & Raposo, A. (2023). Semantic cognition in healthy ageing: Neural signatures of representation and control mechanisms in naming typical and atypical objects. *Neuropsychologia*, 184, 108545. <https://doi.org/10.1016/j.neuropsychologia.2023.108545>
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. *Psychology and Aging*, 17(1), 85-100. <https://doi.org/10.1037/0882-7974.17.1.85>
- Cabeza, R., Albert, M., Belleville, S., Craik, F. I. M., Duarte, A., Grady, C. L., Lindenberger, U., Nyberg, L., Park, D. C., Reuter-Lorenz, P. A., Rugg, M. D., Steffener, J., & Rajah, M. N. (2018). Maintenance, reserve and compensation: The cognitive neuroscience of healthy ageing. *Nature Reviews Neuroscience*, 19, 701-710. <https://doi.org/10.1038/s41583-018-0068-2>
- Cappell, K. A., Gmeindl, L., & Reuter-Lorenz, P. A. (2010). Age differences in prefrontal recruitment during verbal working memory maintenance depend on memory load. *Cortex*, 46(4), 462-473. <https://doi.org/10.1016/j.cortex.2009.11.009>
- Davis, S. W., Dennis, N. A., Daselaar, S. M., Fleck, M. S., & Cabeza, R. (2008). Que PASA? The posterior-anterior shift in aging. *Cerebral Cortex*, 18(5), 1201-1209. <https://doi.org/10.1093/cercor/bhm155>
- D'Esposito, M., Deouell, L. Y., & Gazzaley, A. (2003). Alterations in the BOLD fMRI signal with ageing and disease: A challenge for neuroimaging. *Nature Reviews Neuroscience*, 4(11), 863-872. <https://doi.org/10.1038/nrn1246>
- Elliott, M. L., Knodt, A. R., Ireland, D., Morris, M. L., Poulton, R., Ramrakha, S., Sison, M. L., Moffitt, T. E., Caspi, A., & Hariri, A. R. (2020). What is the test-retest reliability of common task-functional MRI measures? New empirical evidence and a meta-analysis. *Psychological Science*, 31(7), 792-806. <https://doi.org/10.1177/0956797620916786>
- Garcia, A., Cohen, R. A., Porges, E. C., Williamson, J. B., & Woods, A. J. (2022). Functional connectivity of brain networks during semantic processing in older adults. *Frontiers in Aging Neuroscience*, 14, 814882. <https://doi.org/10.3389/fnagi.2022.814882>
- Garcia, A., Cohen, R. A., Langer, K. G., O'Neal, A. G., Porges, E. C., Woods, A. J., & Williamson, J. B. (2024). Semantic processing in older adults is associated with distributed neural activation which varies by association and abstractness of words. *GeroScience*, 46(6), 6195-6212. <https://doi.org/10.1007/s11357-024-01216-x>
- Haight, T. J., Bryan, R. N., Erus, G., Davatzikos, C., Jacobs, D. R., D'Esposito, M., Lewis, C. E., & Launer, L. J. (2015). Vascular risk factors, cerebrovascular reactivity, and the default-mode brain network. *NeuroImage*, 115, 7-16. <https://doi.org/10.1016/j.neuroimage.2015.04.039>
- Haitas, N., Dubuc, J., Massé-Leblanc, C., Chamberland, V., Amiri, M., Glatard, T., Wilson, M., Joannette, Y., & Steffener, J. (2024). Registered report: Age-preserved semantic memory and the CRUNCH effect manifested as differential semantic control networks: An fMRI study. *PLOS ONE*, 19(6), e0289384. <https://doi.org/10.1371/journal.pone.0289384>
- Hennessee, J. P., Webb, C. E., Chen, X., Kennedy, K. M., Wig, G. S., & Park, D. C. (2022). Relationship of prefrontal brain lateralization to optimal cognitive function differs with age. *NeuroImage*, 264, 119736. <https://doi.org/10.1016/j.neuroimage.2022.119736>
- Hoffman, P., & Morcom, A. M. (2018). Age-related changes in the neural networks supporting semantic cognition: A meta-analysis of 47 functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews*, 84, 134-150. <https://doi.org/10.1016/j.neubiorev.2017.11.010>
- Langer, K. G., O'Neal, A. G., Garcia, A., Chen, A., Porges, E. C., Williamson, J. B., Woods, A. J., & Cohen, R. A. (2025). Functional connectivity in distributed cortical networks associated with semantic processing in healthy older adults. *Frontiers in Aging Neuroscience*, 17, 1479861. <https://doi.org/10.3389/fnagi.2025.1479861>
- Mauti, M., Monachesi, B., Taccari, G., & Rumiati, R. I. (2024). Facing healthy and pathological aging: A systematic review of fMRI task-based studies to understand the neural mechanisms of cognitive reserve. *Brain and Cognition*, 182, 106238. <https://doi.org/10.1016/j.bandc.2024.106238>
- Milham, M. P., Erickson, K. I., Banich, M. T., Kramer, A. F., Webb, A., Wszalek, T., & Cohen, N. J. (2002). Attentional control in the aging brain: Insights from an fMRI study of the Stroop task. *Brain and Cognition*, 49(3), 277-296. <https://doi.org/10.1006/brcg.2001.1501>

- Morcom, A. M., & Henson, R. N. A. (2018). Increased prefrontal activity with aging reflects nonspecific neural responses rather than compensation. *The Journal of Neuroscience*, 38(33), 7303-7313. <https://doi.org/10.1523/JNEUROSCI.1701-17.2018>
- Nikolovska, L., Gelova, O., & Spasov, M. (2021). Effects of physical activity with different intensity on adult patients. *KNOWLEDGE - International Journal*, 48(3), 497-502. Retrieved from <https://ojs.ikm.mk/index.php/kij/article/view/4769>
- Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: Aging and neurocognitive scaffolding. *Annual Review of Psychology*, 60, 173-196. <https://doi.org/10.1146/annurev.psych.59.103006.093656>
- Peelle, J. E., Chandrasekaran, K., Powers, J., Smith, E. E., & Grossman, M. (2013). Age-related vulnerability in the neural systems supporting semantic processing. *Frontiers in Aging Neuroscience*, 5, 46. <https://doi.org/10.3389/fnagi.2013.00046>
- Reuter-Lorenz, P. A., & Cappell, K. A. (2008). Neurocognitive aging and the compensation hypothesis. *Current Directions in Psychological Science*, 17(3), 177-182. <https://doi.org/10.1111/j.1467-8721.2008.00570.x>
- Reuter-Lorenz, P. A., & Park, D. C. (2014). How does it STAC up? Revisiting the scaffolding theory of aging and cognition. *Neuropsychology Review*, 24, 355-370. <https://doi.org/10.1007/s11065-014-9270-9>
- Rieck, J. R., Baracchini, G., Nichol, D., Abdi, H., & Grady, C. L. (2021). Reconfiguration and dedifferentiation of functional networks during cognitive control across the adult lifespan. *Neurobiology of Aging*, 106, 80-94. <https://doi.org/10.1016/j.neurobiolaging.2021.03.019>
- Stern, Y., Barnes, C. A., Grady, C., Jones, R. N., & Raz, N. (2019). Brain reserve, cognitive reserve, compensation, and maintenance: Operationalization, validity, and mechanisms of cognitive resilience. *Neurobiology of Aging*, 83, 124-129. <https://doi.org/10.1016/j.neurobiolaging.2019.03.022>
- Stiernman, L., Grill, F., McNulty, C., Bahrd, P., Panes Lundmark, V., Axelsson, J., Salami, A., & Rieckmann, A. (2023). Widespread fMRI BOLD signal overactivations during cognitive control in older adults are not matched by corresponding increases in fPET glucose metabolism. *The Journal of Neuroscience*, 43(14), 2527-2536. <https://doi.org/10.1523/JNEUROSCI.1331-22.2023>
- Talwar, N., Churchill, N. W., Hird, M. A., Tam, F., Graham, S. J., & Schweizer, T. A. (2020). Functional magnetic resonance imaging of the trail-making test in older adults. *PLOS ONE*, 15(5), e0232469. <https://doi.org/10.1371/journal.pone.0232469>
- Tsvetanov, K. A., Henson, R. N. A., Tyler, L. K., Davis, S. W., Shafto, M. A., Taylor, J. R., Williams, N., Cam-CAN, & Rowe, J. B. (2015). The effect of ageing on fMRI: Correction for the confounding effects of vascular reactivity evaluated by joint fMRI and MEG in 335 adults. *Human Brain Mapping*, 36(6), 2248-2269. <https://doi.org/10.1002/hbm.22768>
- Tsvetanov, K. A., Henson, R. N. A., & Rowe, J. B. (2021). Separating vascular and neuronal effects of age on fMRI BOLD signals. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 376(1815), 20190631. <https://doi.org/10.1098/rstb.2019.0631>
- Wu, W., & Hoffman, P. (2023). Age differences in the neural processing of semantics, within and beyond the core semantic network. *Neurobiology of Aging*, 131, 88-105. <https://doi.org/10.1016/j.neurobiolaging.2023.07.022>
- Wu, W., & Hoffman, P. (2024). Functional integration and segregation during semantic cognition: Evidence across age groups. *Cortex*, 178, 157-173. <https://doi.org/10.1016/j.cortex.2024.06.015>

