# Journal of Contemporary Medicine

YEAR: 2024 VOLUME: 14 ISSUE: 4

# JOURNAL OF CONTEMPORARY MEDICINE

e-ISSN 2667-7180

Formerly Çağdaş Tıp Dergisi





**YEAR 2024 VOLUME 14 ISSUE 4**

The Owner and Publishing Manager on behalf of the Journal of Contemporary Medicine

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### Journal article on the Internet

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

### Website

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

### An organization as an author

The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

### Acknowledgements

The source of financial grants and the contribution of colleagues or institutions should be acknowledged.

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Drugs should be referred to by their generic names, rather than brand names.

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JOURNAL OF CONTEMPORARY MEDICINE

Formerly Çağdaş Tıp Dergisi

# CONTENTS

YEAR 2024 VOLUME 14 ISSUE 4 e-ISSN 2667-7180

## ORIGINAL ARTICLES



## CASE REPORT

JOURNAL OF CONTEMPORARY MEDICINE

Formerly Çağdaş Tıp Dergisi

# CONTENTS

YEAR 2024 VOLUME 14 ISSUE 4 e-ISSN 2667-7180

## LETTER TO THE EDITOR



## REVIEW

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CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1459152
J Contemp Med 2024;14(4):160-167

Original Article / Orijinal Araştırma

# Vitamin D Status in Children in the South Marmara Region in Turkey

## Türkiye'nin Güney Marmara Bölgesi'ndeki Çocukların D Vitamini Durumu

**Aynur Karaca[1], Hakan Altın[2]**

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## Abstract

**Aim**: This study aims to investigate the age, gender, and seasonal differences in vitamin D levels in children and to determine the prevalence of vitamin D deficiency.

**Material and Method**: Between January 2022 and December 2023, we retrospectively reviewed the records of children aged 0.1–17 years who had their serum 25-hydroxyvitamin D (25(OH) D) levels checked in the pediatric outpatient clinics of Bursa City Hospital. Children were divided into four groups according to age (0.1–1, 2–5, 6–11, and 12–17 years), three groups according to 25(OH)D levels (vitamin D deficiency=below 12 ng/mL, vitamin D insufficiency=between 12–20 ng/mL, and vitamin D sufficiency=above 20 ng/mL), and four groups according to seasons.

**Results**: The 25(OH)D levels of 41,899 children were analyzed, comprising 19,738 (47.1%) boys and 22,161 (52.9%) girls. The median (minimum-maximum) values were 18.6 (3–145) ng/mL. Girls exhibited lower levels compared to boys [16.8 (3–136) ng/mL in girls vs. 20.3 (3–145) ng/mL in boys, p<0.001]. Vitamin D deficiency was 22.8% (15.5% in boys and 29.2% in girls, p<0.001), and vitamin D insufficiency was 32.9% (32.9% in boys and 32.9% in girls, p=0.970). In 55.6% of patients, 25(OH)D levels were below 20 ng/mL (48.4% of boys and 62.1% of girls, p<0.001). Observations revealed a decline in 25(OH)D levels with advancing age, notably plummeting during winter and spring while peaking in autumn and summer.

**Conclusion**: Adolescents, particularly girls, exhibited the lowest 25(OH)D levels during winter and spring. Consequently, we advocate the development of public health strategies to prevent vitamin D deficiency in this group.

**Keywords**: Vitamin D deficiency, vitamin D insufficiency, 25-hydroxyvitamin D, children

## Öz

**Amaç**: Çalışmamızın amacı çocuklarda D vitamini düzeylerindeki yaş, cinsiyet ve mevsimsel farklılıkları araştırmak ve D vitamini eksikliği prevalansını belirlemektir.

**Gereç ve Yöntem**: Ocak 2022-Aralık 2023 tarihleri arasında Bursa Şehir Hastanesi çocuk polikliniklerinde serum 25-hidroxi vitamin D (25(OH)D) düzeyi ölçümü yapılan 0.1-17 yaş arası çocukların kayıtları retrospektif olarak incelendi. Çocuklar yaşa göre dört gruba (0.1-1, 2-5, 6-11 ve 12-17 yaş); serum 25(OH)D vitamini düzeylerine göre üç gruba (D vitamini eksikliği (12 ng/mL altı), D vitamini yetersizliği (12-20 ng/mL arası) ve D vitamini yeterliliği (20 ng/mL üstü)); ve mevsimlere göre dört gruba ayrıldı.

**Bulgular**: 19738'i (%47,1) erkek ve 22161'sı (%52,9) kız olmak üzere 41899 çocuğun 25(OH)D düzeylerinin ortanca ve (minimum-maximum) 18,6 (3-145) ng/mL olup kızlarda erkeklerden daha düşüktü [kızlarda 16,8 (3-136) ng/mL ve erkeklerde 20,3 (3-145) ng/mL p<0,001]. D vitamini eksikliği %22,8 (erkeklerde %15,5 ve kızlarda %29,2, p<0.001) ve D vitamini yetersizliği %32,9 (erkeklerde %32,9 ve kızlarda %32,9, p=0.970) idi. Hastalarımızın %55,6'sında 25(OH) D düzeyi 20 ng/mL'nin altındaydı (erkeklerin %48,4'ü ve kadınların %62,1'i, p<0,001). 25(OH)D düzeyleri artan yaşla birlikte azalmıştır; en düşük seviyeler kış ve ilkbaharda, en yüksek seviyeler ise sonbahar ve yaz aylarında bulunmuştur.

**Sonuç**: En düşük 25(OH)D düzeyi adolesanlarda, özellikle de kız adolesanlarda kış ve ilkbahar mevsiminde bulunmuştur. Bu nedenle, bu grup için D vitamini eksikliğini önlemeye yönelik halk sağlığı stratejilerinin geliştirilmesi gerektiğini düşünüyoruz.

**Anahtar Kelimeler**: D vitamini eksikliği, D vitamini yetersizliği, 25(OH)D, çocuk

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**Received *(Geliş Tarihi)*:** 26.03.2024 **Accepted *(Kabul Tarihi)*:** 20.05.2024

## INTRODUCTION

Vitamin D, a steroidal prohormone, plays a crucial role in regulating calcium and phosphate metabolism, and influencing the musculoskeletal, renin-angiotensin, cardiovascular systems, and immunity. Vitamin D deficiency can primarily lead to osteomalacia across all age groups and rickets during childhood. Additionally, studies have linked vitamin D deficiency with immune system disorders, type 1 diabetes mellitus, multiple sclerosis, ulcerative colitis, rheumatoid arthritis, cardiovascular diseases, cancer, and mood disorders.[1,2]

The primary source of vitamin D is sunlight. While foods like fish, liver, milk, and eggs contain vitamin D, they can only fulfill a small fraction of the requirements.[3–5] Numerous factors, including skin color, air pollution, season, sun angle, cultural clothing, gender, sedentary lifestyle, genetic predisposition, obesity, and dietary habits, influence Vitamin D levels.[6,7] Two biochemical parameters assess vitamin D levels: 1,25-dihydroxyvitamin D and 25-hydroxyvitamin D (25[OH]D). The 25(OH)D level offers more comprehensive insights into the body's vitamin D reserves due to its longer half-life and significantly higher blood concentration than the other vitamin D metabolites.[5] Therefore, 25(OH)D levels were tested to determine vitamin D status in this study.

Vitamin D deficiency presents a global public health concern. Untreated deficiencies during childhood can predispose individuals to serious ailments later in life. Similar to many countries worldwide, Türkiye conducts epidemiological studies and implements national vitamin D prophylaxis programs to identify at-risk age groups and prevent deficiencies. As part of this effort, oral vitamin D3 prophylaxis at a dose of 400 IU/day is routinely administered to children aged 0–1 year, aligning with practices in many other countries.[8] In the South Marmara Region, where this study is conducted, most of the population resides in Bursa, a densely populated and highly industrialized city characterized by high-rise buildings, which increases the susceptibility to vitamin D deficiency. Assessing the prevalence of vitamin D deficiency in this region is crucial to facilitating the implementation of necessary interventions. Therefore, by collecting data from all regions, regional and national strategies can be developed to prevent vitamin D deficiency.

This study aims to examine the age groups, gender, and seasonal differences of serum 25(OH)D levels in children under the age of 18 who presented to Bursa City Hospital, a third-level hospital in the south Marmara Region of Turkey, to determine the frequency of vitamin D deficiency and to investigate the related factors.

## MATERIAL AND METHOD

The study was carried out with the permission of Bursa City Hospital Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.02.2024, Decision No: 2024-1/8).

This study involved a retrospective review of records belonging to children aged 0.1–17 years, except newborns, who underwent 25(OH)D level testing at the pediatric outpatient clinics of Bursa City Hospital between January 2022 and December 2023. Data on age, gender, and 25(OH)D results of the children were obtained from the hospital automation system. In cases where multiple vitamin D levels were assessed in the same patient, only the initial measurement was considered for inclusion in this study. The determination of 25(OH)D levels was carried out using the chemiluminescence-immunoassay method.

The children were categorized into four age groups: 0.1–1, 2–5, 6–11, and 12–17 years. Following the 2015 global consensus recommendation, 25(OH)D levels were classified into three categories: vitamin D deficiency (below 12 ng/mL), vitamin D insufficiency (between 12–20 ng/mL), and vitamin D sufficiency (above 20 ng/mL).[9] Furthermore, individuals with 25(OH)D levels below 20 ng/mL were identified (comprising both deficiency and insufficiency). They were then further grouped based on the seasons: spring (March to May), summer (June to August), autumn (September to November), and winter (December to February). 25(OH)D levels of children were analyzed according to gender, age groups, and seasons.

### Statistical Analysis

The statistical analysis of this study was conducted using the Statistical Package for the Social Sciences for Windows, version 26.0. Categorical variables were expressed as n (%), while median (minimum-maximum) values were employed when data did not conform to normality. Descriptive analyses were employed to assess the distribution and frequency of the data, with chi-squared tests utilized to compare two independent groups in frequency data. Normality analysis was performed using the Kolmogorov–Smirnov test. The Mann–Whitney U test was applied to compare two independent groups that did not adhere to a normal distribution. The Kruskal–Wallis test was also employed to compare three or more independent groups that did not follow a normal distribution. Post-hoc analysis was conducted using the ANOVA test if a significant difference was detected. The significance level was set at $p < 0.05$ for all statistical analyses.

## RESULTS

This study comprised 41,899 children with a median age of 7 (0.1–17) years. The median ages of the 19,738 (47.1%) boys and 22,161 (52.9%) girls were 8 (0.1–17) and 6 (0.1–17) years, respectively. The median 25(OH)D levels of the children in this study were 18.6 (3–145) ng/mL, which were lower in girls than in boys [16.8 (3–136) ng/mL in girls and 20.3 (3–145) ng/mL in boys, $p<0.001$]. When 25(OH)D levels were compared according to genders in four different age groups, it was found that 25(OH)D levels were statistically significantly lower in boys in the 0.1-1 age group ($p=0.003$) and lower in girls in other age groups ($p<0.001$ in all three age groups, see also. **Table 1**'s Age

section). 25(OH)D levels were consistently lower in girls than in boys across all seasons (p<0.001 in all four seasons) (see **Table 1** and **Figure 1**). When compared by gender in the same season and in different age groups, it was observed that girls generally had lower 25(OH)D levels than boys (see also. **Table 1**'s Seasons section). Additionally, the lowest 25(OH)D levels were found in girls aged 12–17 years [9.6 (3–97) ng/mL in the spring season], while the highest levels were found in boys aged 0.1–1 year [36.1 (3.4–138) ng/mL in the winter season].

**Table 1. Comparison of 25(OH)D serum levels according to gender.**

| Median (min-max) | Male 25 OH) D, ng/mL | Female 25 (OH) D, ng/mL | p |
|---|---|---|---|
| Total | 20.3 (3-145) | 16.8 (3-136) | <0.001 |
| Age (year)/season | | | |
| 0.1-1Spring | 33.6 (3.3-95.7) | 35.1 (3.9-117) | 0.154 |
| Summer | 35.6 (3.2-111) | 35.7 (4.4-96.2) | 0.831 |
| Autumn | 34.0 (3-110) | 35.8 (4.2-117) | 0.073 |
| Winter | 33.2 (3.5-145) | 36.1 (3.4-138) | 0.021 |
| Total | 34.5 (3-145) | 35.7 (3.4-136) | 0.003 |
| 2-5 Spring | 19.6 (3.1-96.7) | 18.7 (3.2-110) | 0.006 |
| Summer | 25.3 (4.3-75.1) | 24.2 (3.6-117) | 0.001 |
| Autumn | 23.5 (3.4-86.8) | 22.3 (4.5-116) | <0.001 |
| Winter | 18.6 (3.2-105) | 18.4 (3.3-139) | 0.511 |
| Total | 22.0 (3.1-105) | 21.1 (3.2-139) | <0.001 |
| 6-11 Spring | 15.4 (3.3-85.2) | 13.4 (3-102) | <0.001 |
| Summer | 23.7 (3.3-82) | 19.9 (3.4-57.9) | <0.001 |
| Autumn | 21.9 (4.9-62.2) | 19.1 (3.1-116) | <0.001 |
| Winter | 15.8 (3.4-94.4) | 13.9 (3-78.3) | <0.001 |
| Total | 19.1 (3.3-94.4) | (3-116) | <0.001 |
| 12-17 Spring | 13.3 (3.3-93.7) | 9.6 (3-97) | <0.001 |
| Summer | 20.6 (3.8-75) | 14.2 (3-116) | <0.001 |
| Autumn | 19.5 (4.4-84.8) | 13.3 (3.1-67.8) | <0.001 |
| Winter | 14.0 (3.1-102) | 10.0 (3-70.6) | <0.001 |
| Total | 17.0 (3.1-102) | 11.7 (3-116) | <0.001 |
| Season | | | |
| Spring | 17.3 (3.1-96.7) | 14.2 (3-117) | <0.001 |
| Summer | 24.1 (3.2-111) | 19.9 (3-117) | <0.001 |
| Autumn | 22.4 (3-110) | 19.0 (3.1–117) | <0.001 |
| Winter | 16.9 (3-145) | 14.0 (3-136) | <0.001 |

25 (OH) D= 25-hydroxyvitaminD

Among the age groups, the highest 25(OH)D levels were found in girls aged 0.1 to 1 year [35.7 (3.4–136) ng/mL], while the lowest value was observed in girls aged 12 to 17 years [11.7 (3–116) ng/mL]. Serum 25(OH)D levels were observed to decrease with increasing age in both sexes across all seasons (p<0.001 for each) (**Table 2**).

Upon examining 25(OH)D levels according to seasons, differences were noted across all seasons, ranked from low to high as winter, spring, autumn, and summer. In boys, no significant difference was observed between the winter and spring seasons, with levels increasing in autumn and summer, respectively. Among girls, 25(OH)D levels were ranked lowest in winter, followed by spring, autumn, and summer. When evaluating 25(OH)D levels according to seasons within age groups, no significant difference was found between seasons in both sexes within the 0.1–1 age group. In other age groups, the seasons with the lowest 25(OH)D levels for both sexes were spring and winter, with no significant difference between them; these seasons were succeeded by autumn and summer from low to high (**Table 3** and **Figure 2**).

In this study, vitamin D deficiency was observed in 22.8% of participants (15.5% in boys and 29.2% in girls, p < 0.001), while vitamin D insufficiency was noted in 32.9% (32.9% in boys and 32.9% in girls, p=0.970). Vitamin D deficiency was least prevalent in boys aged 0.1–1 year (5%) and most prevalent in girls aged 12–17 years (51.6%). When assessing vitamin D deficiency across seasons, the lowest levels were found in boys (4.4%) during the summer season, whereas the highest levels were observed in girls (39.6%) during the spring season (see **Table 4**).

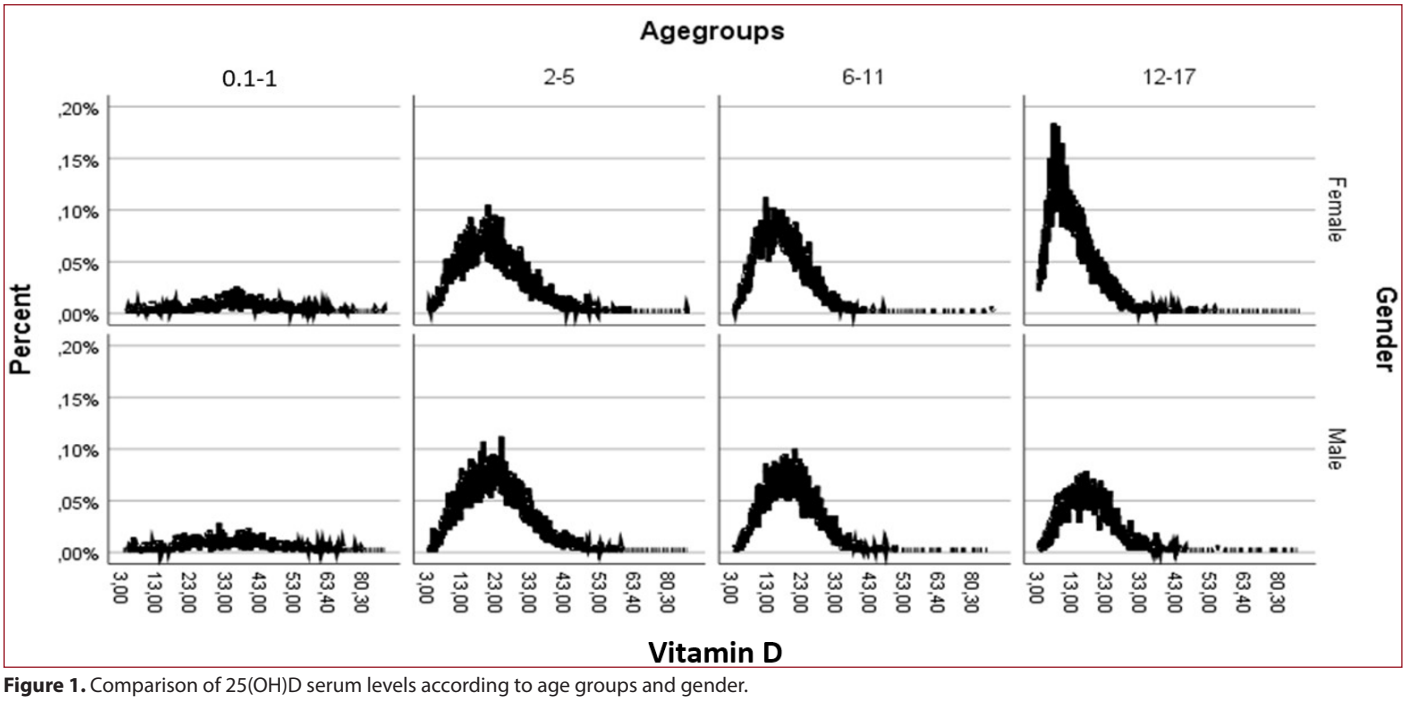


**Figure 1.** Comparison of 25(OH)D serum levels according to age groups and gender.

**Table 2: Comparison of 25(OH)D serum levels according to age groups.**

| Median (min-max) | 0.1-1 year 25(OH)D ng/mL | 2-5 25(OH)D ng/mL | 6-11 25(OH)D ng/mL | 12-17 25(OH)D ng/mL | p (p1-p6) |
|---|---|---|---|---|---|
| M | 34.5 (3-145) | 22.0 (3.1-105) | 19.1 (3.3-94.4) | 17.0 (3.1-102) | <0.001 |
| F | 35.7 (3.4-136) | 21.1 (3.2-139) | 16.5 (3-116) | 11.7 (3-116) | <0.001 |
| Total | 35.1 (3-145) | 21.5 (3.1-139) | 17.7 (3.0-116) | 13.6 (3-116) | <0.001 |
| Seasons | | | | | |
| Spring | | | | | |
| M | 33.6 3.3-95.7) | 19.6 3.1-96.7) | 15.4 3.3-85.2) | 13.3 3.3-93.7) | <0.001 |
| F | 35.1 3.9-117) | 18.7 3.2-110) | 13.4 3-102) | 9.6 3-97) | <0.001 |
| Total | 34.5 3.3-117) | 19.2 3.1-110) | 14.6 3-102) | 11.0 3-97) | <0.001 |
| Summer | | | | | |
| M | 35.6 3.2-111) | 25.3 4.3-75.1) | 23.7 3.3-82) | 20.6 3.8-75) | <0.001 |
| F | 35.7 4.4-96.2) | 24.2 3.6-117) | 19.9 3.4-57.9) | 14.2 3-116) | <0.001 |
| Total | 35.6 3.2-111) | 24.7 3.6-117) | 21.8 3.3-82) | 16.8 3-116) | <0.001 |
| Autumn | | | | | |
| M | 34.0 3-110) | 23.5 3.4-86.8) | 21.9 4.9-62.2) | 15.8 3.4-94.4) | <0.001 |
| F | 35.8 4.2-117) | 22.3 4.5-116) | 19.1 3.1-116) | 13.9 3-78.3) | <0.001 |
| Total | 35.2 3-117) | 23.0 3.4-116 | 20.6 3.1-116) | 14.9 3.0-94.4) | <0.001 |
| Winter | | | | | |
| M | 33.2 3.5-145) | 18.6 3.2-105) | 15.8 3.4-94.4) | 14.0 3.1-102) | <0.001 |
| F | 36.1 3.4-138) | 18.4 3.3-39) | 13.9 3-78.3) | 10.0 3-70.6) | <0.001 |
| Total | 34.9 3.4-145) | 18.4 3.2-139) | 14.9 3.0-94.4) | 11.3 3-102) | <0.001 |

25 (OH) D= 25-hydroxyvitaminD, M=Male, F=Female, p1=0-1/2-5, p2=0-1/6-11, p3=0-1/12-17, p4=2-5/6-11, p5=2-3/12-17, p6=6-11/12-17, p1-p2-p3-p4-p4-p5 and p6 all <0.001

**Table 3: Comparison of 25(OH)D serum levels according to seasons.**

| Median (Min-max) | Spring 25(OH)D ng/mL | Summer 25(OH)D ng/mL | Autumn 25(OH)D ng/mL | Winter 25(OH)D ng/mL | p | p1 | p2 | p3 | p4 | p5 | p6 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| M | 17.3 (3.1-96.7) | 24.1 (3.2-111) | 22.4 (3-110) | 16.9 (3-145) | <0.001 | <0.001 | <0.001 | 0.375 | <0.001 | <0.001 | <0.001 |
| F | 14.2 (3-117) | 19.9 (3-117) | 19 (3.1-117) | 14 (3-136) | <0.001 | <0.001 | <0.001 | 0.049 | <0.001 | <0.001 | <0.001 |
| Total | 15.7 (3-117) | 22.1 (3-117) | 20.8 (3-117) | 15.4 (3-145) | <0.001 | <0.001 | <0.001 | 0.009 | <0.001 | <0.001 | <0.001 |
| Age | | | | | | | | | | | |
| M | 33.6 3.3-95.7) | 35.6 3.2-111) | 34.0 3-110) | 33.2 3.5-145) | 0.129 | | | | | | |
| F | 35.1 3.9-117) | 35.7 4.4-96.2) | 35.8 4.2-117) | 36.1 3.4-138) | 0.920 | | | | | | |
| Total | 34.5 3.3-117) | 35.6 3.2-111) | 35.2 3-117) | 34.9 3.4-145) | 0.229 | | | | | | |
| 2-5 | | | | | | | | | | | |
| M | 19.6 3.1-96.7) | 25.3 4.3-75.1) | 23.5 3.4-86.8) | 18.6 3.2-105) | <0.001 | <0.001 | <0.001 | 0.076 | <0.001 | <0.001 | <0.001 |
| F | 18.7 3.2-110) | 24.2 3.6-117) | 22.3 4.5-116) | 18.4 3.3-39) | <0.001 | <0.001 | <0.001 | 0.795 | <0.001 | <0.001 | <0.001 |
| Total | 19.2 3.1-110) | 24.7 3.6-117) | 23.0 3.4-116) | 18.4 3.2-139) | <0.001 | <0.001 | <0.001 | 0.055 | <0.001 | <0.001 | <0.001 |
| 6-11 | | | | | | | | | | | |
| M | 15.4 3.3-85.2) | 23.7 3.3-82) | 21.9 4.9-62.2) | 15.8 3.4-4.4) | <0.001 | <0.001 | <0.001 | 0.056 | <0.001 | <0.001 | <0.001 |
| F | 13.4 3-102) | 19.9 3.4-57.9) | 19.1 3.1-116) | 13.9 3-78.3) | <0.001 | <0.001 | <0.001 | 0.868 | 0.378 | <0.001 | <0.001 |
| Total | 14.6 3-102) | 21.8 3.3-82) | 20.6 3.1-116) | 14.9 3.0-4.4) | <0.001 | <0.001 | <0.001 | 0.077 | <0.001 | <0.001 | <0.001 |
| 12-7 | | | | | | | | | | | |
| M | 13.3 3.3-93.7) | 20.6 3.8-75) | 19.5 4.4-84.8) | 14.0 3.1-102) | <0.001 | <0.001 | <0.001 | 0.984 | 0.026 | <0.001 | <0.001 |
| F | 9.6 3-97) | 14.2 3-116) | 13.3 3.1-67.8) | 10.0 3-70.6) | <0.001 | <0.001 | <0.001 | 0.983 | <0.001 | <0.001 | <0.001 |
| Total | 11.0 3-97) | 16.8 3-116) | 15.9 3.1-84.8) | 11.3 3-102) | <0.001 | <0.001 | <0.001 | 0.948 | <0.001 | <0.001 | <0.001 |

25 (OH) D= 25-hydroxyvitaminD, M=Male, F=Female, p1=spring-summer, p2=spring-autumn, p3=spring-winter, p4= summer-autumn, p5= summer-winter, p6= autumn-winter

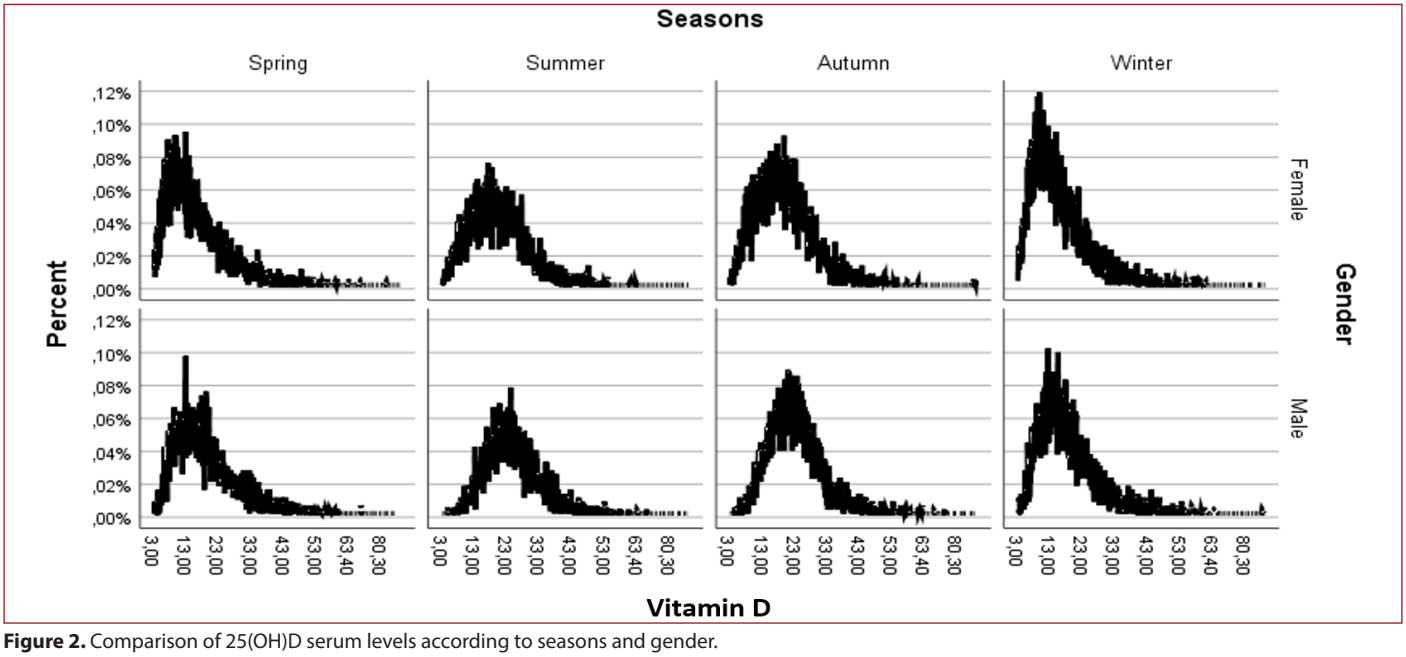


**Figure 2.** Comparison of 25(OH)D serum levels according to seasons and gender.

**Table 4: Distribution of children aged 0-17 years according to vitamin D deficiency-insufficiency and sufficiency groups**

| | Vitamin D deficiency N (%) | Vitamin D insufficiency N (%) | Vitamin D sufficiency N (%) | Total N (%) |
|---|---|---|---|---|
| Male | 3059 (15.5) | 6485 (32.9) | 10194 (51.6) | 19738 (100) |
| Female | 6472 (29.2) | 7298 (32.9) | 8391 (37.9) | 22161 (100) |
| Total | 9531 (22.8) | 13783 (32.9) | 18585 (44.3) | 41899 (100) |
| Age (year) | | | | |
| 0.1-1 | | | | |
| Male | 106 (6.0) | 147 (8.5) | 1475 (85.5) | 1728 (100) |
| Female | 71 (5.0) | 109 (7.7) | 1236 (82.3) | 1416 (100) |
| Total | 177 (5.6) | 256 (8.1) | 2711 (86.3) | 3144 (100) |
| 2-5 | | | | |
| Male | 947 (12.3) | 2234 (29.2) | 4478 (58.5) | 7659 (100) |
| Female | 1014 (14.1) | 2241 (31.2) | 3919 (54.7) | 7174 (100 |
| Total | 1961 (13.2) | 4475 (53.3) | 8397 (56.5) | 14833 (100) |
| 6-11 | | | | |
| Male | 946 (15.8) | 2300 (38.5) | 2732 (45.7) | 5978 (100) |
| Female | 1569 (25.4) | 2577 (41.8) | 2022 (32.8) | 6168 (100) |
| Total | 2515 (20.7) | 4877 (40.2) | 4754 (39.1) | 12146 (100) |
| 12-17 | | | | |
| Male | 1060 (24.2) | 1804 (41.3) | 1509 (34.5) | 4373 (100) |
| Female | 3818 (51.6) | 2371 (32.0) | 1214 (16.4 | 7403 (100) |
| Total | 4878 (41.4) | 4175 (35.5) | 2723 (23.1) | 11776 (100) |
| Season | | | | |
| Spring | | | | |
| Male | 1181 (25.0) | 1715 (36.3) | 1832 (38.7) | 4728 (100) |
| Female | 2066 (39.6) | 1595 (30.6) | 1557 (29.8) | 5218 (100) |
| Total | 3247 (32.7) | 3310 (33.2) | 3389 (34.1) | 9946 (100) |
| Summer | | | | |
| Male | 183 (4.4) | 1052 (25.1) | 2952 (70.5) | 4187 (100) |
| Female | 832 (17.3) | 1577 (32.8) | 2400 (49.9) | 4809 (100) |
| Total | 1015 (11.3) | 2629 (29.2) | 5352 (59.5) | 8996 (100) |
| Autumn | | | | |
| Male | 371 (6.9) | 1640 (30.2) | 3412 (62.9) | 5423 (100) |
| Female | 1189 (19.6) | 2132 (35.1) | 2753 (45.3) | 6074 (100) |
| Total | 1560 (13.6) | 3772 (32.8) | 6165 (53.6) | 11497 (100) |
| Winter | | | | |
| Male | 1324 (24.5) | 2078 (38.5) | 1998 (37.0) | 5400 (100) |
| Female | 2385 (39.4) | 1994 (32.9) | 1681 (27.7) | 6060 (100) |
| Total | 3709 (32.4) | 4072 (35.5) | 3679 (32.1) | 11460 (100) |

Vitamin D deficiency=25 (OH) vitamin D <12 ng/mL; Vitamin D insufficiency=25(OH) vitamin D 12-20 ng/mL; Vitamin D sufficiency=25(OH)D>20 ng/mL.

**Table 5: Comparison of children with 25(OH)D serum levels below 20 ng/mL according to gender.**

| | Male, n=19738 25(OH)D <20 ng/mL N (%) | Female, n= 22161 25(OH)D <20 ng/mL N (%) | Total, n=41899 25(OH)D <20 ng/mL N (%) | p |
|---|---|---|---|---|
| Total | 9544 (48.4%) | 13770 (62.1%) | 23314 (55.6%) | <0.001 |
| Age (year)/season | | | | |
| 0.1-1 | | | | |
| Spring | 65 (14.7) | 53 (14.5) | 118 (14.6) | 0.941 |
| Summer | 41 (10.9) | 32 (10.1) | 73 (10.5) | 0.728 |
| Autumn | 70 (14.8) | 46 (10.8) | 116 (12.9) | 0.074 |
| Winter | 77 (17.7) | 49 (15.8) | 126 (16.9) | 0.493 |
| Total | 253 (14.6%) | 180 (12.7) | 433 (13.8%) | 0.111 |
| 2-5 | | | | |
| Spring | 947 (51.7) | 962 (55) | 1909 (53.3) | 0.049 |
| Summer | 396 (24.9) | 438 (28.8) | 834 (26.8) | 0.014 |
| Autumn | 708 (32.1) | 761 (38) | 1469 (34.9) | <0.001 |
| Winter | 1130 (55.6) | 1094 (57.5) | 2224 (56.5) | 0.235 |
| Total | 3181 (41.5%) | 3255 (45.4%) | 6436 (43.4%) | <0.001 |
| 6-11 | | | | |
| Spring | 1076 (73.8) | 1164 (80.6) | 2240 (77.2) | <0.001 |
| Summer | 350 (27.6) | 665 (51.1) | 1015 (39.5) | <0.001 |
| Autumn | 591 (38.6) | 901 (54.9) | 1492 (47) | <0.001 |
| Winter | 1229 (71.5) | 1416 (79.5) | 2645 (75.5) | <0.001 |
| Total | 3246 (54.3%) | 4146 (67.2) | 7392 (60.1) | <0.001 |
| 12-17 | | | | |
| Spring | 808 (81) | 1482 (89.3) | 2290 (86.2) | <0.001 |
| Summer | 448 (47) | 1274 (76.3) | 1722 (65.7) | <0.001 |
| Autumn | 642 (53) | 1613 (80.4) | 2255 (70.1) | <0.001 |
| Winter | 966 (79.7) | 1820 (88.2) | 2786 (85) | <0.001 |
| Total | 2864 (65.5%) | 6189 (83.6) | 9053 (76.9%) | <0.001 |
| Season | | | | |
| Spring | 2896 (61.3%) | 3661 (70.2%) | 6557 (65.9%) | <0.001 |
| Summer | 1235 (29.5 %) | 2409 (50.1%) | 3644 (40.5%) | <0.001 |
| Autumn | 2011 (37.1%) | 3321 (54.7%) | 5332 (46.4%) | <0.001 |
| Winter | 3402 (63%) | 4379 (72.3%) | 7781 (67.9%) | <0.001 |

25 (OH) D= 25-hydroxyvitaminD

Among the patients, 55.6% had 25(OH)D levels below 20 ng/mL (48.4% in boys and 62.1% in girls, p<0.001). While no difference was observed between sexes in the 0.1–1 age group across all seasons, girls exhibited a higher proportion of children with 25(OH)D levels below 20 ng/mL in both the 6–11 and 12–17 age groups across all seasons. The lowest incidence of children with 25(OH)D levels below 20 ng/mL was found in boys during the summer season in the 0.1–1 age group (10.1%), whereas the highest incidence was observed in girls during the spring season in the 12–17 age group (89.3%) (**Table 5**).

## DISCUSSION

This study observed that vitamin D deficiency was most prevalent among adolescent girls during the winter and spring. Vitamin D deficiency has been linked to various diseases in children, including rickets, asthma, obesity, and autism.[10] Additionally, it has been associated with sepsis, Pediatric Risk of Mortality III score, prolonged hospitalization, and mechanical ventilator stay in critically ill patients admitted to intensive care units.[11] Given the widespread prevalence of vitamin D deficiency in this country and globally, it is paramount to identify at-risk groups and implement necessary preventive measures.

Cui et al.[12] reviewed 308 vitamin D prevalence studies with 7,947,359 participants of all age groups from 81 countries between 2000 and 2022 to investigate global vitamin D levels and reported that the estimated prevalence of serum 25(OH) D was 47.9% below 20 ng/mL and 15.7% below 12 ng/mL. The lowest prevalence of serum 25(OH)D below 20 ng/mL is observed in the African region at 18.9%, while the highest prevalence is reported in the Eastern Mediterranean region at 71.8%. Lower-middle-income countries have reported a prevalence of serum 25(OH)D < 20 ng/mL at 56.0%, whereas upper-middle-income countries have reported this rate at 38.2%.[12] In a 2022 global review of vitamin D status, a prevalence of 25(OH) <12 ng/mL was reported at 5% to 18%, and <20 ng/mL at 24% to 49%, with a relatively low overall prevalence of vitamin D deficiency in South America, Oceania, and North America, and a more moderate prevalence in Europe, Asia, and possibly Africa.[13] A systematic review and meta-analysis of publications from African countries reported

an average 25(OH)D level of 27.1 ng/mL, with a prevalence of 25(OH)D <20 ng/mL at 34.2%, and <12 ng/mL at 18.5%.[14] This study observed a prevalence of 25(OH)D <12 ng/mL at 22.8% and <20 ng/mL at 55.6%, exceeding the world average. This discrepancy may be attributed to factors such as differences in sunlight exposure due to insufficient sunlight angles, limited sunny days owing to this country's high latitude location, reduced sunlight exposure due to factors like high-rise buildings and air pollution in urban areas where the majority of the population resides, as well as the clothing styles influenced by traditional and cultural norms.

The serum 25(OH)D levels were 21.6±13.3 ng/mL (mean± standard deviation) in the study of Yeşiltepe-Mutlu G et al., which included 108,742 subjects of all ages and regions in Turkey. The highest mean 25(OH)D level was 23.5±13.7 ng/mL in the Aegean region, while the lowest was 17.6±12.7 ng/mL in the Black Sea region. In the Marmara region, where this study was conducted, the mean was reported to be 21.6±14 ng/mL. The prevalence of vitamin D deficiency in Turkey as a whole was reported as 27%, with the lowest in the Aegean region at 22% and the highest in the Black Sea region at 42%. In the Marmara region, it was reported as 30%. Additionally, the prevalence of 25(OH)D levels below 20 ng/mL was reported as 51% in Turkey overall and 52% in the Marmara Region.[15] In the Erzincan study involving children aged 0–18 years, 25(OH)D levels were reported to be below 10 ng/mL in 8.36% and below 20 ng/mL in 42.33%.[16] Another study conducted in Ankara with 51,560 children aged 0–18 years reported a mean serum 25(OH)D level of 22.86±16 ng/mL, with 20% of children having vitamin D deficiency.[17] In a study conducted in the Aegean Region, the average serum 25(OH)D level in children aged 0–18 was reported as 28.00±15.55 ng/mL.[18] Furthermore, a study conducted in Gaziantep between March 2021 and March 2022, following the COVID-19 pandemic, reported the prevalence of 25(OH)D <10 ng/mL as 21.2% and <20 ng/mL as 64.5%.[19] The mean 25(OH)D level was reported to be 16.6±11.5 ng/mL in a study including adults in Bursa, where this study was conducted.[20] In this study, the median 25(OH)D level was 18.6 (3–145) ng/mL, with a prevalence of vitamin D deficiency at 22.8%, insufficiency at 32.9%, and 25(OH)D levels below 20 ng/mL at 55.6%. Although not all data from studies conducted in Turkey solely include children, it is notable that the prevalence of vitamin D deficiency and 25(OH)D levels below 20 ng/mL are akin to the Turkish average. Given that this region experiences moderate weather conditions—neither as rainy as the Black Sea region nor as sunny as the Aegean and Mediterranean regions—it is unsurprising that the findings align with the national average.

For various reasons, female adolescents and young adults are more likely to suffer from vitamin D deficiency. According to the global review report by Cui et al., the estimated prevalence of serum 25(OH)D below 20 ng/mL is 45.3% in boys and 53.3% in girls; if it falls below 12 ng/mL, it is 13.6% in boys and 17.8% in girls.[12] In a study of children aged 6–17 years, it was reported that the level of 25(OH)D in Chinese girls (18.7 ng/mL) is lower than in boys (20 ng/mL), and the prevalence of vitamin D deficiency in girls is higher than in boys (50% in boys, 56.5% in girls).[21] Another study involving Chinese individuals of all ages reported the mean 25(OH)D level as 17.6 ng/mL in men and 15.3 ng/mL in women.[22] In a systematic review and meta-analysis conducted in Iran, it was reported that the prevalence of 25(OH)D levels below 20 ng/mL in Iranian children was higher in girls than in boys (61% in girls and 35% in boys).[23] The study of Yeşiltepe-Mutlu G et al., encompassing Turkey, reported that the average 25(OH)D level was lower in girls than in boys (in boys: 23.2±12.5 (1–74.4) ng/mL; in girls: 21±13.4 (0.25–74.5) ng/mL). It was also noted that the prevalence of 25(OH)D levels <12 ng/mL and <20 ng/mL was higher in girls than in boys (18% and 45% in boys; 30% and 52% in girls).[15] Similar to this study, a study conducted with children in Ankara revealed that the average 25(OH)D level was lower in girls than in boys (in boys: 25.1±16.6 ng/mL; in girls: 21.0±15.5 ng/mL). Moreover, it was reported that the prevalence of 25(OH)D levels <12 ng/mL and <20 ng/mL was higher in girls than in boys (13.7% and 45.6% in boys; 26.1% and 61.4% in girls).[16] In another study conducted in adults in Bursa, it was reported that the average 25(OH)D level in women was lower than in men (19.5±9.9 ng/mL in men, 15.8±11.7 ng/mL in women).[20] As reported worldwide and in Turkey, low 25(OH)D levels and a high prevalence of vitamin D deficiency were observed, with <25(OH)D levels of 20 ng/mL being more common in girls in this study. Except for a few seasons in the 0.1–1 and 2–5 age groups, 25(OH)D levels were lower in girls than in boys in all other groups. Furthermore, the prevalence of 25(OH)D levels <20 ng/mL was higher in girls in all age groups except 0.1–1 (all seasons) and 2–5 years (winter).

According to customs and traditions in Turkey, when women reach a certain age, they tend to cover more of their body surface with clothing and spend less time outside the home than men, resulting in reduced sunlight exposure. This condition may explain why women, during a certain age, are more likely to experience vitamin D deficiency.

The primary factor contributing to the development of vitamin D deficiency is inadequate exposure to sunlight. Therefore, it is more prevalent in high-latitude countries where sunlight incidence angles are narrow, in urban areas characterized by high-rise buildings and air pollution, and during the winter and spring seasons when sunlight exposure is reduced.[12,13,21,22,24–26] Yeşiltepe-Mutlu G et al. reported in their study that vitamin D deficiency was most common in the Black Sea region due to its cloudy and rainy weather, particularly in the spring and winter seasons, and least typical in the Aegean region with abundant sunshine, especially during the summer season.[15] Additionally, a study conducted on adults in Bursa noted that the prevalence of 25(OH)D levels <20 ng/mL was highest from March to May and lowest from September to November.[20] This study observed a high prevalence of vitamin D deficiency during the spring and winter seasons, consistent with findings from

studies conducted worldwide and in Turkey. This increase in prevalence during these seasons can be attributed to fewer hours of sunlight, reduced time spent outdoors, and limited sun exposure due to wearing thick clothing covering most parts of the body. Interestingly, it was found that 25(OH) D levels were lower in spring compared to autumn despite similar numbers of sunny days. This discrepancy may be explained by the fact that vitamin D levels, which rise during the summer, do not immediately decrease with the reduction in sunny days during autumn. Similarly, it could be because vitamin D levels, which notably decline during the winter months, do not immediately increase with the rise in the number of sunny days during the spring.

Numerous studies conducted in Turkey have consistently reported that the prevalence of vitamin D deficiency was lowest in the 0–1 age range and highest in adolescence. [15–17] The observation of the highest 25(OH)D levels in 0–1-year-olds indicates that vitamin D deficiency is least common in this age group, suggesting the success of prophylactic vitamin D treatment administered to infants. Like infants, adolescents undergo a period of rapid growth and development, resulting in increased vitamin D requirements. However, while prophylactic vitamin D supplementation is provided for the 0–1 age group, it is not administered to prevent vitamin D deficiency in adolescents. Consequently, although the issue of vitamin D deficiency is effectively addressed in infants, it persists among adolescents.

In this study, consistent with the literature, the lowest prevalence of vitamin D deficiency was found in the 0.1–1 age group and was the highest in adolescents. While assessing seasonal variability within individuals is the most appropriate method to determine whether vitamin D levels fluctuate seasonally, the vitamin D levels of the general population can serve as an indicator of insufficiency or deficiency. Although this study's data showed some variance between genders, its limitations warrant further investigation through more targeted and equivalent group studies to ascertain whether such differences truly exist.

Given the large number of cases in this study and its retrospective design, there are limitations such as the inability to conduct a detailed anamnesis (including factors like urban-rural lifestyle, prior vitamin D treatment, and clothing style), physical examinations, and additional laboratory tests aside from 25(OH)D.

## CONCLUSION

This study observed lower 25(OH)D levels in girls compared to boys, with levels decreasing as age increased. The lowest levels were found during winter and spring, while the highest levels were observed during autumn and summer. Considering that the lowest 25(OH)D levels are seen in adolescents, particularly female adolescents, during winter and spring, this study advocates for the development of public health strategies to address vitamin D deficiency in this group. These strategies may include maximizing sunlight exposure, promoting outdoor physical activity, advocating for vitamin D-rich diets, and implementing prophylactic vitamin D therapy. In addition, the possibility of rickets should be taken into consideration in growing children whose 25(OH)D values are less than 20 ng/mL. Serum alkaline phosphatase, calcium, phosphorus, and parathyroid hormone levels should be measured in these children. If the child is younger than three years old or if there is a strong clinical suspicion of rickets due to risk factors or physical symptoms, a radiographic evaluation for rickets should be carried out. Although this study's data revealed some disparity between genders, given the study's limitations, further investigation through more targeted and equivalent group studies is warranted to clarify the extent of such differences.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Bursa City Hospital Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.02.2024, Decision No: 2024-1/8).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1463530
J Contemp Med 2024;14(4):168-173

Original Article / Orijinal Araştırma

# Evaluation of Mean Platelet Volume and 25 Hydroxy Vitamin D Levels In Gestational Diabetic Women

## Gestasyonel Diyabetli Kadınlarda Ortalama Platelet Hacmi ve 25 Hidroksi D Vitamini Düzeylerinin Değerlendirilmesi

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## Abstract

**Aim**: According to few studies which tried to evaluate mean platelet volume (MPV) and 25 hydroxy vitamin D, have shown conflicting results in gestational diabetic patients. In this study we aimed to compare main platelet volume and 25 hydroxy vitamin D values between gestational diabetic patients and healty individual pregnant womens.

**Material and Method**: The patients were selected from 24-28 weeks pregnant people who made gestational diabetes screening and oral glucose tolerance test from obstetric-gynecology, diabetes and endocrinology polyclinics of Okmeydanı Training and Research Hospital. After the searching 52 gestational diabetic patients and 52 healty pregnant women included to the study. We estimated MPV and vitamin D level. In addition, demographic and clinical data of subjects were recorded.

**Results**: Mean platelet volume (MPV) value was found 8.5±1.0 fl and 8.3±1.1 fl. in gestational diabetic and control group respectively. There was no statistically significant differences in MPV value between case and the control group (p>0.05). Mean 25 hydroxy vitamin D value was found 20.5±11.0 ng/ml and 21.1±9.3 ng/ml. gestational diabetic and control group respectively. There was no statistically significant differences in 25 hydroxy (OH) vitamin D value between case and control group.

**Conclusion**: In our study we found no statistically significant differences in MPV and 25-OH vitamin D values between gastational diabetic pregnant group and healty pregnant group.

**Keywords**: Gestational diabetes, main platelet volume, vitamin D

## Öz

**Amaç**: Gestasyonel diyabeti olan hastalarda ortalama trombosit hacmi (MPV) ve 25-OH hidroksi vitamin D düzeylerini değerlendirmeye çalışan az sayıdaki çalışmaya göre, çelişkili sonuçlar ortaya çıkmıştır. Bu çalışmada gestasyonel diyabetik ve sağlıklı gebelerde MPV ve serum 25-OH vitamin D düzeylerini değerlendirmeyi ve karşılaştırmayı amaçladık.

**Gereç ve Yöntem**: Hastalar Okmeydanı Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum, Diyabet ve Endokrinoloji polikliniklerinden gestasyonel diyabet taraması ve oral glukoz tolerans testi yapılmış 24-28 haftalık gebelerden seçildi. Araştırma sonucunda 52 gestasyonel diyabet hastası ve 52 sağlıklı gebe çalışmaya dahil edildi. MPV ve D vitamini seviyeleri tespit edildi. Ayrıca hastaların demografik ve klinik verileri kaydedildi.

**Bulgular**: Çalışmaya alınan gestasyonel diyabetik gebe grubunun ortalama MPV değeri 8,5±1,0 fl; kontrol grubunda ise ortalama MPV 8,3±1,1 fl saptandı. Çalışmaya alınan hasta grubu ile kontrol grubu arasında ortalama MPV değeri dağılımda istatistiksel olarak anlamlı bir farklılık görülmedi (p>0,05). Gestasyonel diyabetik gebe grubunun ortalama 25-OH vitamin D değeri 20,5±11,0 ng/ml; kontrol grubunda ise 21,1±9,3 ng/ml saptandı. Çalışmaya alınan hasta grubu ile kontrol grubu arasında ortalama 25-OH vitamin D değeri dağılımda istatiksel olarak anlamlı bir farklılık görülmedi (p>0,05)

**Sonuç**: Bizim çalışmamızda gestasyonel diyabetik gebe grubu ile sağlıklı gebe grubu arasında MPV ve 25-OH vitamin düzeyleri arasında istatistiksel olarak anlamlı bir fark saptanmadı.

**Anahtar Kelimeler**: Gestasyonel diyabet, ortalama trombosit hacmi, D vitamini

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**Received *(Geliş Tarihi)*:** 02.04.2024 **Accepted *(Kabul Tarihi)*:** 22.07.2024

## INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a glucose tolerance disorder that first appears during pregnancy or is diagnosed during pregnancy.[1] Its true incidence is not fully known; Data in the literature vary depending on the society in which the studies were conducted and the diagnostic criteria. According to IDF (International Diabetes Federation) 2013 data, the frequency of hyperglycemia in pregnant women between the ages of 20-49 is reported to be 16.9%. While the prevalence is 25% in Southeast Asia, it was found to be 10.4% in North America.[2] The frequency of GDM is increasing in studies conducted today. This may be due to the increased frequency of obesity or the decrease in threshold values in diagnosis and tests.[3]

It has been reported that there are changes in platelet function and morphology in diabetic patients.[4] These changes are associated with an increased risk of vascular disease and venous thromboembolism. Platelet volumes are an indicator of platelet synthesis. Platelet volume is one of the determinants of platelet functions because larger platelets are more metabolically active. Increased MPV indicates platelet functions and activation and is considered an indicator of increased cardiovascular disease risk. The slight increase in platelet aggregation that occurs during normal pregnancy causes an increase in platelet number and volume.[4,5] Increased MPV level may accompany acute myocardial infarction, acute ischemic stroke, preeclampsia and renal artery stenosis.[6] Conflicting results regarding MPV have been found in the few studies conducted in gestational diabetic patients.

Vitamin D level in pregnant women is also a subject that has attracted the attention of researchers. Some studies have shown that pregnant women are more prone to vitamin D deficiency[7] and that there is a relationship between vitamin D deficiency and insulin resistance.[8,9] In addition to studies showing the relationship between vitamin D deficiency and insulin resistance in pregnant women and that 25-OH vitamin D concentration is significantly lower in GDM patients than in the control group,[9] there are also studies showing that GDM rates are similar in those with and without vitamin D deficiency.[10]

Vitamin D receptors are expressed in tissues that play a role in the regulation of glucose metabolism, such as muscle and pancreas.[11] In our study, we wanted to study this issue, which has not been clarified in previous studies, in order to find answers to the questions of whether MPV levels can be a factor in the increase in thrombophilia in GDM and what is the relationship between vitamin D deficiency and GDM.

## MATERIAL AND METHOD

The study was approved by the institutional ethics committee with 190 protocol no in 08.04.2014. Written informed consent was obtained from each subject following a detailed explanation of the protocol of the study. All study procedures were conducted in accordance with the ethical principles stated in the "Declaration of Helsinki".

Pregnant women aged 24-28 weeks who applied to Okmeydanı Training and Research Hospital Gynecology and Obstetrics, Diabetes and Endocrinology outpatient clinic for gestational diabetes screening between September 2013 and March 2014 were included in the study. These pregnant women underwent an oral glucose tolerance test (OGTT) with 50, 75g or 100g of glucose. Pregnant women whose glucose value was ≥140 mg/dl at the 2nd hour with 75 g glucose or at the 1st hour with 50 g glucose or who were diagnosed with gestational diabetes by a three-hour sugar loading test with 100 g glucose were included in the case group. Pregnant women who were not diagnosed with gestational diabetes by OGTT were included in the control group. Patients diagnosed with anemia, hemoglobinopathy, preeclampsia, pregestational diabetes, or a systemic disease were excluded from the study.

Of the 104 people included in the study, 52 were gestational diabetics and 52 were nondiabetic healthy pregnant women with similar ages and demographic characteristics. Demographic characteristics of both groups were recorded. Weight measurements were made with thin clothing and no shoes on the same scale (Arzum Peso Model AR535, China, 2008). Height measurements were made on bare foot. Body mass index (BMI) was calculated with the weight (kg)/height2 (m) formula. Waist circumference (WC) was measured with a measuring tape at the level of the umbilicus. Blood pressure of the patients was measured from both arms after a rest of at least 15 minutes using a sphygmomanometer (Erka, Germany).

Glucose, total, very-low-density lipoprotein (VLDL) and high-density lipoprotein (HDL)-cholesterol, triglyceride and insulin levels of the patients were measured in the venous blood sample drawn after 12-hour fasting by a clinical biochemistry otoanalyzer (Olympus AU2700). LDL-cholesterol value was calculated using the Fridewalt formula.

Hemogram, MPV and 25-OH vitamin D levels were checked. For complete blood count, blood is taken into 2 cc EDTA tubes; The study was carried out with the LH 789 device from Beckman Coulter. 25-OH vitamin D level in serum was analyzed by the HLPC method with commercial kits (Immuchrom GmbH, Happenheim, Germany) on an HLPC device (Agilent 1100, Minneapolis, USA). A 25-OH vitamin D level <30 ng/ml was considered vitamin D deficiency.

Pregnant women who were diagnosed with gestational diabetes with a 75 g OGTT two-hour or 50-g OGTT 1st-hour glucose value ≥140 mg/dl and a 100-g OGTT three-hour glucose loading test performed on patients who applied for gestational diabetes screening at 24-28 weeks of gestation were included in the case group was included. The control group included healthy pregnant women who applied for routine gestational diabetes screening at 24-28 weeks of gestation and who were not diagnosed with gestational diabetes by OGTT. Patients diagnosed with anemia, hemoglobinopathy, preeclampsia, pre-gestational diabetes, or a systemic disease were excluded from the study.

Statistical analyses were conducted using the SPPSS 22.0 program. Descriptive statistics of the data were used mean, standard deviation, median, minimum-maximum, rate and frequency values. The distribution of variables were checked with the Kolmogorov Smirnov test. Unpaired t test and Mann Whitney U test was used for comparisons based on the distribution pattern of the numerical data. Chi-square test was used to compare categorical data. Associations between the parameters were evaluated with the Pearson and Spearman's correlation. Analyses where apporpriate. Results were evaluated as significant when $p<0.05$ with in a 95% confidence interval.

## RESULTS

The average age of the GDM group was found to be 31.2±3.4 years. The average age of the control group was 31.0±4.7 years. There was no statistically significant difference between the ages, heights, body weights, BMI, number of pregnancies, and number of weeks of gestation of the GDM group included in the study and the control group. ($p>0.05$) (**Table 1**). The rate of DM history in first-degree relatives of the GDM group was significantly higher than the control group ($p<0.05$) (**Table 1**). While the presence of DM in first-degree relatives was seen in 38.5% of the GDM group; It was seen in 13.5% in the control group.

The average MPV value of the GDM group was 8.5±1.0 fl; In the control group, it was found to be 8.3±1.1 fl. MPV was found to be higher in the patient group included in the study, but the difference with the control group was not significant ($p>0.05$) (**Table 2**).

The average 25-OH vitamin D value of the GDM group was 20.5±11.0 ng/ml; In the control group, it was found to be 21.1±9.3 ng/ml. There was no statistically significant difference between the average 25-OH vitamin D value between the patient group included in the study and the control group ($p>0.05$) (**Table 2**)

There was no statistically significant difference between the patient and control groups in terms of the prevalence of 25-OH vitamin D deficiency ($p>0.05$) (**Table 2**).

There was no statistically significant difference between mean haemoglobin (Hb), platelet (PLT), platelet distribution width (PDW), parathormone (PTH), calcium, phosphorus, alkaline phosphatase (ALP), albumin values between the patient group included in the study and the control group. ($p>0.05$).

The average HbA1C value was 5.3±0.5 (%) in the GDM group and 4.6±0.3 (%) in the control group. A statistically significant difference was detected between the mean HbA1C values of the patient and control groups included in the study ($p<0.05$).

The correlation analysis of the patients' MPV and serum 25-OH vitamin D levels with other clinical and laboratory data is shown in **Table 4**.

There was no significant ($p>0.05$) correlation between MPV level and 25-OH vitamin D value, Hb, PDW, HbA1C, PTH, phosphorus, ALP, albumin, and number of pregnancies. There was a significant ($p<0.05$) negative correlation between MPV value, PLT value and gestational week. There was a significant ($p<0.05$) positive correlation between the MPV value and the calcium value (**Table 4**).

There was no significant ($p>0.05$) correlation between 25-OH vitamin D level and Hb, PLT, PDW, HbA1C, PLT, calcium, phosphorus, ALP, albumin, pregnancy number, and gestational week. There was a significant ($p<0.05$) negative correlation between 25-OH vitamin D level and PTH level (**Table 4**)

**Table 1. Averages of demographic and anthropometric characteristics of the patient and control groups**

| | | Patient GroupGDM) | | | Control Group | | | p-value |
|---|---|---|---|---|---|---|---|---|
| | | Mean + s.d./n-% | Median | min-max | Mean + s.d./n-% | Median | min-max | |
| Ageyears) | | 31.2±3.4 | 32 | 24.0 - 37.0 | 31.0±4.7 | 30 | 24 - 40 | 0.462 |
| Heightcm) | | 160.5±5.1 | 160 | 150.0 - 172.0 | 160.1±5.3 | 160 | 150 - 170 | 0.674 |
| Body weightkg) | | 74.8±7.7 | 75 | 60.0 - 92.0 | 74.1±13.0 | 72 | 55 - 120 | 0.233 |
| BMIkg/m2) | | 29.1±3.2 | 29 | 23.1 - 37.8 | 28.9±4.6 | 29 | 22 - 44 | 0.393 |
| First degree relatives of patients with DM | Yes<br>No | 20 38.5%<br>32 61.5% | | | 7 13.5%<br>45 86.5% | | | **0.004** |
| Number of pregnancy | | 2.2±0.9 | 2 | 1.0 - 4.0 | 2.2±1.0 | 2 | 1 - 5 | 0.522 |
| Gestational Week | | 26.2±1.6 | 26 | 24.0 - 28.0 | 26.0±1.4 | 26 | 24 - 28 | 0.493 |

Mann-whitney u test / Chi-squared test

**Table 2. Average MPV, 25-OH vitamin D and 25-OH vitamin D deficiency averages of the patient and control groups.**

| | | Patient Group(GDM) | | Control Group | | |
|---|---|---|---|---|---|---|
| | | Mean±s.d./n-% | Median (min-max) | Mean + s.d./n-% | Median (min-max) | p-value |
| MPV(fl) | | 8.5±1.0 | 8 (6.5 - 10.7) | 8.3±1.1 | 8 (7 - 12) | 0.303 |
| 25 OH Vit D (ng/ml) | | 20.5±11.0 | 21 (4.2 - 62.0) | 21.1±9.3 | 22 (4 - 50) | 0.477 |
| Vitamin D deficiency <30 | No<br>Yes | 8 15.4%<br>44 84.6% | | 6 11.5%<br>46 88.5% | | 0/566 |

Independent!Samples t test / Mann-whitney u test / Chi-squared test

**Table 3. Mean laboratory parameter of case and control groups**

| | Patient Group (GDM) | | | Control Group | | | p-value |
|---|---|---|---|---|---|---|---|
| | Mean±s.d. | Median | min-max | Mean±s.d. | Median | min-max | |
| Hb (g/dl) | 11.5±0.9 | 12 | 9.5 - 13.3 | 11.4±0.7 | 11 | 10 - 13 | 0.563 |
| PLT (x10$^3$) | 206.3±41.0 | 202 | 122.0 - 336.0 | 211.3±40.7 | 212 | 133 - 282 | 0.411 |
| PDW | 17.1±0.7 | 17 | 16.1 - 19.0 | 17.0±0.6 | 17 | 1·6 - 19 | 0.225 |
| H bAIC (%) | 5.3±0.5 | 5 | 4.5 - 7.1 | 4.6±0.3 | 5 | 4 - 6 | **0.000** |
| PTH (pg/ml) | 33.3±13.4 | 32 | 12.0 - 67.5 | 32.8±16.3 | 33 | 11 - 104 | 0.587 |
| Calcium (mg/dl) | 9.1±0.4 | 9 | 8.0 - 10.0 | 9.2±0.4 | 9 | 8 - 11 | 0.136 |
| Phosphorus( mg/dl) | 3.4±0.4 | 3 | 2.7 - 5.0 | 3.3±0.4 | 4 | 2 - 4 | 0.995 |
| ALP (U/L) | 78.3±19.1 | 78 | 43.0 - 123.0 | 87.2±23.0 | 87 | 49 - 153 | 0.067 |
| Albumin(g/dl) | 3.4±0.3 | 3 | 2.9 - 3.9 | 3.4±0.3 | 3 | 3 - 4 | 0.536 |

Independent Samples t test I Mann-whitney test

**Table 4. Correlation between MPV, serum 25-0H vitamin D level of patients and other clinical with laboratory datas.**

| | | 25 OH Vit D | Hb | PLT | PDW | HbAIC | PTH |
|---|---|---|---|---|---|---|---|
| MPV (fl) | r | 0.002 | 0.126 | -0.396 | 0.152 | 0.141 | -0.106 |
| | P | 0.983 | 0.204 | **0.000** | 0.124 | 0.153 | 0.285 |
| 25OH vit D (ng/ml) | r | | 0.088 | 0.017 | -0.117 | -0.028 | -0.356 |
| | P | | 0.377 | 0.866 | 0.235 | 0.776 | **0.000** |
| | | **Calcium** | **Phosphorus** | **ALP** | **Albumin** | **Number of pregnancy** | **Gestational Week** |
| MPV (fl) | r | 0.205 | 0.030 | -0.168 | 0.144 | -0.077 | -0.208 |
| | P | **0.036** | 0.763 | 0.088 | 0.144 | 0.438 | **0.034** |
| 25OH vit D (ng/ml) | r | 0.134 | 0.046 | -0.101 | -0.043 | -0.128 | 0.064 |
| | P | 0.174 | 0.643 | 0.310 | 0.663 | 0.197 | 0.519 |

Spearman Correlation

## DISCUSSION

Studies have shown that larger platelets are more active and clot better. Large platelets collapse more easily with platelet aggregation agonists such as ADP, collagen, and adrenaline. These larger platelets produce more prothrombotic and vasoactive factors such as arachidonic acid metabolites, serotonin and ATP, and have denser granules.[12,13]

Changes in platelet morphology have been reported in diabetic patients.[14] Increased platelet aggregation is seen in diabetic patients and this correlates with increased cardiovascular events. Platelet activation is increased in diabetic patients compared to nondiabetic patients.[15]

Increased platelet and leukocyte activity increases adhesion to endothelial cells, leading to inflammation and thrombosis. During normal pregnancy, MPV is constant.[12,16-18] There is no difference between MPV values in Type 1 and Type 2 diabetes mellitus.[12,17] In diabetes mellitus, hemostasis shifts towards a prethrombotic state, leading to microangiopathic late complications. It has been found that MPV in diabetic patients is higher than in the normal population. It is known that this height is one of the factors causing impaired hemostasis and prethrombotic state in diabetes. It is a matter of debate whether tight metabolic control can normalize this hyperactivity in diabetes. There are also studies linking this volume increase in platelets to stem cell dysfunction in the megakaryocyte series.[16,19] Although some studies found that MPV levels of macroangiopathic diabetic patients were higher than normal controls, no statistical relationship was found between vascular complications and MPV in many other studies.[19,20] Studies have reported that changes in MPV, rather than qualitative changes in platelet functions, are responsible for hypercoagulable platelets, as in diabetes mellitus.[21]

MPV was found to be high in diabetics with or without complications, but no correlation could be shown between high glucose levels and glycated hemoglobin (HbA1c) and MPV. In type 1 diabetes patients, platelet activation may be associated with poor metabolic control.[21] When blood sugar drops effectively, MPV decreases significantly.[6] MPV levels are higher in diabetic patients than in the control group.[22] High MPV levels have also been reported in prediabetic patients.[23]

Different results have been reported in the few studies conducted on MPV in GDM patients. While several of these studies reported that MPV levels were significantly higher in gestational diabetic pregnant women than in healthy pregnant women, no significant difference was found in other studies. In our study, no statistically significant difference was shown between pregnant women with gestational diabetes and healthy pregnant women in terms of both MPV and platelet count.

Bozkurt et al.[24] showed that gestational diabetic patients had higher MPV levels and lower platelet counts than the control group, and explained the low platelet count with the shorter platelet lifespan in diabetic patients.

In a similar study conducted by Balkan et al.[25] on a total of 89 pregnant women, 38 with gestational diabetes and 51 healthy pregnant women; MPV and HbA1C values of the gestational diabetic group were found to be significantly higher than those of healthy pregnant women.

Having a history of diabetes in first-degree relatives is considered a risk factor in the development of gestational diabetes.[26] In our study, presence of a history of diabetes in first-degree relatives; It was found to be 38.5% in the gestational diabetes patient group and 13.5% in the healthy pregnant group, and was found to be statistically significantly higher (**Table 1**).

In our study, in the correlation analysis of the MPV level of the patients with other clinical and laboratory data; There was a significant negative correlation between MPV value, platelet count and gestational week. There was a significant positive correlation between MPV value and calcium value. However, this was not statistically significant (**Table 4**).

In studies where the MPV value is found to be significantly higher, the gestational week is generally 32-36 weeks. In our study, MPV values at 24-28 weeks of gestation were evaluated. The fact that the MPV value did not show a statistically significant difference between the two groups in our study suggested that this might be due to the fact that the study was conducted at an earlier gestational week.

Vitamin D deficiency is quite common in the general population, and its prevalence in the pregnant population has been known for a long time.[27] Vitamin D has been associated with many negative health outcomes, starting from the preconception period, pregnancy, perinatal period, childhood and adulthood.[27,28] There is also increasing evidence regarding the role of adequate vitamin D levels in maintaining normal glucose homeostasis. It has been observed in the literature that studies evaluating the effect of vitamin D deficiency in patients with gestational diabetes have contradictory results.

There is no international consensus on the reference range of serum 25-OH vitamin D level that best reflects vitamin D status in the normal population and pregnant women. The standard definition of normal values of vitamin D levels in the normal population is the 25-OH vitamin D level that will not cause an increase in PTH level.[32] In our study, when vitamin D deficiency was categorized according to the cut-off value of <30 ng/ml, the deficiency rates were found to be 84.6% in the gestational diabetes group and 88.5% in the healthy pregnant group. The average 25-OH vitamin D level of the gestational pregnant group was found to be lower than that of healthy pregnant women, but no statistically significant difference was shown between them in terms of both rate and level.

When the literature was reviewed in terms of data showing the relationship between vitamin D deficiency and gestational diabetes in pregnant women, in a cross-sectional study conducted by Maghbooli et al.[9] at 24-28 weeks of gestation, the rate of severe vitamin D deficiency was found to be statistically significantly higher in the GDM group than in the control group. Additionally, it was shown that the average 25-OH vitamin D levels were statistically significantly lower in the GDM group than in the control group.

Similarly, in the case-control study conducted by Zhang et al.[11] it was shown that vitamin D deficiency was higher in the GDM group than in the control group, and the average maternal plasma 25-OH vitamin D concentration was statistically significantly lower in the GDM group than in the control group. There are also studies in the literature that do not associate vitamin D deficiency with the risk of GDM. In the case-control study conducted by Baker et al.[29] the relationship between vitamin D deficiency and GDM in the first trimester was evaluated. In this study, first trimester maternal 25-OH vitamin D deficiency rates were found to be similarly low in the GDM group and healthy controls.

In another case-control study by Makgoba et al.[30] in which the relationship between the development of GDM and the first trimester 25-OH vitamin D level was evaluated, no statistically significant difference was detected in the GDM group and the normoglycemic control group in terms of vitamin D deficiency. In a cross-sectional study conducted by Farrant et al.[10] 25-OH vitamin D levels were found to be similar in the GDM group and the healthy pregnant group, and the prevalence of vitamin D deficiency was shown to be 66%.

Studies have reported vitamin D deficiency in pregnant women at rates ranging from 7.2% (2-53) to 78.4%.[31] The prevalence of vitamin D deficiency in our study is higher than other studies. These differences are thought to be caused by many factors that can affect serum 25-OH vitamin D levels, such as the ethnic group in which the study was conducted, clothing style, physical activity status, BMI, and socioeconomic status. There is also not enough data to measure vitamin D levels during pregnancy and evaluate the effectiveness of vitamin D replacement if deficiency is detected. In cases where women during pregnancy and lactation require at least 600 IU vitamin D per day and 25-OH vitamin D levels are <20 ng/ml, 1000-2000 IU/day vitamin D replacement is recommended by The American Congress of Obstetricians and Gynecolgists (ACOG).[33,34]

## CONCLUSION

As a result, in our study, consistent with the literature, the presence of a history of diabetes in first-degree relatives was found to be higher in the GDM group than in the control group. For this reason, we believe that pregnant women with a history of diabetes in their first-degree relatives should be closely monitored for gestational diabetes.

However, vitamin D deficiency was found to be quite common in all pregnant women. Therefore, we believe that measuring vitamin D in all pregnant women is useful.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of İstanbul Okmeydan Training and Research Hospital Clinical Researches Ethics Committee (Date: 08.04.2014, Decision No: 190).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The Work was developed at Van Training and Research Hospital, Van, Turkey.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1467668
J Contemp Med 2024;14(4):174-179

Original Article / Orijinal Araştırma

# A Neurophysical Hypothesis on the Role of the Intensity of the Electromagnetic Field Generated by the Cerebral Hemispheres in the Determination of Laterality, in Line with Einstein's Unified Field Theory

## Einstein'ın Birleşik Alan Teorisi Doğrultusunda, Lateralitenin Belirlenmesinde Serebral Hemisferler Tarafından Oluşturulan Elektromanyetik Alanın Yoğunluğunun Rolü Üzerine Nörofiziksel Bir Hipotez

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## Abstract

**Aim**: Traditional models of cerebral laterality, focusing primarily on anatomical and functional asymmetries, fall short of explaining the underlying physical dynamics. This study pioneers a novel perspective by hypothesizing that the intensity of the electromagnetic field generated by the cerebral hemispheres plays a crucial role in determining laterality. Inspired by Einstein's unified field theory, we explore this hypothesis through an interdisciplinary approach that merges principles of physics with neurophysiology.

**Material and Method**: Our research employed an innovative experimental design involving three groups of male Wistar albino rats categorized based on handedness: right-handed, left-handed, and ambidextrous. We utilized electroencephalography (EEG) to measure the electromagnetic field intensity of the cerebral hemispheres, analyzing the data through a lens that combines traditional neuroscientific methods with concepts adapted from field theory.

**Results**: The findings reveal a significant correlation between the intensity of the electromagnetic field in the dominant hemisphere and handedness, with dominant hemispheres displaying higher field intensities. Notably, ambidextrous rats exhibited no significant difference in field intensity between hemispheres, underscoring the potential influence of electromagnetic fields on hemispheric dominance.

**Conclusion**: This study's implications suggest a radical rethinking of how cerebral functions might be influenced by electromagnetic phenomena. The integration of Einstein's unified field theory into the study of cerebral laterality opens new pathways for research. Our findings advocate for a broader, more integrated understanding of brain functionality, highlighting the need for further interdisciplinary research in this nascent field.

**Keywords**: Laterality, hemisphere, electroencephalography, electromagnetic field

## Öz

**Amaç**: Öncelikle anatomik ve fonksiyonel asimetrilere odaklanan geleneksel serebral lateralite modelleri, altta yatan fiziksel dinamikleri açıklamakta yetersiz kalmaktadır. Bu çalışma, serebral hemisferler tarafından üretilen elektromanyetik alanın yoğunluğunun lateralitenin belirlenmesinde çok önemli bir rol oynadığını varsayarak yeni bir bakış açısına öncülük etmektedir. Einstein'ın birleşik alan teorisinden esinlenerek, bu hipotezi fizik prensiplerini nörofizyoloji ile birleştiren disiplinler arası bir yaklaşımla araştırıyoruz.

**Gereç ve Yöntem**: Araştırmamızda, sağ elini kullanan, sol elini kullanan ve iki elini de kullanabilen olmak üzere üç grup erkek Wistar albino sıçanı içeren yenilikçi bir deneysel tasarım kullanılmıştır. Serebral hemisferlerin elektromanyetik alan yoğunluğunu ölçmek için elektroensefalografi (EEG) kullandık ve verileri geleneksel sinirbilimsel yöntemleri alan teorisinden uyarlanan kavramlarla birleştiren bir mercek aracılığıyla analiz ettik.

**Bulgular**: Bulgular, baskın hemisferdeki elektromanyetik alan yoğunluğu ile el kullanımı arasında anlamlı bir korelasyon olduğunu ve baskın hemisferlerin daha yüksek alan yoğunluğu sergilediğini ortaya koymaktadır. Özellikle, iki elini de kullanabilen sıçanlar, hemisferler arasındaki alan yoğunluğunda önemli bir fark sergilememiş ve elektromanyetik alanların hemisferik baskınlık üzerindeki potansiyel etkisinin altını çizmiştir.

**Sonuç**: Bu çalışmanın sonuçları serebral fonksiyonların elektromanyetik olaylardan nasıl etkilenebileceğine dair radikal bir yeniden düşünme önermektedir. Einstein'ın birleşik alan teorisinin serebral lateralite çalışmasına entegrasyonu, araştırmalar için yeni yollar açmaktadır. Bulgularımız, beyin işlevselliğinin daha geniş, daha entegre bir şekilde anlaşılmasını savunmakta ve bu yeni gelişen alanda daha fazla disiplinlerarası araştırmaya duyulan ihtiyacı vurgulamaktadır.

**Anahtar Kelimeler**: Lateralite, hemisfer, elektroensefalografi, elektromanyetik alan

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**Received *(Geliş Tarihi)*:** 12.04.2024 **Accepted *(Kabul Tarihi)*:** 12.07.2024

## INTRODUCTION

The human brain, an electrical and biochemical organ, naturally generates electromagnetic fields through the activities of its neurons. Neurons communicate via synaptic transmissions, electrical impulses that propagate through neural circuits.[1] This electrical activity generates localized electromagnetic fields, detectable through methods such as electroencephalography (EEG).[2]

The proposition that the intensity of these electromagnetic fields plays a role in determining cerebral laterality is inspired by the unified field theory's foundational concept: the interrelation of forces within a unified framework.[3] In the context of our hypothesis, we extrapolate this concept to suggest that just as the unified field theory seeks to describe different forces within a single framework, the electromagnetic fields generated by cerebral activity could be integral to the brain's functional organization, specifically in the determination of hemispheric dominance.

An electromagnetic field is produced by moving electric charges.[4] It propagates at the speed of moving electric-loaded particles and interacts with charges and currents. The magnetic field creates the electric field by moving charged particles or currents. These two fields can be viewed as a combination of electric and magnetic fields.[5] Unified field theory is usually considered a combination of electric and magnetic fields for a single physical field.[6] According to unified field theory, electric and magnetic fields can generate each other, transform into each other, and affect each other in the surrounding electric and magnetic fields.[7]

The corpus callosum connects the two hemispheres anatomically and physiologically and plays a vital role in the decision-making process and knowledge transportation between the two hemispheres.[8] Information integration across the corpus callosum depends on its structural integrity and functionality.[9] It is a bridge that carries sensory-motor impulses and regulates lateralized behaviors.[10] Corpus callosum abnormalities have adverse effects on the decision-making process.[11] Various studies examined the relationship between corpus callosum size and hand preference.[12-14]

The exploration of cerebral laterality has predominantly been constrained within the boundaries of neuroanatomy and psychology, largely overlooking the profound potential of physical sciences to unravel the mysteries of the brain.[15] The unified field theory, a cornerstone of theoretical physics proposed by Einstein,[3] offers a tantalizing framework for reimagining the principles underlying cerebral functions. Existing literature on cerebral laterality has primarily focused on structural, genetic, and functional aspects, often neglecting the electromagnetic properties intrinsic to neural operations.[16]

In our opinion, although both hemispheres seem to vibrate simultaneously, due to the structural differences of the hemispheres, the hemispheric circulation, and the phase difference in the hemispheric electrodynamic activities, the electromagnetic fields produced by the hemispheres also differ. As a result, the formed electromagnetic waves can interact symmetrically, asymmetrically, or even oppositely to create a combination field of varying intensities. Most likely, the corpus callosum rebalances the static, dynamic, or kinetic storms between the two hemispheres, which is beneficial for the brain.

At the core of this hypothesis is the proposition that the brain's electromagnetic fields, generated by the electrical activity of neurons, could be fundamentally influenced by principles akin to those of the unified field theory. Neurons communicate through electrical impulses, creating localized electromagnetic fields detectable by techniques such as EEG. This neural activity, and consequently the electromagnetic fields it generates, can be conceptualized as being influenced by the same principles that govern the interaction of electromagnetic and gravitational fields in the unified field theory.

In the context of cerebral laterality, this theoretical integration suggests that the dominance of one hemisphere could be attributed, in part, to variations in the intensity of electromagnetic fields generated within the brain. These variations may influence the functional organization and specialization of the hemispheres, affecting cognitive and motor processes that are lateralized, such as handedness.

The application of unified field theory principles to understand brain electromagnetic fields opens new vistas for interpreting brain function and dysfunction. For example, asymmetries in electromagnetic field intensity between hemispheres could underlie the lateralization of certain cognitive functions or predispositions to neurological conditions. This perspective could lead to novel diagnostic approaches, where imbalances in electromagnetic field intensities are used as biomarkers for early detection of cerebral laterality disorders or neurodegenerative diseases.

## MATERIAL AND METHOD

Fifteen male Wistar albino rats weighing 250±50 gr were used. Animals were fed with standard laboratory chow and water. The research methodology and necessary authorizations underwent a thorough examination and received approval from the Committee on Animal Experiment Ethics (Date: 29.04.2024, Decision No: 97) at the Medical Faculty of Ataturk University in Turkey. Both the care of the animals involved in the study and the execution of the experimental procedures adhered strictly to the standards and regulations provided by this ethics committee. There are paw preference tests for different species, such as mice, rats, cats, and dogs, for various topics in the literature.[17-20] We applied a food reaching test to determine the paw preference and food catching time. The rats were placed in steel cages with two holes, separated by 1 cm (**Figure 1**). The openings are proper for using forearms to reach food but small for a snout. Since the paw preference stabilized in five days,[21] we regularly observed the animals

for six days and used the fifth-day results for the handedness assessment in line with the literature.[21,22] We obtained five right-pawed (GI; n=5), five left-pawed (GII; n=5), and five mixed-pawed (GIII, n=5).

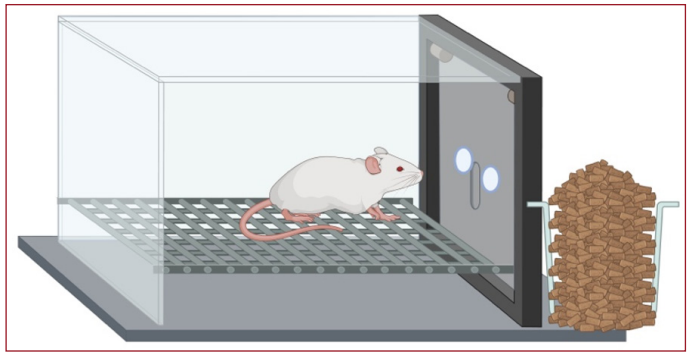

**Figure 1**. Experimental rat placed in steel a cage with two holes separated with 1 cm. Rat can eat food by reaching out through hole(s) (Created with BioRender.com).

Without making any distinction between right-handedness and left-handedness, the time taken by the rats to catch food was taken as a basis. EEG was taken under general anesthesia using conventional methods (MP 100 A-CE (Biopac Systems, USA). At the end of the experiment, the subjects were sacrificed the animals with high-dose anesthesia.

The total length (L) of the five-second EEG wave path taken by the load (number of neurons: n/mm3) in the unit volume of the brain; the total area under these EEG waves (F) is the force exerted by this charge, and the product of these two parameters is considered as the work (W) done by the unit volume of the load. The total work done in five milliseconds is calculated by W=L.F. The W values were compared among groups with the t-test.

### Histological Analysis

In our study, we meticulously prepared brain tissues by fixing them in 10% formalin, embedding them in paraffin, and sectioning at five microns to closely examine the corpus callosum. This region was chosen for its critical role in hemispheric communication and its potential relevance to our investigation of electromagnetic field intensity and cerebral laterality. Hematoxylin and Eosin (H&E) staining was employed to highlight the structural integrity and cellular density of the corpus callosum, offering a clear contrast between neural components and the surrounding matrix.

### Statistical Analysis

Statistical analysis was integral to our examination of histological differences between the groups. Using the Mann-Whitney U test, we compared the neuronal density and structural features within the corpus callosum of right-handed, left-handed, and ambidextrous rats. This non-parametric test was chosen for its suitability in analyzing small, non-normally distributed samples, typical of histological studies.[23]

## RESULTS

As seen in **Figure 2A**, an electric field is formed by the magnetic fields rotating in opposite directions at the edges of a metal disc spun in a U magnet and by the effect of the magnetic field created. This translates into the composite area represented in **Figure 2B**. When the brain is examined with the same laws, it is seen that these laws are also valid in the brain (**Figure 2C**). Because of the corpus callosum U magnet, falx fixed plate. However, the rotating disk has been replaced by the relatively vibrating brain. While the "n" electrically charged neurons (Qn) in a unit volume in the cerebral cortex vibrate and form their fields at different field strengths (yellow-red circles) on the left (LMF) and right (RMF), the combined area of the two hemispheres (UMF) is formed through the corpus callosum.

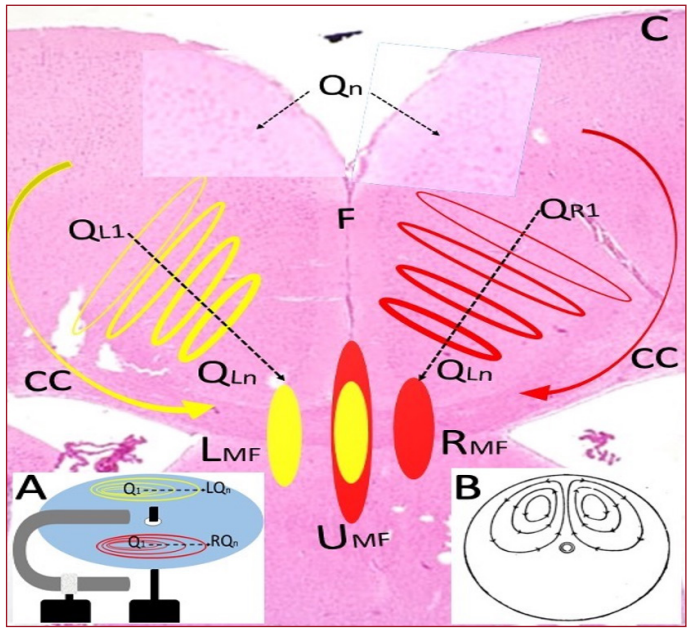


**Figure 2.** A) An electric field is formed by the magnetic fields rotating in opposite directions with each other, B) The magnetic field is translated into the composite area, C) The corpus callosum (CC) U magnet, falx fixed plate. The n electrically charged neurons (Qn) in a unit volume in the cerebral cortex vibrate and form their fields at different field strengths (yellow-red circles) on the left (LMF) and right (RMF): the combined area of the two hemispheres (UMF) is formed through the CC.

The five-millisecond alpha sequence of electroencephalography waves (f(x)) created by the action potential (red curve) formed by a neuronal discharge, magnetic fields (red circles) formed by the vibration resultant of these, and electromagnetic pulsations of the brain in a two-dimensional plane is observed in **Figure 3**. We determined the area between the points where the deepest of these alpha waves intersect the x-axis and five consecutive alpha waves as the representative intensity of the unit combined area of the hemispheres. By calling the smallest unit f, we considered the field strength as its multiples. Here, f(x) is the wave function, l is the wavelength, and F is the area it occupies. The total area intensity (W) is the distance (L) multiplied by the force (F). So: W=L.F

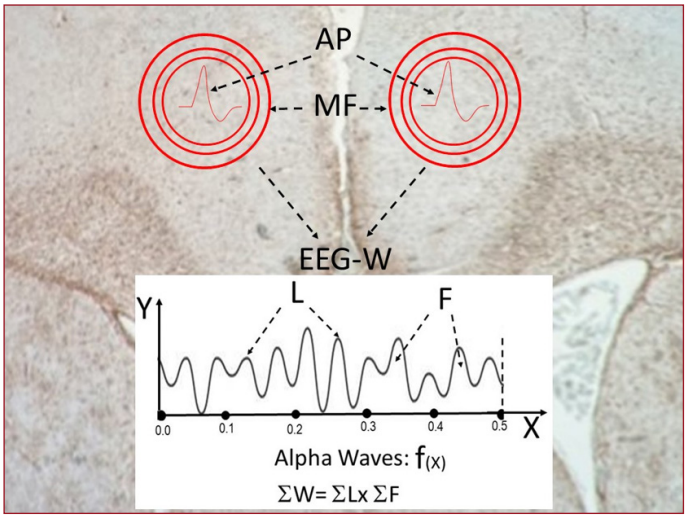


**Figure 3.** The five-millisecond alpha sequence of electroencephalographic waves (f(x)) generated by the action potential (red curve) produced by a neuronal discharge, the magnetic fields (red circles) produced by the resulting oscillations, and the electromagnetic pulsations of the brain are observed in a two-dimensional plane. Here, f(x) is the wave function, L is the wavelength, and F is the area it occupies. The total area intensity (W) is the distance (L) multiplied by the force (F).

The distribution of W values according to the groups is shown in **Table 1**. W values of the dominant hemispheres of GI/GII were significantly higher than the non-dominant ones ($p<0.0005$). The differences between the dominant hemispheres of subjects in GI/GII were insignificant ($p<0.005$). In addition, the differences between the two hemispheres were insignificant in two-handed GIII ($p<0.005$). However, differences between two-handed GIII and GI/GII dominant hemispheres were significant ($p<0.0001$).

**Table 1. The distribution of W values according to the groups**

| | GI | GII | GIII |
|---|---|---|---|
| W/Dominant Hemisphere | 27±3 | 32±5 | 38±6 |
| W/Non-Dominant Hemisphere | 21±2 | 26±4 | 35±5 |
| W/Equal Dominant | - | - | 36±4 |

The relationship between the W values and neuron density of EEG-recorded parietal cortices was compared statistically. Although there was a significant relationship between neuron density and W values, these results were not included in the discussion to avoid prolonging the article.

## DISCUSSION

This study introduces a groundbreaking hypothesis suggesting that the intensity of electromagnetic fields generated by cerebral hemispheres significantly influences hemispheric dominance and, consequently, cerebral laterality. Our findings provide empirical support for this hypothesis, demonstrating a notable correlation between electromagnetic field intensity in the dominant hemisphere and handedness in Wistar albino rats. The implications of these results extend beyond the scope of traditional neurophysiological and neuroanatomical considerations, potentially heralding a paradigm shift in our understanding of brain functionality.

According to Euclidean theory, the shortest line between two points or between the ends of two overlapping line segments is a line segment.[24] According to the geometry of curved spaces and quantum physics laws using non-Euclidean methods,[25] the brain also needs the shortest-time path in physics-time geometry. According to current science, this path is the cycloid or cytochrome curve described by Bernoulli, Galileo, and Huygens.[26] The brachistochrone is the shortest-time curve for the shortest travel time.[27]

Handedness or hand preference is a popular neuroscience subject and has been researched for a long time.[28] In the literature, the language-controlling hemisphere is described as the dominant hemisphere, and the left hemisphere officiates in most human individuals.[29] Half of left-handed and about all right-handed humans are left cerebral dominant.[30] However, the right hemisphere hypothesis refers to the superiority of the right cerebrum in emotional conditions contributing to emotional brain lateralization.[31] Besides, mice represent right-hemisphere hippocampus-dependent 5–7 Hz oscillations in case of observational fear.[32] The right central nucleus of the amygdala performs increased neuronal activity compared to the left one during an acute injury.[33] In some vertebrates, the left hemisphere is a part of routine activities, while the right hemisphere plays a crucial role in emergencies. Animals mostly use the left hemisphere (right side of their bodies) during routine feeding.[34] In the view of such information, left or right-handed and related laterality varies in numerous conditions. Therefore, we can suggest our experimental animals' dominant hemispheres in terms of their hand preference when reaching food.

The corpus callosum has a curious role in determining laterality.[35] Anatomical or functional hemispheric asymmetries emerge as the left and right hemispheres dominate different task-processing aspects.[9] This latter result suggests that during evolution, brain size expansion led to functional lateralization to avoid excessive conduction delays between the hemispheres.[36] Corpus callosum agenesia leads to decision-making compromise and potential negative social consequences.[37] Reaction time increases with callosal agenesia-owned patients.[38] These data on the corpus callosum have been partially confirmed by radiological analysis.[39]

In the regulation of intrahemispheric and interhemispheric electromagnetic field oscillations, the corpus callosum, which connects two hemispheres like two battery cables, may also equalize the capacitances of the hemispheres. According to our theory, this function of the corpus callosum protects the brain from electromagnetic storms. It determines laterality instantly or continuously by adjusting the current balance between the two hemispheres. In determining the laterality, the single hemispheres vary depending on

the electromagnetic field intensity of the hemispheres, the number of neurons they contain, the pulsation frequency of the brain, and the regulatory role of the corpus callosum, and the combined field strength of the whole brain may play an important role.

Cognition and behavior, fundamentally rooted in the complex interplay of neural circuits across both hemispheres, might also be subject to the modulatory effects of these electromagnetic fields. For instance, variations in field intensity could influence cognitive processes such as attention, memory, and language, which are known to be lateralized to some extent. This suggests a possible mechanism by which electromagnetic fields could subtly influence the efficiency or preference of one hemisphere over another for certain cognitive functions.

Moreover, the concept of brain behavior, particularly the lateralization of functions such as handedness, emotional processing, and decision-making, could be re-evaluated in light of our findings. The differential electromagnetic signatures of the hemispheres might provide a physical basis for understanding how certain behaviors or cognitive styles become dominant. This perspective could also inform our understanding of disorders characterized by atypical lateralization, offering new pathways for therapeutic intervention. In essence, by acknowledging the role of electromagnetic fields in the cerebral hemispheres, our study not only contributes to the nuanced understanding of cerebral laterality but also invites a re-examination of how we conceptualize brain function and organization.

**Theoretical Implications for Cerebral Laterality**

In bridging this concept with cerebral laterality, we propose the following theoretical implications:

**Electromagnetic field intensity as a determinant of hemispheric dominance:** The differential intensity of electromagnetic fields generated by each hemisphere could influence the dominance for certain cognitive and motor functions. This aligns with the unified field theory by suggesting that a fundamental physical property (field intensity) underlies diverse neurological phenomena (laterality).

**Interhemispheric interaction and unified field dynamics:** The corpus callosum, facilitating interhemispheric communication, may function analogously to a "field modulator" in the brain's unified field. It could regulate the interaction between the hemispheres' electromagnetic fields, ensuring balanced functionality and coherence in brain operations, akin to the theoretical role of unified fields in maintaining equilibrium among physical forces.

**Empirical exploration of unified field theory concepts in neurology:** By applying concepts from the unified field theory to neurophysiology, we not only explore a novel hypothesis for cerebral laterality but also provide a unique empirical framework to test aspects of unified field theory principles, specifically the interplay and balance of forces (fields) within a complex system (the brain).

**Limitations and Future Insight**

Despite the groundbreaking insights provided by our study, it is important to acknowledge its limitations and outline avenues for future research. One of the primary constraints is the reliance on an animal model to infer cerebral laterality and electromagnetic field implications in humans. While offering valuable preliminary data, the direct applicability of these findings to human neurophysiology requires further validation.

Additionally, the complexity of electromagnetic field measurements and their interpretation within the neural context presents challenges in standardization and replication of the study's methods. Future research should aim to refine these measurement techniques and explore their applicability across a broader spectrum of subjects, including human participants, to substantiate the universality of the observed phenomena.

Furthermore, investigating the interaction between electromagnetic fields and other neural attributes, such as synaptic plasticity and neurotransmitter levels, could provide a more comprehensive understanding of the mechanisms underpinning cerebral laterality. Ultimately, our study lays the groundwork for a novel interdisciplinary approach to exploring brain functionality, urging the scientific community to further investigate the electromagnetic dimension of neural processes and its implications for understanding and treating neurological conditions.

## CONCLUSION

Incorporating a detailed explanation of the unified field theory's principles and their relation to electromagnetic fields in the brain provides a theoretical foundation for our hypothesis. It not only enriched the manuscript by bridging physics and neurophysiology but also invited readers into an interdisciplinary dialogue, potentially catalyzing future research that further explores these connections. By elucidating these concepts, we aimed to make the theoretical underpinnings accessible to readers across disciplines, fostering a deeper understanding of our hypothesis and its implications for cerebral laterality and beyond.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: All animal applications, including surgical and medical procedures, were accepted by the Animal Experiments Local Ethics Committee, Atatürk University (Date: 29.04.2024, Decision No: 97).

**Informed Consent:** Not available.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Acknowledgment**: We are grateful to all of those with whom we have had the pleasure to work during this article.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1475337
J Contemp Med 2024;14(4):180-188

Original Article / Orijinal Araştırma


# The Effect of Oral Care Protocols on Mucositis in Pediatric Cancer Patients: A Randomized Controlled Trial

## Çocuk Kanser Hastalarında Ağız Bakım Protokollerinin Mukozite Etkisi: Randomize Kontrollü Bir Çalışma

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## Abstract

**Aim**: Standard oral care protocols can reduce the incidence of mucositis. This study aimed to evaluate the effect of the "Oral Care Protocol" containing sodium bicarbonate or saline on mucositis development, degree, and duration in pediatric cancer patients.

**Material and Method**: This study is a blind, parallel trial design, randomized controlled study. Patients (n=43) who received inpatient chemotherapy treatment for more than three days at the Pediatric Hematology and Oncology Unit were included. The oral care protocol with saline was given to the patients in the control group (n=22), and the oral care protocol with sodium bicarbonate was given to the patients in the study group (n=21). The primary outcome was the development of mucositis. The secondary outcomes were mucositis degree, patient data at the time of mucositis development, and the duration of mucositis. The characteristics of the patients in the study and control groups and the data of patients with and without mucositis were compared with Fisher's exact test, t-test, and chi-square analysis.

**Results**: No statistically significant difference was found between the study and control groups in terms of mean age, gender, diagnosis, relapse status, treatment stage, risk group, and treatment protocols. Mucositis developed in 18.2% of the patients in the control group and 9.5% of the patients in the study group. No statistically significant difference was found in terms of mucositis development, degree, and duration.

**Conclusion**: The oral care protocol with sodium bicarbonate can be used to prevent mucositis in pediatric cancer patients. ClinicalTrials.gov Identifier: NCT04586491.

**Keywords**: Children, cancer, mucositis, oral care, sodium bicarbonate

## Öz

**Amaç**: Standart ağız bakım protokolleri mukozit insidansını azaltabilir. Bu çalışmada, pediatrik kanser hastalarında sodyum bikarbonat veya salin içeren "Ağız Bakım Protokolü"nün mukozit gelişimi, derecesi ve süresi üzerine etkisinin değerlendirilmesi amaçlandı.

**Gereç ve Yöntem**: Bu çalışma kör, paralel deneme tasarımına sahip, randomize kontrollü bir çalışmadır. Çocuk Hematoloji ve Onkoloji Ünitesinde üç günden fazla yatarak kemoterapi tedavisi gören hastalar (n=43) çalışmaya dahil edildi. Kontrol grubundaki hastalara (n=22) salin ile ağız bakım protokolü, çalışma grubundaki hastalara (n=21) ise sodyum bikarbonat ile ağız bakım protokolü verildi. Birincil sonuç mukozit gelişimiydi. İkincil sonuçlar mukozit derecesi, mukozit gelişimi sırasındaki hasta verileri ve mukozitin süresiydi. Çalışma ve kontrol grubundaki hastaların özellikleri ile mukoziti olan ve olmayan hastaların verileri Fisher'in kesin testi, t-testi ve ki-kare analizi ile karşılaştırıldı.

**Bulgular**: Çalışma ve kontrol grupları arasında yaş ortalaması, cinsiyet, tanı, relaps durumu, tedavi evresi, risk grubu ve tedavi protokolleri açısından istatistiksel olarak anlamlı fark bulunamadı. Kontrol grubundaki hastaların %18,2'sinde, çalışma grubundaki hastaların ise %9,5'inde mukozit gelişti. Mukozit gelişimi, derecesi ve süresi açısından istatistiksel olarak anlamlı fark bulunamadı.

**Sonuç**: Sodyum bikarbonat içeren ağız bakım protokolü pediatrik kanser hastalarında mukozitin önlenmesinde kullanılabilir. ClinicalTrials.gov Tanımlayıcı: NCT04586491.

**Anahtar Kelimeler**: Çocuklar, kanser, mukozit, ağız bakımı, sodyum bikarbonat

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**Received *(Geliş Tarihi)*:** 15.05.2024 **Accepted *(Kabul Tarihi)*:** 27.06.2024

## INTRODUCTION

Oral hygiene is one of the applications in which the individual most needs hygienic care. Oral hygiene in children is essential for minimizing the risk of infection and for strong healthy tooth development. Inadequate oral care may cause dry mouth, dental caries, periodontal diseases, bad breath, stomatitis, and mucositis.[1] The pediatric population is one of the patient groups that most need oral care. Oral care is standard practice, especially in pediatric hematology-oncology units to prevent chemotherapy-related mucositis.[2] Oral evaluation helps to determine the frequency of oral care in case of mucositis. Perry et al.[3] stated that the knowledge of pediatric hematology and oncology nurses on oral care, prevention, and management of complications is variable. Nurses need professional oral care training and cooperation. Oral care is one of the most common care practices that pediatric nurses should use in pediatric patients, but it can often be neglected.[4] The development of mucositis can cause both pain and feeding difficulties in patients and greatly affects the comfort of the child and his family. The most important intervention is to prevent the development of mucositis. Quick and relaxing interventions are required during the treatment process. Additionally, in patients who develop severe mucositis, the chemotherapy protocol may need to be interrupted, and the hospitalization period will be prolonged. It is vital to prevent mucositis from developing, as well as preventing it from reaching serious mucositis.[1-4]

The effectiveness of preventive and therapeutic oral care protocols must be evaluated.[5] Chlorhexidine, saline, sodium bicarbonate, benzydamine, sucralfate, granulocyte stimulating factor, low-dose laser therapy, and cryotherapy can be used to prevent mucositis, but none are definitively effective in chemotherapy-associated mucositis.[6-8] In a guideline for children with oral and oropharyngeal mucositis who have received cancer treatment or HSCT (bone marrow transplantation), it is stated that there are weak recommendations regarding the use of low-dose laser therapy, cryotherapy, and keratinocyte growth factor.[9] In a systematic review and meta-analysis study for children with cancer, prophylactic low-dose laser therapy was reported to reduce mucositis.[10] In a systematic review examining interventions in the treatment of oral mucositis in patients undergoing cancer treatment, comparisons of benzydamine HCl versus placebo, sucralfate versus placebo, low-dose laser versus placebo, and the low-dose laser found effective at reducing mucositis. In pain control, patient-controlled analgesia, continuous infusion, and cognitive behavioral therapy can be used. The use of fewer opioids is recommended for patient-controlled analgesia versus continuous infusion. New interventions in the treatment of mucositis and controlled studies evaluating the effectiveness of the interventions are needed.[11] In randomized controlled studies, mouthwash with morphine was found to be effective in reducing pain due to mucositis associated with chemotherapy.[12,13] Nasogastric tube feeding, and total parenteral nutrition (TPN) are recommended in pediatric cancer patients with gastrointestinal mucositis, but oral intake can be continued by preventing the development of mucositis.[14]

In a systematic review, that used dental care, saline, sodium bicarbonate, mixed mouthwashes, and chlorhexidine for managing oral mucositis (OM) in cancer patients, there was insufficient evidence for these products. It is recommended to develop oral care protocols and evaluate their effectiveness.[15] Yarom et al.[16] recommended in favor of zinc and a recommendation against glutamine. The use of benzydamine mouthwash was also recommended.[17] In a review of the use of various agents, an effective agent was not recommended, and they stated that pilocarpine and pentoxifylline were ineffective.[18]

In a study on the effectiveness of sodium bicarbonate in the prevention and management of mucositis, salt and soda, chlorhexidine, and mouthwash were compared, and no difference was found between the groups. The use of soda was suggested for chemotherapy-induced mucositis.[19] In another systematic review, no difference was found when chlorhexidine, sterile water, and NaCl 0.9% were compared, and the use of chlorhexidine mouthwash was not supported.[20] Another study suggested the use of chlorhexidine to reduce oral mucosal damage in children with cancer.[21] In the prevention and treatment of OM, sodium bicarbonate mouthwash is not recommended in any guidelines for children, and there is insufficient and weak evidence, in studies directed at the adult population. However, since it is harmless, sodium bicarbonate can frequently be used in maintaining oral hygiene. The use of sodium bicarbonate in children may not be beneficial, and it is unpleasant and irritating, the saline can be used in children.[15] There are differences in terms of the agents used in oral care in patients initiating chemotherapy. Sodium bicarbonate is a frequently used and easily accessible preparation. However, studies evaluating its effectiveness in the pediatric population are limited.[22]

Bhatt et al.[23] applied a standardized mucositis protocol for the prevention and management of oral mucositis in HSCT patients receiving high-dose chemotherapy. They stated that the standardized oral care protocol is effective in the management of mucositis. Yavuz and Bal Yılmaz[24] found that the planned oral care training given before chemotherapy reduced the degree of mucositis and pain levels in children. In another study, the standard oral care protocol reduced the incidence of mucositis in children with cancer.[25]

### Aim

This study was conducted to determine the effects of oral care protocol containing sodium bicarbonate or saline solution in the prevention of oral mucositis (OM), mucositis degree, and duration in children with cancer.

### Study hypothesis

There is a difference in oral mucositis, OM degree, and duration between groups.

There is a difference in variables in patients with and without mucositis.

## MATERIAL AND METHOD

### Study design and participants

This study was conducted as a randomized controlled trial with a parallel design. The study participants were composed of children with cancer who received chemotherapy in the Pediatric Hematology and Oncology Unit of a university hospital in Turkey, between October 2019 and February 2020. This trial was approved by the Ethics Committee of the Hospital. It is registered also at the NIH (NCT04586491). This study was guided by the CONSORT checklist.[26]

The sample size was calculated according to Alkhouli et al.'s[27] study using the G*Power software (v. 3.1.9.4). The significant level was set at 0.05 and the statistical power of the study was set at 80%. It estimated that three patients for each group were required to demonstrate an effect size (0.99). The study sample was comprised of 43 children with cancer aged 1-17 years, who received chemotherapy for ≥3 days at inpatient clinics between October 2019 and February 2020, and whose families agreed to their participation in the study (**Figure 1**). Patients excluded who have oral ulceration or mucositis, taking any antiviral or antifungal therapy for OM before enrollment, and at the terminal period. Written informed consent was obtained from children and parents.

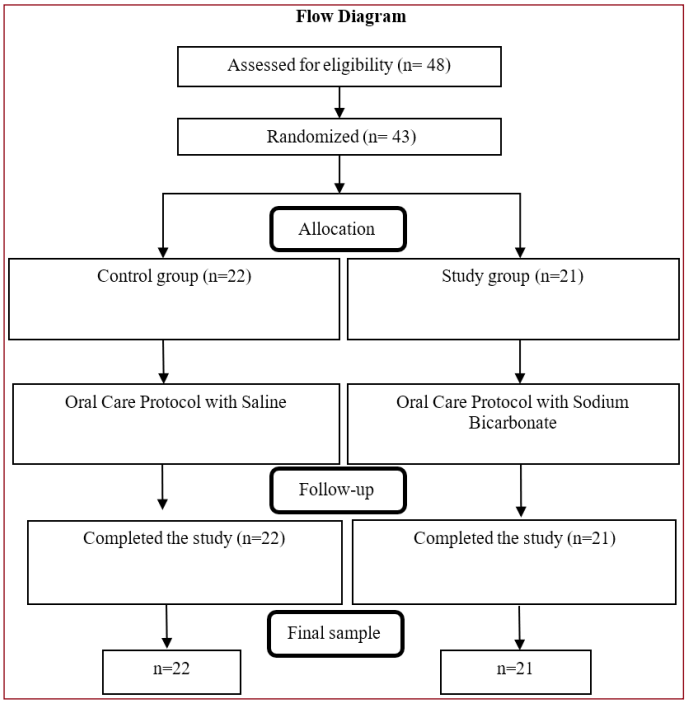


**Figure 1**. Flow diagram of this study

This trial was blinded and the patients/parents, nurses, and investigators had no idea about the groups. The nurse interns who were not in the study randomly assigned all patients into groups.

### Randomization

After the child was included in the sample, he/she was included in the study or control group by stratified randomization method. Randomization was achieved between the study and control groups by stratifying the patients in terms of gender, age, and diagnosis variables. Increasing age and the diagnosis were conditions that prolonged the duration of severe oral mucositis.[28] Therefore, the stratified randomization method was used. In the study, the gender variable was naturally divided into 2 layers, and the age divided into 5 layers as "<1 year, 1-3 years old,> 3-6 years old, 6-12 years old,> 12 years old". The diagnostic variable is divided into 3 layers "Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), and Oncological tumors". In this case, 2×5×3=30 combinations made between variables. According to this randomization method, the possibility of imbalance occurring between the groups is limited.

### Study procedure

Informed consent was obtained from parents of children before the study. The nurse interns who were not in the study randomly assigned all patients into groups; study group/ oral care protocol with sodium bicarbonate 8.4% solution, control group/ oral care protocol with saline solution. All patients took standard oral care protocol in the unit.

### Oral care protocol

- Oral care training for the child and family
- Daily evaluation of the inside of the mouth with the World Health Organization (WHO) Oral Mucositis Grading Scale
- Oral care 4 times a day if oral grade 0, 6 times a day if grade 1, 8 times a day if grade 2, 12 times a day if grade 3, and 24 times a day if grade 4
- Mouthwash with saline (control group) or sodium bicarbonate 8.4% solution (study group) according to the oral care times
- If the patient is unable to mouthwash (<3-4 years), wipe the inside of the mouth with saline (control group) or sodium bicarbonate 8.4% solution (study group) with a sterile sponge
- Brushing teeth with a soft toothbrush (<3-4 years) if platelet value was >50000 mm³
- If the platelet value was <50000 mm³, wipe the inside of the mouth with a sterile sponge soaked with saline (control group) or sodium bicarbonate solution (study group).
- If grade ≥ 1 or 2 mucositis developed and is accompanied by pain, it included mouthwash with saline containing morphine (1cc of morphine is mixed into 19 cc of saline, and the patient is allowed to mouthwash with saline containing 5cc of morphine 4 times a day).
- If grade ≥ 1 mucositis developed, the patients were fed via nasogastric tube.

In the control group, the saline solutions in 500 cc bottles were stored in patient rooms. In the study group, 1 ampoule (10 cc) of 8.4% sodium bicarbonate was added to 500 cc saline solution and stored in the patient rooms. The solutions were renewed every two days. The use of glutamine and mycostatin is recommended for every patient in the unit. However, it is not the standard approach. Patients may not use it at their own discretion.

### Outcomes

The primary outcome was the development of mucositis. The secondary outcomes were mucositis degree, patient data at the time of mucositis development, and the duration of mucositis. During hospitalization, the development status of mucositis and its degree was followed by the WHO Oral Mucositis Grading Scale. If the child with mucositis was older than 8 years old, the ChIMES and Wong-Baker Faces Pain Rating Scale were also applied for the mucositis-related pain. The patient's data about mucositis, the OM duration time, and medical records were recorded in the Mucositis Follow-up Form.

### Study Instruments

**Socio-Demographic Data Collection Form:** It consisted of questions about sociodemographic and treatment-related characteristics of the children; age, gender, socioeconomic level, diagnosis, date of diagnosis, relapse status, treatment stage, diagnosis risk classification, chemotherapy cure, and chemotherapy drugs.[2,12,13,19,27]

**The Mucositis Follow-up Form:** It included the presence of daily mucositis, duration of mucositis, the use of glutamine and Mycostatin, the chemotherapy drugs on the day of mucositis, the number of neutrophils and thrombocytes on the day of mucositis, and the use of analgesic and morphine mouthwash due to mucositis.

**The World Health Organization Mucositis Scale:** It is based on the ability to eat and drink. WHO mucositis scores are 0 (no symptoms), 1 (oral pain) erythema-no change in oral intake, 2 (oral erythema and ulcers, solid diet tolerable- soft foods only), 3 (oral ulcers, liquid diet only), 4 (oral feeding impossible). High scores for the WHO mucositis scale indicated severe mucositis. (29) In the clinic where the study was carried out, patients were routinely evaluated with this tool every day.

**International Child Mucositis Rating Scale (ChIMES):** ChIMES was developed by Tomlinson et al.[30] It evaluates oral mucositis and mucositis-related findings in pediatric oncology patients between 8 and 18 years. ChIMES include the severity of oral pain, the effect of pain on swallowing, eating, drinking, pain relief status, and reason. It consists of six items to evaluate the presence/absence of oral ulcers. Each item of ChIMES 1, 2, 3, and 4 are evaluated with the lowest 0, the highest 5 points; Item 5 is evaluated with the lowest 0, the highest 2 points; Item 6 is evaluated with the lowest 0 and the highest 1 point. When all items are answered, the minimum score obtained from the scale is "0", and the maximum score is "23". The higher the total score obtained from the scale indicates the severity of the mucositis grade. Turkish validity and reliability study of ChIMES is done.[31] The Cronbach's alpha coefficient was 0.91. This scale was used in this study in children with > 0 Grade OM.

**Wong-Baker Faces Pain Rating Scale (WB-FACES):** It is used to measure pain intensity.[32] Mucositis-related pain is evaluated with the 0-10 WB-FACES in children with OM. It was used in this study in children with > 0 Grade OM.

### Ethics

The procedures complied with ethical guidelines and received the Ethics Committee of Dokuz Eylül University (3481GOA 2019/03-55). Written informed consent was obtained from children and parents.

### Data analysis

Numbers, percentages, and averages are used to evaluate demographic data. Kolmogorov Smirnov test was used to determine if data was molded by a normal distribution. Mann Whitney U test and Chi-Square analysis were used to compare mucositis development status, degree, and duration in the study and control groups. Mann Whitney U test, Fisher's exact test, and Chi-Square analysis were used to evaluate patients with and without mucositis in terms of some variables. The research data were analyzed using SPSS (23.0). The p-value accepted as statistically significant <.05.

## RESULTS

### Sample characteristics

There were no statistically significant differences in terms of gender, age, diagnosis, relapse status, the time between the date of diagnosis and study inclusion, and neutrophil and platelet values at the time of inclusion in the study and control groups (p > .05) (**Table 1**).

### Mucositis Development, grade, and duration

Mucositis developed in 18.2% (n=4) of the patients in the control group and 9.5% (n=2) of the patients in the study group. Three patients with mucositis in the control group were in Grade 1, and one patient was in Grade 2. Two patients with mucositis in the study group were Grade 1. Mucositis duration followed in patients with mucositis, and the mucositis of the patients in the control group recovered in 0.8±2.5 days and the study group in 0.1±0.6 days (**Table 2**).

**Table 1. Patient demographics**

| | Control Group / Oral Care Protocol with Saline (n=22) | Study Group / Oral Care Protocol with Sodium Bicarbonate (n=21) | |
|---|---|---|---|
| Gender | n (%) | n (%) | |
| Girl<br>Boy | 6 (27.3)<br>16 (72.7) | 11 (52.4)<br>10 (47.6) | X2= 2.833<br>p= .092 |
| Age (years) M±SD | 7.2±4.6 | 8.4±5.4 | U=208.500<br>p= .583 |
| Age group n (%) | | | |
| ≤6<br>7-12<br>13-18 | 11 (50.0)<br>7 (31.8)<br>4 (18.2) | 9 (42.8)<br>6 (28.6)<br>6 (28.6) | X2= .654<br>p= .721 |
| Diagnosis | | | |
| ALL or AML<br>Oncological tumors | 9 (40.9)<br>13 (59.1) | 5 (23.8)<br>16 (76.2) | X2= 1.431<br>p= .232 |
| Relapse status | | | |
| Yes<br>No | 4 (18.2)<br>18 (81.8) | 5 (23.8)<br>16 (76.2) | X2= .206<br>p= .650 |
| The time between diagnosis and inclusion in the study (month) | | | |
| <6 month<br>>6 month | 12 (54.5)<br>10 (45.5) | 13 (61.9)<br>8 (38.1) | X2= .239<br>p= .625 |
| Neutrophil value | | | |
| <500/µl<br>>500-1,000/µl<br>>1,000 µl | 7 (31.8)<br>7 (31.8)<br>8 (36.4) | 6 (28.6)<br>6 (28.6)<br>9 (42.8) | X2= .190<br>p= .910 |
| Platelet value | | | |
| <50000 mm³<br>>50000 mm³ | 16 (72.7)<br>6 (27.3) | 17 (81.0)<br>4 (19.0) | X2= .407<br>p= .523 |

ALL= Acute Lymphoblastic Leukemia, AML= Acute Myeloid Leukemia

**Table 2: Mucositis development, degree, and duration according to the groups**

| | Control Group (n=22) | Study Group (n=21) | |
|---|---|---|---|
| Mucositis development | n (%) | n (%) | |
| Yes<br>No | 4 (18.2)<br>18 (81.8) | 2 (9.5)<br>19 (90.5) | X2= .671<br>p= .413 |
| Mucositis grade | | | |
| Grade 1<br>Grade 2 | 3 (13.6)<br>1 (4.5) | 2 (9.5)<br>- | - |
| Mucositis duration (day) | M±SD<br>0.8±2.5 | M±SD<br>0.1±0.6 | U=209.500<br>p= .386 |

### Characteristics of Patients with and without Mucositis

Of the patients with mucositis, 66.7% (n=4) were male, and 50% (n=3) were between the ages of 1-6 years. There was no difference between patients with and without mucositis in terms of age group, average age, and gender ($p > .05$).

Of the patients with mucositis 50% were diagnosed with ALL (n=3) and 50% (n=3) were diagnosed with oncological tumors. A difference was found between patients with and without mucositis in terms of diagnosis ($p < .05$). While mucositis did not develop in any patients with AML, mucositis developed in 3 of 7 patients with ALL, and 3 of 27 patients with oncological tumors. There was no difference in terms of the average number of chemotherapy cycles and relapse status of patients with and without mucositis.

When the risk classification of patients with mucositis is examined, it is seen that 66.7% (n=4) of them are at standard risk. Of the patients with mucositis, 66.7% (n=4) were in the consolidation treatment, and 33.3% (n=2) were in maintenance treatment. When the time between diagnosis and including date of the study of patients with mucositis was examined, 50% (n=3) had been receiving chemotherapy for more than 6 months. There was no difference in risk classification, treatment stage, and mean time between diagnosis and including the date of the study in patients with and without mucositis ($p < .05$).

When the chemotherapies received by the patients were examined, of the patients with mucositis 33.3% (n=2) were taking etoposide, 83.3% (n=5) were taking doxorubicin, 33.3% (n=2) were taking vincristine, and 16.7% (n=1) were taking dexamethasone. Two of 6 patients were receiving etoposide and 1 of 6 patients were receiving dexamethasone, and a difference was found between the use of etoposide and dexamethasone in patients with and without mucositis ($p < .05$).

All patients with mucositis were using glutamine and Mycostatin. A difference was found in terms of glutamine and Mycostatin use in patients with and without mucositis ($p < .05$) (**Table 3**).

### The patient's data at the time of mucositis

Of these patients with mucositis, 33.3% had agranulocytosis (ANC < 200/µl) (n=2), 33.3% had moderate neutropenia (ANC: 200-500/µl; n=2) and 33.3% had mild neutropenia (ANC: 500-1,000/µl; n=2). Platelet counts of all patients with mucositis were between 20,000 and 50,000mm³. All patients (n=6) with mucositis were fed by a nasogastric catheter. Morphine mouthwash was applied to five patients with mucositis (83.3%); regular analgesics were administered to four patients with mucositis (66.7%). Three of the patients with mucositis were in the younger age group, so the pain levels associated with mucositis could not be evaluated, and the mean pain score of three patients in the 7-12 age group evaluated by WB-FACES was 6.3±0.5 (min: 6, max: 7) (**Table 4**). The OM and pain associated with mucositis in these three patients were also evaluated with the ChIMES. The intensity of the oral pain was 2.0±0.0 (min: 2 max: 2). The effect of pain on swallowing was 1.6±0.5 (min: 1 max: 2), on eating was 2.0±0.0 (min: 2 max: 2), on drinking was 1.6±0.5 (min: 1 max: 2). Taking painkillers was 1.6±0.5 (min: 1 max: 2), and presence/absence of oral ulcer was 1.6±0.5 (min: 1 max: 2). The mean total score of the ChIMES was 10.6±2.3 (min: 8 max: 12).

**Table 3: Comparison of Patients with and without Mucositis**

| | Patients with mucositis (n=6) | Patients without mucositis (n=37) | |
|---|---|---|---|
| | n (%) | n (%) | |
| Gender | | | |
| Girl | 2 (33.3) | 15 (40.5) | p=1.000** |
| Boy | 4 (66.7) | 22 (59.5) | |
| Age group | | | |
| 1-6 | 3 (50.0) | 10 (27.0) | p=1.000** |
| 7-18 | 3 (50.0) | 17 (73.0) | |
| Age (years) M±SD | 6.3±3.7 | 8.0±5.2 | U=94.000 p= .572 |
| Diagnosis n (%) | | | |
| ALL or AML | 3 (50.0) | 11 (21.7) | p=.373** |
| Oncological tumors | 3 (50.0) | 26 (70.3) | |
| Relapse status | | | |
| Yes | 1 (16.7) | 8 (21.6) | p=1.000** |
| No | 5 (83.3) | 29 (78.4) | |
| Total chemotherapy cycle M±SD | 5.8±5.1 | 4.9±5.6 | U=97.500 p= .644 |
| Risk Categories n (%) | | | |
| Standard-risk group | 4 (66.7) | 24 (64.9) | p=1.000** |
| Medium or High-risk group | 2 (33.3) | 13 (35.1) | |
| Treatment stage | | | |
| Induction or Consolidation | 4 (66.7) | 21 (56.8) | p=1.000** |
| Maintenance | 2 (33.3) | 16 (43.2) | |
| The time between diagnosis and inclusion in the study (month) | | | |
| <6 month | 3 (50.0) | 22 (59.5) | p= .683** |
| >6 month | 3 (50.0) | 15 (40.5) | |
| Chemotherapy used when the mucositis develops* | | | |
| Etoposide (yes/no) | 2 (33.3) / 4 (66.7) | / 37 (100.0) | X2=12.935 p= .000 |
| Doxorubicin (yes/no) | 5 (83.3) / 1 (16.7) | 21 (56.8) / 16 (43.2) | X2=1.525 p= .217 |
| Vincristine (yes/no) | 2 (33.3) / 4 (66.7) | 8 (21.6) / 29 (78.4) | X2=.397 p= .529 |
| Dexamethasone (yes/no) | 1 (16.7) / 5 (83.3) | / 37 (100.0) | X2=6.313 p= .012 |
| Glutamine use | | | |
| Yes/no | 6 (100.0) / - | 10 (27.0) / 27 (73.0) | X2=11.767 p= .001 |
| Mycostatin use | | | |
| Yes/no | 6 (100.0) / - | 19 (51.4) / 18 (48.6) | X2=5.021 p= .025 |

*Most patients use more than one chemotherapy. **Fisher's exact test.

**Table 4. Descriptive Characteristics of Patients with Mucositis**

| Patient no | Study/ Control group | Age | Gender | Diagnosis | Chemotherapies when the mucositis developed | WHO mucositis grade | Neutrophil (µl)/ Platelet (mm³) | WB-FACES Score | Use of analgesics | Use of Morphine mouthwash | Mucositis duration (day) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| P12 | S | 9 | F | Solid tumor | Etoposide-Doxorubicin | 1 | 300/36000 | 6 | no | yes | 3 |
| P21 | C | 11 | M | ALL | Dexamethasone-Vincristine | 1 | 800/32000 | 6 | yes | yes | 1 |
| P22 | C | 3 | F | ALL | Doxorubicin | 1 | 1300/22500 | - | yes | yes | 11 |
| P25 | C | 9 | M | Solid tumor | Etoposide-Doxorubicin-Vincristine | 2 | 440/34000 | 7 | yes | yes | 2 |
| P26 | C | 2 | M | ALL | Doxorubicin | 1 | 100/32000 | - | yes | yes | 5 |
| P36 | S | 4 | M | Solid tumor | Doxorubicin | 1 | 200/49000 | - | no | no | 1 |

## DISCUSSION

The effectiveness of oral protocol containing saline or sodium bicarbonate on the development of mucositis, mucositis degree, and healing time was evaluated in this study. The mucositis developed in 18.2% (n=4) of the patients with an oral protocol containing saline. Although there was no statistical difference, mucositis developed more in the group that used the saline-containing oral care protocol than in the group that used the sodium bicarbonate-containing oral care protocol. Basic oral care in children with cancer usually includes oral care education, regular tooth brushing, and the use of oral saline solutions.[9] None of the mouth rinses such as chlorhexidine, normal saline, sodium bicarbonate, and benzydamine had shown to be effective in preventing chemotherapy-induced OM in children.[6] In a study comparing Aloe-Vera and sodium bicarbonate in children with

ALL (n=22), no statistically significant difference was found in the frequency of OM in the 1st, 5th, 6th, and 8th weeks of the study.[33] However, studies on the pediatric cancer population evaluating the effectiveness of sodium bicarbonate are quite limited.[34,35] There is insufficient evidence for the use of chlorhexidine in children with OM, prophylactic use of 0.12% chlorhexidine gluconate can reduce the frequency of OM.[36] It is seen that the incidence of OM decreased in studies in which regular oral care and training were applied, and standard oral care protocols were used.[22-24]

There was no difference in terms of mucositis degree in this study. Grade 2 mucositis developed in one patient in the control group. The fact that two patients with mucositis in the oral care protocol containing sodium bicarbonate group were grade 1 suggested that sodium bicarbonate might be effective in preventing the increase of mucositis degree. Alkhouli et al.[33] found a statistically significant difference in the occurrence of different OM degrees between groups. Patients in the sodium bicarbonate group began OM sooner than the aloe vera group.[33] In a study comparing propolis and placebo in children with severe OM, 42% of patients had OM in the propolis group, and 48% of patients had OM in the placebo group. Almost half of the patients suffered from severe OM, propolis cannot be recommended for severe OM treatment.[37] In a study using an oral care protocol that includes regular brushing with a soft brush and fluoridated toothpaste and the use of a 0.2% alcohol-free chlorhexidine mouthwash after brushing, children with grade 4 OM were 88% less likely to use the oral care protocol than children with grade 1 OM.[38] The absence of severe OM was pleasing in our study. It showed that our standard oral care protocol is effective in preventing severe OM. Complementary alternative therapies are frequently used in studies, but the content and frequency of the basic oral care approach are often not mentioned in these studies.[33,37]

Although there was no difference in terms of recovery time in this study, we observed that the number of days with OM was low in both groups. In only one patient in the control group, OM continued for 11 days. In Hurrell et al.'s[38] study, the duration of OM was 7 days. In the study of Bhatt et al.[23] their standardized mucositis protocol reduced the incidence and duration of mucositis. Future studies should aim at reducing the grade and duration of OM as well as preventing the development of mucositis.

Pain management is also important for these patients. Oral cryotherapy cannot reduce the incidence of severe OM and oral pain in these patients.[39] Therapeutic LLLT can reduce the severity of oral mucositis and oral pain.[10] Management of OM-related pain should also be addressed in studies. In our study, OM-related pain was also evaluated. The Wong-Baker Faces Pain Scale can be used to evaluate the pain in the mouth due to mucositis.[40] The ChIMES is one of the scales that can be used to evaluate mucositis in children with cancer.[30] In Hurrell et al.'s study,[38] the ChIMES pain score showed an increase in the likelihood of severe OM and the use of CHX mouthwash. In our study, the pain scores of only three patients with mucositis were evaluated due to age group, and mouthwash with morphine was used for pain management. There are no self-report scales for the assessment of OM or OM-related pain in the younger age group such as 3-6 years. Validated screening and assessment tools are especially important for these pediatric patients. Clinical assessment of OM should be a routine care component for children receiving treatment for cancer. Children of different age groups were included in the study. Pain management associated with mucositis should be carried out considering the age group.

In this study, patients with mucositis were using glutamine and Mycostatin. Glutamine can be used to promote mucosal healing during cancer treatment[41] and prevent OM in children with ALL.[42] The keratinocyte growth factor,[9] low-level laser therapy,[43,44] or palifermin can also be used for children with severe mucositis.[45] Honey and olive oil are effective as a preventative and therapeutic measure for OM.[27,46] Probiotics are also effective in reducing OM.[47]

Mucositis developed in 3 of the 7 ALL patients included in the study. OM is more common in children with ALL due to the intensity of treatment.[38] OM management should be given more importance, especially in hematological cancers. Most of the patients with OM were receiving chemotherapy for more than six months. In this study, mucositis developed in two patients on maintenance therapy. Mucositis can develop at any stage of chemotherapy treatment. Therefore, oral care should never be neglected, and a supportive and prophylactic approach should be maintained. Of the six patients with mucositis, two were receiving etoposide and one was receiving dexamethasone. The chemotherapeutic agents are mostly related to severe OM and the interruption in chemotherapy, especially the alkylating agents and antimetabolites.[48] This study revealed that the effective variables in the development of mucositis are diagnosis, risk group, chemotherapy, glutamine, and Mycostatin use. In a study, the presence of HSV, thrombocyte count, Candida spp. found to be associated with an increased degree of mucositis in children and adolescents receiving ALL induction therapy.[49]

The present study had some limitations. There was no age limitation in this study, the younger patients could consider that mucositis was more common in the younger age group. Although stratified randomization was achieved, the patient population is quite large. Only children with leukemia could be studied. If the use of Mycostatin and glutamine were the standard approach in all patients, the effect of the oral care protocol containing saline, or sodium bicarbonate could be more clearly demonstrated. WB-FACES and ChIMES were evaluated in patients with mucositis. However, before the development of OM patients could be evaluated daily with ChIMES.

### Implications

The standardized oral care protocols are effective in the management of mucositis. Chlorhexidine, saline, sodium bicarbonate, benzydamine, sucralfate, granulocyte stimulating factor, low-dose laser therapy, and cryotherapy can be used to prevent oral mucositis in children with cancer. In the prevention of OM, mouthwash with sodium bicarbonate is not recommended in any guidelines for children. There is insufficient and weak evidence for sodium bicarbonate mouthwash, studies directed at the adult population mostly. In this study, mucositis developed less in patients who applied oral care protocol with sodium bicarbonate. The mouthwash with sodium bicarbonate can be used in children with cancer. It is recommended to conduct studies in which the standard approach to preventing mucositis is clearly stated, in younger age groups, in cases of ALL. Studies using comparative products should be conducted in pediatric hematology-oncology units where sodium bicarbonate or other agents are used as the standard approach.

## CONCLUSION

Mucositis developed in 18.2% of the patients in the control group and 9.5% of the patients in the study group. Less mucositis developed in the patients with the oral care protocol containing sodium bicarbonate. There was no difference in terms of mucositis degree and recovery time in this study. Mucositis developed in 3 of the 7 ALL patients included in the study. The standard oral care protocol was used in this study, which deals with the development of mucositis and the recovery period in 43 children treated with chemotherapy. The oral care protocol containing sodium bicarbonate mouthwash was found to be more effective in preventing the development of mucositis in pediatric cancer patients.

The prevention and treatment of OM are difficult, with several methods and pharmacologic agents tested. Standardized oral care protocols are effective in the management of OM. Accordingly, the standard oral care protocol applied in this study, and the efficacy of mouthwash with saline and sodium bicarbonate evaluated, which is frequently used, but there is inadequate evidence in the pediatric population. Prophylactic use of mouthwash with sodium bicarbonate can be recommended in the pediatric cancer population. The incidence and duration of mucositis and mucositis-related pain can be evaluated in younger pediatric patients receiving high-dose chemotherapy with ALL.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Dokuz Eylül University Ethics Committee (Decision No: 3481GOA 2019/03-55).

**Informed Consent:** Written informed consent was obtained from children and parents.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Acknowledgment:** The authors are grateful for the kind cooperation of pediatric oncology patients, pediatric oncology/hematology nursing staffs, and intern nurses.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1496012
J Contemp Med 2024;14(4):189-192

Original Article / Orijinal Araştırma

# Pediatric Modification for Alvarado Score: Appearance of Patients with Apandisitis

## Alvarado Skoru için Pediatrik Modifikasyon: Apandisitli Hastaların Görünümü

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## Abstract

**Aim**: For decreasing the morbidity rate in emergency pediatric surgery clinics, this study evaluated the reliability of an acute appendicitis diagnosis score defined by us as "appearance of the patient with appendicitis (APA)", a new modification of Alvarado Score (AS).

**Material and Method**: One hundred eighty patients, that admitted to Van Training and Research Hospital between February 2018 and June 2018 and were consulted to pediatric surgery with acute appendicitis suspicion; were analyzed as a randomized prospective study. In the new scoring system which we define as APA, instead of a left shift of neutrophils – a state of the patients lying still in the bed, reluctant to speak, with dry lips, with tired eyes, upset and with a troubled expression at the face is placed. For all the patients, AS (AS 1-4, AS 5-6 and AS 7-10) and APA (APA 1-4, APA 5-6 and APA 7-10) scores were independently calculated as three groups and were compared to each other.

**Results**: 180 children (108 males – 72 female) with an average age of 11 (range, 6 – 15) were included in the study. Distribution of patients in the three groups of AS was determined as 1-4: 90 (50%), AS 5-7: 48 (26.7%) and AS 8-10: 42 (23.3%) respectively. Distribution of patients with respect to APA score were as APA 1-4: 72 (40%), APA 5-7: 69 (38.3%) and APA 8-10: 39 (21.7%). Appendectomy was performed on 3 patients from the AS 1-4 group, on 15 patients from AS 5-6 group and on 33 patients from AS 7-10 group. Whereas none of the patients from the APA 1-4 group had an appendectomy, 18 patients from APA 5-6 group and 33 patients from APA 7-10 group had an appendectomy.

**Conclusion**: By means of APA which we define as a combination of AS and clinical judgment (CJ), the number of pediatric cases with appendicitis suspicion to be kept under observation was increased and unnecessary – too early or too late- surgical intervention incidence was decreased. Our study shows CJ and scoring systems are not alternative methods for each other and collective use of both can decrease morbidity and mortality in acute appendicitis treatment.

**Keywords**: Alvarado score, appendicitis, pediatrics

## Öz

**Amaç**: Bu çalışmada, acil çocuk cerrahisi kliniklerinde morbidite oranının azaltılması amacıyla Alvarado'nun yeni bir modifikasyonu olan ve "apandisitli hastanın görünümü (APA)" olarak tanımladığımız akut apandisit tanı skorunun güvenilirliği değerlendirilmektedir. Puan (AS).

**Gereç ve Yöntem**: Şubat 2018 ile Haziran 2018 tarihleri arasında Van Eğitim ve Araştırma Hastanesi'ne başvuran ve akut apandisit şüphesiyle çocuk cerrahisine başvuran 180 hasta; randomize prospektif bir çalışma olarak analiz edildi. APA olarak tanımladığımız yeni puanlama sisteminde nötrofillerin sola kayması yerine hastaların yatakta hareketsiz yatması, konuşmak istememesi, dudakları kuru, gözleri yorgun, üzgün ve yüzünde sıkıntılı bir ifade olması durumu. yüz yerleştirilir. Tüm hastaların AS (AS 1-4, AS 5-6 ve AS 7-10) ve APA (APA 1-4, APA 5-6 ve APA 7-10) skorları üç grup halinde bağımsız olarak hesaplandı ve karşılaştırıldı. birbirlerine.

**Bulgular**: Araştırmaya yaş ortalaması 11 (6-15 yaş aralığı) olan 180 çocuk (108 erkek – 72 kız) dahil edildi. AS'nin üç gruba göre dağılımı sırasıyla 1-4: 90 (%50), AS 5-7: 48 (%26,7) ve AS 8-10: 42 (%23,3) olarak belirlendi. Hastaların APA skoruna göre dağılımı APA 1-4:72 (%40), APA 5-7:69 (%38,3) ve APA 8-10:39 (%21,7) şeklindeydi. AS 1-4 grubundan 3 hastaya, AS 5-6 grubundan 15 hastaya ve AS 7-10 grubundan 33 hastaya apendektomi yapıldı. APA 1-4 grubundaki hastaların hiçbirinde apendektomi yapılmazken, APA 5-6 grubunda 18, APA 7-10 grubunda ise 33 hastaya apendektomi uygulandı.

**Sonuç**: AS ve klinik yargının (CJ) birleşimi olarak tanımladığımız APA sayesinde, apandisit şüphesi ile gözlem altında tutulması gereken pediatrik olguların sayısı artırılmış ve gereksiz -çok erken veya çok geç- cerrahi müdahale sıklığı azaltılmıştır. azaldı. Çalışmamız CJ ve skorlama sistemlerinin birbirine alternatif yöntemler olmadığını ve her ikisinin birlikte kullanımının akut apandisit tedavisinde morbidite ve mortaliteyi azaltabileceğini göstermektedir.

**Anahtar Kelimeler**: Alvarado skoru, apandisit, pediatri

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**Received *(Geliş Tarihi)*:** 24.06.2024 **Accepted *(Kabul Tarihi)*:** 19.07.2024

## INTRODUCTION

Alvarado score (AS) is a well-tested and commonly used clinical scoring system for acute appendicitis diagnosis.[1] Prospective studies reported that just AS could be used as a diagnostic method.[2] Apart from utility and cost effectiveness of AS, its insufficiency may also be in question.[3] Thus, it should be supported with additional parameters in pediatric cases. Some surgeons remark that acute appendicitis can be clinically diagnosed without routine imaging.[4] In studies in where clinical judgment (CJ) and AS were compared, no superiority of AS over CJ could be proved.[5] Objective redefinition of CJ and its incorporation into AS as a parameter may increase the diagnostic value and practical use of AS.

This study intended to evaluate the reliability of CJ, which defined by us as "appearance of patient with appendicitis" (APA). We used APA as a new parameter in AS to develop a new pediatric modified system. We named this modification as "Appearance of Patient with Appendicitis-modified Alvarado Score" (APA m-AS).

## MATERIAL AND METHOD

The study was carried out with the permission of Van Training and Research Hospital Ethics Committee (Date: 03.05.2018, Decision No: 2018/08). This work was carried out in accordance with the Helsinki Declaration principles.

This prospective case control study was conducted in Van Training and Research Hospital as a public institution. One hundred eighty patients that admitted to our clinic between February-June 2018 were included in the work. Our clinic is a reference center for appendicitis surgery. The rates of appendicitis are high, since patients examined by other clinicians (e.g., pediatricians) are directed to our clinic. All patients admitted to the hospital with a right lower quadrant pain were identified with an initial diagnosis of appendicitis, after being assessed using scoring systems. None of the patients were given painkillers during the observation. Patients were divided into three groups regarding to AS score: 1-4 point (discharge), 5-6 point (observation with scoring repeated in 12h), and 7-10 point (urgent surgery).

Instead of a left shift of neutrophils, we preferred to use APA in our newly defined APA m-AS score system included a state of the patients: a) lying still in the bed, b) reluctant to speak, c) dry lips, d) tired looking eyes, and e) upset and troubled expression at the face. These are most common findings about general appearance in acute appendicitis. According to APA m-AS, at least existence of three out of five signs was considered as 1 point.

Similar to AS groups, patients were divided into three groups: APA m-AS 1-4 (discharge), APA m-AS 5-6 (observation with scoring repeated in 12h) and APA m-AS 7-10 (urgent surgery).

AS and APA m-AS scores were compared. Discharged group was followed with phone calls by pediatric surgery nurses. All observed groups were re-evaluated after 12 hours. These patients were either discharged or admitted to the pediatric surgery clinic. This study did not contain pathological results.

### Statistical Analysis

Statistical assessment was performed using SPSS Inc., Chicago, IL, USA (version 15). Normality controls were done using Shapiro–Wilk test. Groups were compared in terms of appendectomy rate, negative pathology rate and hospitalization periods, using independent sample t-test. The statistical significance level was set at $P < 0.05$.

## RESULTS

One hundred eighty patients were included in the work. Average age of the patients was 11 years (range, 6-15 years). Children under six-year-old were excluded from the study because of the difficulty in clinical observation. 108 out of 180 patients (60%) were male and 72 were female. Distribution of patients relative to AS scores was as follows: AS 1-4: 90 (50%), AS 5-6: 48 (26.7%), and AS 7-10: 42 (23.3%). Distribution of patients according to APA m-AS scores was as follows: APA m-AS 1-4: 72 (40%), APA m-AS 5-6: 69 (38.3%), and APA m-AS 7-10: 39 (21.7%). AS and Comparison of AS and APA m-AS scores was exhibited in Figure 1. Appendectomy was performed in 51 of 180 patients (28.3%). Appendectomy was performed in 3 patients from group AS 1-4, 15 patients from group AS 5-6, and 33 patients from group AS 7-10. None of the patients from group APA m-AS 1-4 underwent appendectomy, but 18 patients from group APA m-AS 5-6 and 33 patients from group APA m-AS 7-10 underwent appendectomy. 6 patients in AS 1-4 group were transferred to APA m-AS 5-6 group, and also 6 patients in AS 7-10 group were transferred to APA m-AS 5-6 group without operation.

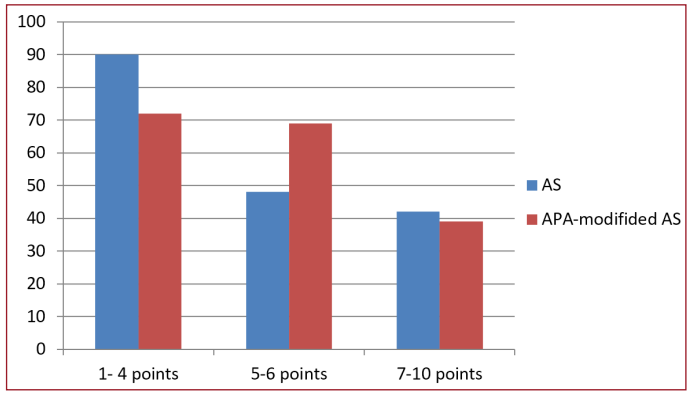


**Figure 1.** Comparison of AS and APA-Modified AS

There was no significant difference between AS group and APA m-AS group in terms of negative pathology and laparotomy rates ($p>0.05$). In the APA m-AS group, we determined that the suspected group (APA m-AS 5-6 points) increased ($p<0.05$). APA was correlated with leukocytosis ($p<0.05$). APA m-AS reduced significantly perforated appendicitis and hospitalization periods ($p<0.05$).

## DISCUSSION

Acute appendicitis is the most frequently performed emergency surgical intervention in all age groups, including children.6 However, due to the mimicking of other diseases, difficulties may be encountered in acute appendicitis diagnosis in children.[7-9] In one of every three pediatric cases examined by clinicians, appendicitis is missed.[10] Due to negative appendectomies with misdiagnosis or too late operations, perforations may occur and thus this lead to an increase of morbidity and mortality.[4,10] Negative appendectomy incidence is reported between 6-32% in previous studies.[11-13] Perforation incidence is almost 100% in infants under a certain age, but it decreases with age and is 65% in children under 4-year-old.[14] Thus, we consider that especially in pediatric surgery clinics, diagnostic methods employed for acute appendicitis should be improved.

AS, first suggested by Alvarado in 19861, is a scoring system, rating the clinical and laboratory findings of patients with possible appendicitis. It is denoted that AS is the best prediction method available for appendicitis diagnosis.2 However, true diagnosis incidence of AS alone is reported as 70%.[3] For this reason, many modified scoring systems have been developed to increase the success rate of AS.[15-17] However, instead of introducing an unaccustomed, many parameters, brand new scoring systems, we consider that AS is more appropriate to improve with modifications since it is the most commonly used and adapted scoring system. Techniques as ultrasonography and computed tomography are referred as well in appendicitis diagnosis.[3,15-18] Such complementary techniques along with AS increase the success rate of AS; however, there are some disadvantages as follows: a) ultrasonography is noticeably dependent to the experience of the physician and b) computed tomography is not available in all the emergency rooms owing to its cost.[17-19] CJ can be considered as another technique in diagnosis.5 Man denoted that CJ was more reliable than AS.[5] Zakaria reported that negative appendectomy reduced in studies used CJ and ultrasonography together, and they defined this method as "modified clinical practice grading score".[20,21] However, Man remarked that especially in clinics without an emergency surgeon, and for less experienced surgeons, AS was more useful.[5]

In our study, with the purpose of increasing the success rate of AS, we developed APA m-AS scoring system. We designed the system as a combination of AS and CJ. Most important disadvantage of CJ is its subjectivity by including the clinical experiences of a surgeon. There is a necessity to eliminate the subjectivity of CJ and make it easier to comprehend for non-surgeon physicians and for less experienced surgeons. In this study, we defined CJ as a state of the patients (lying still in the bed, reluctant to speak, with dry lips, with tired looking eyes, and with upset and troubled expression at the face). Because some symptoms such as anorexia and nausea, which are placed between AS parameters are commonly seen in any other inflammatory disease. Judgment formation is a puzzle. We believe that togetherness of all these subjective parameters are the pieces of this puzzle.

We removed the left shift of neutrophils from AS, and included the patient state into the system. Thus, we defined a newly modified system (APA m-AS). This allowed us, without too much change in the assessment system of AS, to combine CJ and AS. By means of APA m-AS, no appendectomy was performed for patients in discharge group. Transfer of patients that not required appendectomy from AS urgent surgery group to APA m-AS observation group is achieved. Re-evaluation may reduce potential complications with the advantage of early intervention before clinical deterioration.[21,22] Foremost advantage of APA m-AS versus AS is increasing the number of patients in observation group and thus prevent unnecessary–too early or too late- surgical interventions. This method may perhaps reduce morbidity and mortality.

This study reduced the number of misdiagnosed patients and thus increased the number of patients to be kept under observation. We didn't interfere to do decision of surgeon on the call and we didn't give any information about data of patients in any step of management. With this method, the number of patients under observation group increases. Thus, the length of hospital stay associated with complicated surgeries decreases.

## CONCLUSION

By means of APA m-AS, a combination of AS and CJ, number of pediatric cases with appendicitis suspicion to be kept under observation was increased. This study shows that CJ and AS are not alternative methods for each other, and collective use of both can decrease morbidity and mortality in acute appendicitis treatment. Foremost advantage of APA m-AS is retaining the assessment system of well-comprehended, commonly used and cost-effective AS. We consider that APA m-AS will be useful for non-surgeon doctors and less experienced surgeons.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Van Training and Research Hospital Ethics Committee (Date: 03.05.2018, Decision No: 2018/08).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The Work was developed at Van Training and Research Hospital, Van, Turkey.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1499755
J Contemp Med 2024;14(4):193-203

Original Article / Orijinal Araştırma


# A Study on Phubbing, Differentiation of Self and Contribution in Adolescents

## Ergen Bireylerde Phubbing, Benliğin Farklılaşması ve Katkı Üzerine Bir İnceleme

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## Abstract

**Aim**: The present study examined the phenomenon of "phubbing" in adolescents and its potential impact on the development of self-concept.

**Material and Method**: The study was conducted with 436 individuals using a convenience sampling method. This study employs a quantitative research design to examine the mediating role of phubbing in the relationship between self-differentiation and contribution in adolescents. Quantitative research is a method of testing objective theories by examining the relationship between different variables.

**Result**: The results indicated that there was a significant difference in the total scores of emotional reactivity, self-position, differentiation of self and total scores of self-abstraction, contribution to self, contribution to community and contribution, depending on whether the participants were engaged in an activity that they found enjoyable. Furthermore, it was demonstrated that there was a significant difference in emotional reactivity, family, community and contribution total scores in participants who were engaged in an activity to feel good. This study revealed a partial mediation effect of phubbing between differentiation of self and contribution.

**Conclusion**: The findings of the research were discussed in the context of previous studies and suggestions were made.

**Keywords:** Phubbing, differentiation of self, contribution, adolescent ındividual

## Öz

**Amaç**: Bu çalışmada ergen bireylerde phubbing, benliğin farklılaşması ile katkı ele alınmıştır.

**Gereç ve Yöntem**: Çalışma uygun örnekleme yöntemi kullanılarak 436 kişi ile gerçekleştirilmiştir. Bu çalışma, ergenlerde kendini farklılaştırma ve katkı sağlama arasındaki ilişkide phubbing'in aracılık rolünü inceleyen nicel bir araştırmadır. Nicel araştırma, farklı değişkenler arasındaki ilişkiyi inceleyerek nesnel teorileri test etme yöntemidir.

**Bulgular**: Analizlerde gönüllü faaliyetlerde bulunan katılımcıların kendine ve topluluğa katkı ile katkı toplam puanında anlamlı farklılık olduğu, aile ile birlikte faaliyetlerde bulunan katılımcıların aile, topluluk ve katkı toplam puanlarında anlamlı farklılık olduğu bulunmuştur. Katılımcılar keyifli olduklarında bir etkinlikle uğraşmalarına bağlı olarak duygusal tepkisellik, ben pozisyonu, benliğin farklılaşması toplam puan ile kendini soyutlama, kendine katkı, topluluğa katkı ve katkı toplam puanlarında anlamlı farklılık görülmüştür. Ayrıca kendini iyi hissetmek adına bir şeyle uğraşan katılımcılarda duygusal tepkisellik, aile, topluluk ve katkı toplam puanlarında anlamlı farklılık olduğu bulunmuştur.

**Sonuç**: Bu çalışmada benliğin farklılaşması ile katkı arasında phubbingin kısmi aracılık bulgusuna ulaşılmıştır. Araştırma bulguları alanyazındaki çalışmalarla tartışılmış ve önerilerde bulunulmuştur.

**Anahtar Kelimeler**: Phubbing, benliğin farklılaşması, katkı, ergen bireyler

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**Received *(Geliş Tarihi)*:** 11.06.2024 **Accepted *(Kabul Tarihi)*:** 26.07.2024

## INTRODUCTION

Adolescence is a period of storm and stress as well as a stage in which the identity structure of the individual is shaped. In this period, multifaceted changes such as physical, social-emotional, cognitive and physiological symptoms affect the development of the self. These changes support the development of an introverted or extroverted self-perception.[1] Self-awareness is the individual's feeling and awareness of himself/herself as a self that is independent and separated from other individuals.[2] Differentiation of the self is the individual's self-regulation skills in the interpersonal dimension. It includes the ability to control the desired emotional reactions in order to establish social relationships with other individuals. Differentiation of the self in individuals and families refers to a period of time and can differentiate in the process. As the level of differentiation of family members increases, the cooperation between them increases. As differentiation decreases, cooperation, bonds and sacrifices of family members decrease.[3] It includes the individual's ability to create a flexible self while maintaining relationships with people. It includes the ability to control emotional reactivity to establish desired and social relationships.[4]

Differentiation of the self takes place in the process, some individuals have a high level of differentiation while others have a low level. Individuals with a high level of self-differentiation maintain their sense of self when relationships are stressed and establish meaningful relationships with others. Therefore, they can manage stress and relationships in a healthier way.[4] Individuals with undifferentiated selves are quickly affected by emotional processes. Revenge, condemnation, internal detachment behavior, cognitive fusion and emotional avoidance showing unforgiveness can be shown as barriers to the differentiation of the self.[5] Individuals with undifferentiated selves are easily affected by emotional processes. They cannot act independently in matters of concern.[6] Individuals with low level of differentiation cannot distinguish between facts and feelings. They act in the direction of their feelings. They make decisions according to their feelings. They spend intense energy on feelings of love and affection. They cannot realize their cognitive skills due to excitement. They tend to react instantly to their environment. They are caught between family dilemmas. They live their lives by punishing individuals they disapprove of. They often experience emotional and physical problems. They have low energy in jobs that involve them in social production.[3]

Differentiation of the self does not have a negative connotation such as detachment from one's parents or society. What is emphasized here is expressed as a process spent in unity and solidarity by strengthening the sense of belonging with parents.[7] Unity and uniqueness are two important forces in the differentiation of the self. Differentiation of the self is affected by these two forces that affect the relationships of individuals and that we expect to create balance in these relationships. Higher level differentiation enables the individual to maintain his/her sense of self in differentiated conditions and in positions where intense romantic/emotional relationships are active in marriages. Differentiation at a higher level also enables the individual to reduce the anxiety of others and to be psychologically robust against the anxiety developed by others that may be disruptive.[3,8] In a study conducted by Yıldız with 283 university students on differentiation of the self, it was found that there was a moderate negative relationship between differentiation of the self and repetitive negative thoughts (rumination), obsessive thinking and deep thinking.[4]

Differentiation of the self supports the individual's contribution to self, family and community/society. Differentiation of the self is important for the individual to contribute to himself/herself. The individual can contribute to himself/herself in three dimensions.[9] The first is the contribution to oneself. The second is the contribution to his/her family. The third is the contribution to society.[10] Individuals engage in different activities to feel good about themselves. These are activities such as visiting social service institutions, participating in volunteer activities, walking, knitting. These activities provide a spiritual improvement in the individual. In addition, the individual supports the spiritual strengthening of his/her parents and other people in the community. At the end of this process, they contribute to themselves, their parents and society. Inspired by positive youth change, the three-dimensional contribution is linked to positive outcomes such as self-control as well as to characteristics such as self-confidence, caring, relationships and temperament. The three-dimensional contribution is inspired by the understanding that contributions and ideologies in adolescence are influential in the development of the individual. According to the three-dimensional contribution, an individual's contribution to self, family and society is important for the development of an effective society.[11]

The individual develops positively by interacting with the community. The community to which the individual belongs also makes positive contributions to the individual.[12,13] Friend groups can contribute to the development of a sense of belonging. Organized events such as sports competitions and spontaneous events such as conversations have an important place in the development of positive emotions. They contribute to the active development of the individual.[14] The individual's willing and active participation in these activities contributes positively to his/her development. Therefore, the sense of belonging develops further.[15] From this point of view, it can be interpreted that an individual with a differentiated self will contribute more easily. Couple and family relationships are one of the areas to contribute. Polat and İlhan reported that individuals with differentiated

selves had an increase in couple adjustment. Again, differentiation of the self supports the individual to adapt better to different situations and conditions(16). Mert and Çetiner reported that university students with differentiated selves have high levels of adjustment and can take on their own identity.[17] Lampis, Cataudella, Busonera, and Skowron found that self-differentiation is more important than relationship fit in explaining dependent behavior. It has been revealed that people with high levels of differentiation show less dependent behaviors in relationships. This, in turn, increased relationship adjustment by establishing warmer relationships and having an optimistic approach to themselves and their partners.[18] In Skowron and Dendy's study, people with high levels of self-differentiation have more secure ties in relationships. While the highest relationship with attachment anxiety was found in the emotional reactivity sub-dimension, a strong relationship was found between attachment avoidance and emotional detachment. In addition, it was found that there was a strong relationship between effortful control, which is defined as the ability to control one's behaviors with a conscious effort, and self-positioning.[19] Accordingly, it was observed that individuals with high self-positioning levels were more successful in directing and focusing attention, preventing maladaptive behavior and being flexible. Ross and Murdock, in their study focusing on individualistic and collectivistic structures within culture, observed that the differentiation of the self is significantly positively related to the development of the autonomous self, while it is significantly negatively related to the relational self. In particular, strong correlations were found between relational self and interconnectedness with others and emotional reactivity. It was found that autonomous self-construal levels positively predicted life satisfaction and negatively predicted psychological symptoms.[20] On the other hand, relational self-construal was positively correlated with life satisfaction, but also positively correlated with psychological symptoms. Emotional reactivity fully mediated the relationship between relational self-construal and psychological problems. A significant positive correlation was found between interconnectedness with others and life satisfaction.

In case of differentiation of the self, individuals support others to develop positively. However, with the integration of technology into our lives, it interrupts mutual interaction in the social environment where we come together and affects friendship and parental relationships.[4] While the individual should be in communication with one or more people while in a social environment, the fact that there is a one-way communication and the other person is not involved in this interaction disrupts communication. Especially with the intensive use of smartphones recently, people are always interested in their phones and do not continue communication by ignoring the other person.[21]

The widespread use of smartphones has significantly affected people's social interactions. While people interact on social networks via smartphones, they ignore the other person during social interaction when they physically come together.[22] Instead of improving social interaction between people, the intensive use of smartphones has led to the emergence of a problem area called "Phubbing (Sociotelism)" that will negatively affect relationships.[23] Phubbing (sociotelism) is a situation in which people do not interact in a physical social environment and focus on their smartphones, ignoring and ignoring the people in their environment. Over time, it has become a concept frequently used by researchers working on smartphone use.[21]

Phubbing is the act of social isolation by using smartphones and tablets during social activities, constantly following social media and paying attention to social media on the smartphone, ignoring the other person.[23,24] In other words, Sociotelism is when people focus on their smartphones instead of paying attention and listening to others while verbally interacting with them in the same environment. Not only social media but also online messaging and other chat applications are included in this act. Phubbing can be seen in any environment. Here, the person avoids interaction in the physical environment by constantly looking at the smartphone and focusing on it.[25] People can exhibit this behavior even in activities such as eating, listening to lectures, attending meetings, and spending time with family and friends. People who engage in this behavior (Phubbers) often ignore and neglect maintaining and developing relationships with other individuals.[26] As a result, partners' enjoyment of the relationship may decrease, jealousy and depression increase. In addition, social norms may be violated through hurtful and rude behaviors, and trust, empathy, intimacy and satisfaction from conversations between individuals may decrease.[27]

Phubbing leads to social miscommunication. Intensive use of smartphones leads to a decrease in the skills of individuals in the social communication process.[28] While interaction and friendship ties are strengthened in individuals who come together on an activity basis, these ties are weakened with phubbing.[29] Satisfaction between relationships decreases with phubbing. At the same time, conflicts between relationships increase. However, relationship satisfaction decreases and the sense of personal peace is damaged.[23] In addition, phubbing reduces the time spent together, negatively affects the emotional support that individuals provide to each other, and decreases the feeling of closeness.[30] In addition to being relational, phubbing increases stress and anxiety,[31] which can negatively affect mood. Not limited to these, phubbing damages the individual's sense of belonging.[32] This behavior, which even causes passive social exclusion,[33] negatively affects emotional loyalty,[34] and causes compulsive behaviors.[35]

The aim of this study is to examine how contributing tendencies of individuals with differentiated selves are shaped and to reveal what kind of an effect phubbing has in this process. The fact that the literature does not directly address how differentiation of self, phubbing and contribution affect each other made it necessary to conduct the current study. In addition, it was deemed necessary to reveal the mediating role of phubbing in increasing the contribution of the differentiation of the self, which helps the individual to be shaped positively.

- **RQ1.** Does differentiation of self correlate with contribution?
- **RQ2.** Does differentiation of self correlate with the phenomenon of phubbing?
- **RQ3.** Does a correlation exist between the act of contributing and the phenomenon of phubbing?
- **RQ4.** Does the phenomenon of "phubbing" serve as a mediator in the relationship between differentiation of self and contribution?

## MATERIAL AND METHOD

### Research Methodology

This study is a quantitative research examining the mediating role of phubbing in the relationship between self-differentiation and contribution in adolescents. Quantitative research is a method of testing objective theories by examining the relationship between different variables. The measurement of these variables is largely carried out with measurement tools and the raw data, which are thus converted into numerical form, are analyzed through statistical calculations.[36] In addition, a correlational research design was utilized in this study.[37] The relational survey design aims to reveal how the characteristics of the individual affect other variables.[38]

### Working Group

The study group consisted of 436 adolescents between the ages of 15 and 18. The study group was determined through convenience sampling. Convenient sampling is a method that is preferred because it minimizes the loss of time and provides savings in labor force as well as being economical.[38] The age range of the study group varied between 15 and 18 ($\bar{x}$=16.9, SD=1.53). Demographic information of the individuals in the study group is presented in **Table 1**.

**Table 1. Distribution According to Gender**

| Gender | N | % |
|---|---|---|
| Female | 251 | 57.6 |
| Male | 185 | 42.4 |
| Total | 436 | 100 |

When the information on the gender of the participants is analyzed in **Table 1**, 57.6% of the adult individuals are female and 42.4% are male.

**Table 2. Type of School Attended**

| Education Status | N | % |
|---|---|---|
| Science High School | 53 | 12.2 |
| Imam Hatip High School | 69 | 15.8 |
| Social Sciences High School | 108 | 24.8 |
| Vocational Technical Anatolian High School | 102 | 23.4 |
| Anatolian High School | 104 | 23.8 |
| Total | 436 | 100 |

**Table 2** provides information on the type of school the participants attended. It is understood that the participants received education in five different school types.

**Table 3. Duration of Smartphone Use**

| Duration | N | % |
|---|---|---|
| 0-1 hour a day | 23 | 5.28 |
| 2-3 hour a day | 121 | 27.75 |
| 3-4 hour a day | 138 | 31.65 |
| 5 hours or more per day | 124 | 28.44 |
| Not specified | 30 | 6.88 |
| Total | 436 | 100 |

**Table 3** shows the duration of the participants' smartphone usage during the day. Here, it is seen that the participants spend the most time with their smartphones for 3-4 hours a day (38.50%) and the least time with their smartphones for 0-1 hour a day (5.30%).

**Table 4. Participation in Any Volunteer Activity in the Last Month**

| Voluntary activity | N | % |
|---|---|---|
| I participated in voluntary activity | 65 | 14.91 |
| I did not participate in voluntary activities | 361 | 82.80 |
| Not specified | 10 | 2.29 |
| Total | 436 | 100 |

**Table 4** shows whether the participants have participated in any volunteer activity in the last month. **Table 4** shows that the majority of the participants (82.80%) did not take part in any volunteer activity.

**Table 5. Doing Something in Pleasant Times**

| Doing things at leisure | N | % |
|---|---|---|
| Activity available | 410 | 94 |
| No activity | 26 | 6 |
| Total | 436 | 100 |

**Table 5** shows that most of the participants (94%) were engaged in something when they felt joyful, while very few (6%) did not do anything.

**Table 6. Doing Something to Feel Good When Feeling Bad**

| Doing something when you feel bad | N | % |
|---|---|---|
| Activity available | 367 | 84.20 |
| No activity | 69 | 15.80 |
| Total | 436 | 100 |

When **Table 6** is analyzed, it is understood that most of the participants (84.2%) spend time doing something to feel better when they feel bad, while some (15.8%) do not spend time doing anything.

### Data Collection Tools

Three different measurement tools were utilized in the data collection process. The Differentiation of Self Inventory Short Form, Three Dimensional Contribution Scale and General Phubbing Scale were used together with the personal information form created by the researchers according to the literature reviews.

**Differentiation of self ınventory short form:** The Differentiation of Self Inventory Short Form (DSI-SF) was developed.[39] The scale consists of 20 items in a 6-point Likert-type scale ranging from "not at all suitable for me" to "completely suitable for me". The sub-dimensions of the scale are emotional reactivity, self-positioning, emotional detachment and intertwining with others. There are reverse items in the instrument. Cronbach's alpha reliability coefficient for the entire instrument was .88; emotional reactivity .80, self-positioning .70, emotional detachment .79 and intertwining .68. The test-retest reliability coefficients for the measurement tool were .85, .82, .74, .81 and .72, respectively. The Turkish adaptation of the measurement tool and its reliability and validity studies were conducted.[40] Confirmatory factor analysis was conducted for the construct validity of the measurement tool. In this context, the analyses were conducted with 20 items in the measurement tool. After the analyses, it was seen that the goodness of fit values of the measurement tool were at acceptable values (RMSEA=.07, AGFI=.86, CFI=.91, IFI=.91, GFI=.89). In the reliability analysis studies of the measurement tool, Cronbach's alpha internal consistency coefficient was found to be .82 for the total score, .61 for the self-position sub-dimension, .78 for the emotional reactivity sub-dimension, .66 for the emotional detachment sub-dimension, and .72 for the internalization sub-dimension.[40] For the current study, the Cronbach's apha internal consistency coefficient of the BFE-CFS was calculated as .67 for the total score, .54 for the self-position subscale, .71 for the emotional reactivity subscale, .70 for the emotional detachment subscale, and .66 for the internalizing subscale.

**Three dimensional contribution scale:** The Three-Dimensional Contribution Scale was developed.[9] The adaptation process of the measurement tool into Turkish was carried out.[41] The validity and reliability studies of the scale were conducted with 207 individuals. The original structure of the scale consists of three sub-dimensions and a total of 15 items. There are no reverse items in the five-point Likert-type measurement tool. The lowest score that can be obtained from the measurement tool is 15 and the highest score is 75.[9]

The factor structure of the scale was confirmed by confirmatory factor analysis and it was found that the three-dimensional structure of the scale showed acceptable fit (RMSEA= .07, AGFI= .86, GFI= .90, IFI= .93, RMR=.07). The Cronbach alpha internal consistency coefficient was calculated as .86 in the reliability analysis of the scale. In order to determine the similar scale validity of the scale, a significant relationship of .85 was determined between the scale and the five-dimensional well-being scale for adolescents.[41] These findings show that the Three-Dimensional Contribution Scale is a valid and reliable measurement tool. In this study, the Cronbach alpha internal consistency coefficient of the measurement tool was calculated as .88 for the total score, .78 for the self-contribution dimension, .80 for the family contribution dimension, and .77 for the community contribution dimension.

**General Phubbing Scale:** The General Phubbing Scale (GPS) was developed.[42] The adaptation process of the measurement tool into Turkish was carried out.[43] The validation study of the measurement tool in adolescent individuals was conducted.[44] The validity and reliability studies of the scale were conducted with 206 adolescents. The original structure of the seven-point Likert-type scale consists of four sub-dimensions and a total of 15 items. There are no reverse items in the five-point Likert-type scale. The lowest score that can be obtained from the measurement tool is 15 and the highest score is 105.[44]

The factor structure of the scale was confirmed by confirmatory factor analysis and it was found that the four-dimensional structure of the scale showed an acceptable fit (RMSEA= .08, CFI= .95, TLI= .94, IFI= .95). In the reliability analysis studies conducted for the scale, Cronbach alpha internal consistency coefficients were 0.78, 0.85, 0.92, 0.77 and 0.94 for nomophobia, interpersonal conflict, self-isolation, problem acceptance sub-dimensions and total score, respectively.[44] These findings indicate that the GPG is a valid and reliable measurement tool. In this study, the Cronbach alpha internal consistency coefficient of the instrument was calculated as 0.83, 0.81, 0.88, 0.66, and 0.90 for nomophobia, interpersonal conflict, self-isolation, problem acceptance sub-dimensions and total score, respectively.

**Table 7. Normality Analysis of the Distribution**

| | n | Min | Max | Average | SS | Skewness | SH | Kurtosis | SH |
|---|---|---|---|---|---|---|---|---|---|
| DSI | 436 | 25 | 115 | 71.66 | 12.75 | .123 | .117 | 1.480 | .233 |
| GPS | 36 | 15 | 105 | 44.78 | 18.67 | .843 | .117 | .603 | .233 |
| TDCS | 36 | 15 | 75 | 54.92 | 10.87 | -.398 | .117 | .303 | .233 |

**Table 7** shows the minimum-maximum values, mean and standard deviations, skewness kurtosis coefficients and standard errors of the participants' scores obtained from the differentiation of self, three-dimensional contribution and general phubbing scale. In order for the data to be considered normally distributed, the skewness coefficient should take a value between -3, +3 (or -2, +2).[45] Based on the results obtained, it was seen that the scale scores exhibited a normal distribution.

**Personal Information Form:** It was prepared to determine the status of individuals according to various variables.

### Data Collection Process

Ethics committee permission was obtained for the research and the process started. The quantitative data of the study were collected in two different ways, online and offline. Individuals who volunteered to participate in the study were administered the DSI-SF, Three-Dimensional Contribution Scale, and General Phubbing Scale along with the personal information form. The research was conducted with 436 individuals. The data of 436 individuals were analyzed in this study.

### Data Analysis

IBM SPSS 21 and AMOS programs were used to process and interpret the quantitative data collected from the individuals who participated in the study. The raw data were first transferred to these programs and made ready for analysis. IBM SPSS 21 and AMOS programs were then used for analysis. In the data analysis process, frequency analysis and percentage for descriptive statistics; Pearson correlation analysis and structural equation modeling[46-48] were used for the series of relationships and predictors between CPI-CF, contribution and Phubbing.

### Ethics of the Study

This study was approved by the ethics committee of Tokat Gaziosmanpaşa University on 30 January 2024, with decision number 01-65.

### Findings

**Table 8. Distribution of Age, Duration, Scale Total and Sub-dimensions of the Volunteer Activity Group**

| Variables | Participation in any voluntary activity in the last month | | p |
|---|---|---|---|
| | Yes | No | |
| | Ort±SS | Ort±SS | |
| Age | 16.77±0.84 | 16.93±1.64 | 0.438 |
| duration | 2.58±0.88 | 2.66±0.82 | 0.491 |
| DSI_ emotional_cutoff | 3.15±1.45 | 3.26±1.32 | 0.555 |
| DSI_emotional_ reactivity | 3.73±1.17 | 3.76±1.1 | 0.818 |
| DSI_ fusion_with | 2.77±1.06 | 2.91±1.1 | 0.355 |
| DSI_ I position | 4.45±0.98 | 4.12±0.93 | 0.009 |
| DSI_TOTAL | 3.53±0.62 | 3.51±0.68 | 0.878 |
| GPS_ nomophobia | 14.29±6.64 | 14.62±6.31 | 0.699 |
| GPS_ interpersonal conflict | 8.69±4.99 | 10.42±6 | 0.029 |
| GPS_ self-isolation | 9.09±5.79 | 10.8±6.33 | 0.043 |
| GPS_ problem_acknowledgment | 8.85±4.42 | 9.85±4.63 | 0.106 |
| GPS_TOTAL | 40.92±16.87 | 45.7±18.88 | 0.057 |
| TDCS_ to_self | 21.6±3 | 18.96±3.99 | <0.001 |
| TDCS _ to_ family | 18.74±4.92 | 17.81±4.52 | 0.135 |
| TDCS _ to_ community | 19.14±4.21 | 17.2±4.33 | 0.001 |
| TDCS _TOTAL | 59.48±9.94 | 53.98±10.67 | <0.001 |

Note: Significance test was used for the difference between two means.

When **Table 8** is examined, it is seen that there is a significant difference in the self-position dimension of DSI (p=.009), self-contribution (p=.001), community-contribution (p=.001) and total mean scores (p<.001) of the PPIQ compared to those who did not participate in volunteer activities in the last month. In this context, the participants who took part in voluntary activities were as follows: taking part in a Red Crescent aid organization (f=1), collecting money to help a baby with SMA (f=1), participating in any voluntary activity (f=15), participating in a knowledge contest (f=1), taking part in a poetry reading activity (f=3), attending a martyr condolence (f=1), acting as a presenter (f=1), reading activity (f=9), participating in a project (f=1), taking care of the students who came as part of eramus (f=6), preparing food for a bazaar (f=3), participating in a school club activity (f=1), participating in the Human Rights and Freedoms Humanitarian Relief Foundation (IHH) (f=7), participating in an essay (f=1), preparing a Tübitak project (f=2), playing a match on the astroturf (f=1), accompanying kindergarten students on a university trip (f=1), attending TEKNOFEST (f=2), participating in a quiz (f=1), going to the movies (f=1), going to a football match (f=3), chatting with friends (f=1), playing games with friends (f=1), sharing food with friends (f=1), participating in sportive activities (f=6), feeding animals (f=1), donating blood (f=1), playing instruments (f=1), taking part in Disaster and Emergency Situations (AFAD) (f=1), participating in excursions (f=1) .

**Table 9. Distribution of Age, Duration, Scale Total and Sub-dimensions of the Family Activity Group**

| Variables | What You Do to Spend Time with Your Family | | p |
|---|---|---|---|
| | No activity | Activity available | |
| | Ort±SS | Ort±SS | |
| Age | 16.85±0.78 | 16.91±1.57 | 0.844 |
| Duration | 2.46±0.9 | 2.66±0.83 | 0.236 |
| DSI _ emotional_ cutoff | 3.32±1.35 | 3.22±1.34 | 0.721 |
| DSI _ emotional_ reactivity | 3.43±1.11 | 3.77±1.1 | 0.126 |
| DSI_ fusion_with | 3.03±0.93 | 2.87±1.1 | 0.471 |
| DSI _ I position | 3.97±0.82 | 4.19±0.95 | 0.245 |
| DSI_TOTAL | 3.44±0.77 | 3.51±0.66 | 0.571 |
| GPS_ nomophobia | 13.04±5.81 | 14.58±6.37 | 0.230 |
| GPS_ interpersonal conflict | 10.58±5.32 | 10.12±5.91 | 0.701 |
| GPS_ self-isolation | 11.77±7.31 | 10.39±6.21 | 0.276 |
| GPS_ problem_acknowledgment | 9.04±4.18 | 9.72±4.62 | 0.461 |
| GPS_TOTAL | 44.42±19.01 | 44.81±18.68 | 0.919 |
| TDCS_ to_self | 18.42±4.3 | 19.47±4 | 0.198 |
| TDCS_ to _family | 15.12±4.1 | 18.14±4.57 | 0.001 |
| TDCS_ to_ community | 15.08±3.8 | 17.71±4.38 | 0.003 |
| TDCS_TOTAL | 48.62±9.5 | 55.32±10.84 | 0.002 |

Note: Significance test was used for the difference between two means.

**Table 9** shows that there is a significant difference in the mean scores of contribution to family (p=.001), contribution to community (p=.003) and total score (p=.006) of the UCBS for individuals who do something to spend time with their families compared to those who do not share anything. At this point, the participants who did something to spend time with their families had the following activities: picnics (f=4),

spending time together in the evenings (f=3), shopping (f=3), chatting (f=53), going out (f=37), eating together (f=156), doing activities (f=15), going to the village (f=37), cooking (f=15), drinking coffee (f=1), spending time in the garden (f=1), playing games (f=41), visiting family elders (f=39), helping with housework (f=43), playing games (f=1), discussion sessions on history (f=1), traveling (f=72), going to the movies (f=103), hiking (f=69), helping with housework (f=54), playing chess (f=9), playing games (f=61), drinking tea (f=75), knitting (f=7 ).

**Table 10. Distribution of Age, Duration, Scale Total and Sub-dimensions of the Leisure Group**

| Veriables | What You Do to Spend Time with Your Family | | p |
|---|---|---|---|
| | No activity | Activity available | |
| | Ort±SS | Ort±SS | |
| Age | 16.88±0.82 | 16.9±1.56 | 0.948 |
| Duration | 2.54±0.86 | 2.66±0.83 | 0.485 |
| DSI_ emotional_ cutoff | 3.12±1.31 | 3.24±1.35 | 0.656 |
| DCI_ emotional_ reactivity | 3.18±1.05 | 3.79±1.1 | 0.006 |
| DCI_fusion_with | 2.72±0.87 | 2.89±1.1 | 0.446 |
| DCI_ I position | 3.77±0.94 | 4.2±0.94 | 0.023 |
| DCI_TOTAL | 3.2±0.72 | 3.53±0.66 | 0.014 |
| GPS_ nomophobia | 12.27±7.04 | 14.63±6.28 | 0.066 |
| GPS_ interpersonal conflict | 11.23±7.1 | 10.08±5.79 | 0.333 |
| GPS_ self-isolation | 12.88±7.86 | 10.31±6.14 | 0.043 |
| GPS_ problem_acknowledgment | 8.85±4.83 | 9.74±4.58 | 0.339 |
| GPS_TOTAL | 45.23±23.97 | 44.76±18.33 | 0.901 |
| TDCS_ to_self | 17.5±4.57 | 19.53±3.96 | 0.012 |
| TDCS_to_family | 17.12±4.44 | 18.01±4.6 | 0.333 |
| TDCS_ to_community | 15.38±4.12 | 17.69±4.38 | 0.009 |
| TDCS_TOTAL | 50±10.32 | 55.23±10.84 | 0.017 |

Note: Significance test was used for the difference between two means.

When **Table 10** is examined, a significant difference was observed in the mean scores of the participants who did something when they were pleasant compared to the participants who did not do anything, in the emotional reactivity (p=.006), self-position (p=.023) and total score (p=.014) dimensions of the DSI, in the self isolation (p=.043), in the self-contribution (p=.012), in the community-contribution (p=.009) and in the total score (p=.017) dimensions of the PPCQ. When the participants' annotated responses were examined, it was seen that the participants who did something when they enjoyed it were listening to music (f=12), eating (f=10), reading books (f=39), spending time with friends (f=12), spending time with family (f=15), doing sports (f=6), watching TV series (f=10), playing guitar (f=3), drawing pictures (f=12), spending time on the phone (f=11), texting with friends (f=1), picnicking (f=1), eating olives (f=1), playing chess (f=2), traveling (f=2), cycling (f=2), spending time in the kitchen (f=1), playing games (f=21), eating (f=10), playing basketball (f=1), playing games on the playstation (f=1), playing football (f=6 ).

**Table 11. Distribution of Age, Duration, Total and Sub-dimensions of the Activities to be Done to Feel Good When Feeling Bad**

| Veriables | When you feel bad. what do you do to feel good? Explain. | | p |
|---|---|---|---|
| | No activity | Activity available | |
| | Ort±SS | Ort±SS | |
| Age | 16.99±0.7 | 16.89±1.64 | 0.629 |
| Duration | 2.61±0.93 | 2.66±0.81 | 0.661 |
| DSI_ emotional_ cutoff | 3.19±1.27 | 3.24±1.36 | 0.783 |
| DSI_ emotional_ reactivity | 3.5±1.09 | 3.8±1.1 | 0.044 |
| DSI_fusion_with | 2.87±1.12 | 2.88±1.09 | 0.942 |
| DSI_ I position | 3.99±0.93 | 4.21±0.95 | 0.067 |
| DSI_TOTAL | 3.39±0.66 | 3.53±0.67 | 0.100 |
| GPS_ nomophobia | 14.12±6.23 | 14.56±6.37 | 0.595 |
| GPS_ interpersonal conflict | 11.28±6.99 | 9.93±5.63 | 0.082 |
| GPS_ self-isolation | 11.3±7.1 | 10.31±6.11 | 0.228 |
| GPS_ problem_acknowledgment | 9±4.69 | 9.81±4.57 | 0.179 |
| GPS_TOTAL | 45.7±21.87 | 44.62±18.04 | 0.660 |
| TDCS_ to_self | 18.61±4.14 | 19.56±3.99 | 0.072 |
| TDCS_to_family | 16.54±4.84 | 18.23±4.5 | 0.005 |
| TDCS_ to_ community | 16.58±4.48 | 17.73±4.36 | 0.045 |
| TDCS_TOTAL | 51.72±11.41 | 55.52±10.67 | 0.008 |

Note: Significance test was used for the difference between two means.

**Table 11** shows that participants who did something to feel good when they felt bad compared to participants who did nothing showed a significant difference in the mean scores of DSI's emotional reactivity (p=.044), PPI's contribution to family (p=005), contribution to community (p=.045) and PPI's total score (p=.008). When the explanatory responses of the participants were examined, it was found that when they felt bad, they took a walk (f=6), listened to music (f=74), ate (f=7), slept (f=42), read a book (f=20), stayed alone (f=11), spent time with their lovers (f=1), and lay down on the bed (f=3) to feel better, showering (f=5), skin care (f=1), playing games with friends (f=2), sharing with friends (f=1), playing football (f=3), sharing family (f=8), watching movies (f=7), spending time in nature (f=2), watching favorite videos (f=1), sleeping (f=9), going out with mother (f=2), playing sports (f=7), writing poetry (f=1), spending time on social media (f=2), thinking about good things (f=3), playing volleyball (f=2), not thinking about things that make you feel bad (f=2), praying (f=4), reading the Quran (f=1), doing social activities (f=1), playing chess (f=1), cycling (f=2), playing computer games (f=7), painting (f=7), thinking about their dreams (f=2), crying (f=6), talking to someone (f=7), spending time with a sibling (f=1), riding a motorcycle (f=6), watching tiktok (f=1), praying (f=1), waiting calmly (f=1), playing betting coupons (f=1) and giving motivational speeches (f=2) .

**Table 12. Pearson Correlation Analysis for the Relationships Between DSI,TDCS, and GPS**

| | DSI | TDCS | GPS |
|---|---|---|---|
| DSI | 1 | | |
| TDCS | .12** | 1 | |
| GPS | .10** | -.18** | 1 |

* p< .05, ** p< .01

When **Table 12** is examined in detail, a positive (r= .12, p<.01), negative (r= -.18, p<.01) and positive (r= .10, p<.01) significant relationship was found between DSI and TDCS, and GPS, and DSI and GPS, respectively.

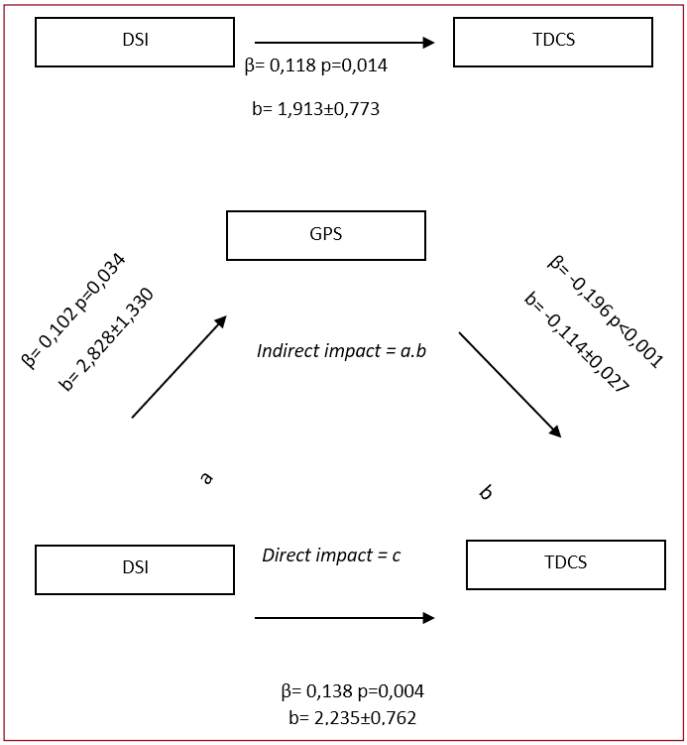


**Figure 1.** The mediating role of gps in the effect of dsı on. The mediating role of gps in the effect of dsı on tdcs

Indirect Impact+ Direct Impact= Total Impact

a.b c=a.b+c

(2,828 x -0,114) + (2,235)=1,913

In the model established in Figure 1, according to the results of the regression analysis, the assumption that DSI, which is required for mediation analysis, has a significant effect on TDCS is provided (β= 0.118 p=0.014). Upon examination of Figure 2, the results of the regression analysis within the established model indicate that the assumption that DSI, which is required for mediation analysis, also has a significant effect on GPS is met. (β= 0.102 p=0.034).Similarly, since GPS, which is another mediating variable assumption in Figure 1, also meets the assumption of significance of GPS on TDCS (β= -0.196; p<0.001), it is understood that GPS is a mediating variable.

Therefore, GPS has a mediating effect in the relationship between DSI and TDCS. It is understood that the effect of DSI on TDCS is an indirect effect. Because, after the model in Figure 1 is established, the direct effect from DSI to TDCS maintains its significance (β= 0.138 p=0.004). Therefore, the GPS acts as a partial mediating variable. Here, the ratio of the indirect effect to the total effect, calculated as (a.b/(a.b+c)) (2.828*-0.114 2.828*-0.114+2.235)=-0.169), is 16.9%. This ratio can be interpreted as 16.9% of the direct impact on DSI is provided as indirect impact.

## DISCUSSION

In the study, it was concluded that there was a significant difference in the total scores of self-positioning, self-contribution, community participation and contribution of individuals who had participated in any volunteer activity in the last month. It is thought that participating in volunteer activities positively empowers the individual. It is seen that the findings obtained in the literature overlap with the results of the current analysis. Aldemir reported that when dealing with anyone, the person has a positive mood, reaches an awareness, connects to life, creates a purpose for life, can cope with negative moods and can more easily overcome their prejudices.[49] Lerner vd, also found that contribution enables the individual to have positive emotions, thoughts and experiences by taking actions. In the same study, it was also revealed that participating in social activities, using leisure time meaningfully and interacting with other people have a significant impact on an individual's well-being.[50] Seligman states that the factors that determine an individual's level of happiness are attitudes towards happiness, living conditions and participation in voluntary activities.[51] Morrow-Howell, Hinterlong, Rozario and Tang, who looked at the relationship between participation in volunteer activities and well-being, also reported that individuals who participated in volunteer activities increased their well-being levels.[52]

In the current study, it was concluded that the activities carried out with the family created a significant difference in the individual's contribution to the family, contribution to the community and contribution total scores. It is acknowledged that the outcomes align with those observed in other studies. Eccles, Early, Frasier, Belansky and McCarthy posited that positive experiences within the family environment facilitate the acquisition of positive experiences in other contexts, including school and peer groups.[53] Cook, Herman, Phillips and Settersten revealed that an individual who has positive experiences with his/her social environment will gain positive experiences with other interaction areas (family, school, etc.) and himself/herself (autonomy).[54]

The other result of the study was that participants who engaged in an activity when they were enjoying themselves showed a significant difference in emotional reactivity, self-position, DSI total score, self-abstraction, self-contribution, contribution to the community and TDCS total score. The considerable divergence observed in both positive and negative dimensions may be attributed to the activities undertaken by the participants. Accordingly, it suggests that there may be situations where the usefulness of the activity is ignored while the participants prefer activities that they think will be good for them. When the literature is examined, it is understood that there are similar studies that overlap with the results. Bailey and Fernando[55] found that participating in leisure time activities and spending this participation in a quality way creates an inner pleasure, which helps the individual to be happy. Şahan[61] reported that sportive

activities will help the individual to be away from concepts such as self-interest and benefit. In the same study, the researcher reports that sportive activities are also important in gaining the skills of being sincere, being fair and belonging. Kelly, Miller-Ott, and Duran reported that excessive use of smartphones will negatively affect communicative expectations.[56] Wirth vd, reported that excessive phone use leads to passive social exclusion.[33]

In this study, when the participants were asked what they were dealing with when they felt bad, it was concluded that there was a significant difference in emotional reactivity, contribution to the family, contribution to the community and TDCS. In the result obtained, the significant difference in the positive and negative dimensions in order to feel good may be due to whether the participants personally participate in the actions they perform. The findings of the Dupuis and Smale[57] study, which was conducted with individuals aged 55 and over, indicated that those who engaged in hobby and handicraft activities on a regular basis exhibited higher levels of psychological well-being than those who engaged in these activities on a moderate or infrequent basis. Vernon, Modecki, and Barber found a positive relationship between problematic use of social media, which is among leisure time activities, and depressive mood.[58]

In this study, it was concluded that there was a low level positive significant relationship between differentiation of self and contribution. It is understood that the result is similar to the results of the research in the literature. Yıldız[4] reported that differentiation of self helps individuals to establish meaningful relationships with other people. Sandage and Jankowski,[5] on the other hand, revealed that the undifferentiated self leads the individual to be in destructive relationships with other people. In different studies, it has been reported that a high level of differentiation of the self helps the individual to reduce his/her worries and helps him/her to remain psychologically strong against the worries that other people may cause on the individual.[4,8] In their 2017 study, Lampis and colleagues observed that individuals with high levels of self-differentiation exhibited less dependent behaviours in relationships. Skowron and Dendy found that individuals with a high level of self-positioning are better at being flexible, preventing maladaptive behavior, and directing attention. Therefore, it can be interpreted that individuals with differentiated selves make positive contributions to themselves and other people.[19]

Another result obtained from the research is that there is a low level positive significant relationship between differentiation of self and phubbing. It is thought that the sub-dimensions are effective in obtaining such a result in the research. It is understood that the results obtained overlap with the results in the literature. Roberts and David reported that phubbing reduces satisfaction between relationships and leads to conflicts. In the same study, it was revealed that phubbing reduces relationship satisfaction between individuals, damages feelings of personal peace and negatively affects communication.[23] McDaniel and Coyne reported that phubbing reduces the time spent together, leads to a feeling of lack of emotional support and causes a decrease in the feeling of closeness.[30] Karaaziz and Keskindağ reported that frequent smartphone use is associated with stress and anxiety.[31]

Another result obtained in the current study is that phubbing has a low level negative relationship with contribution. It is seen that the result obtained overlaps with different study problems when the literature is examined. Kelly, Miller-Ott, and Duran reported that excessive use of smartphones will negatively affect communicative expectations and lead to dissatisfaction.[56] Ranie and Zickuhr stated that phubbing can lead to negative and hurtful consequences in human communication.[59] Han, Min, and Lee revealed that the sense of belonging of people exposed to phubbing may be damaged.[32] In different studies, it has been reported that phubbing causes passive social exclusion,[33] negatively affects emotional loyalty,[34] and causes compulsive behaviors.[35]

Another result obtained from the study is that GPS has an indirect effect on DSI's prediction of TDCS. When the literature is examined, it is understood that phubbing has a disruptive effect on an individual's self-regulation and interaction with individuals. In this context, it is understood that the results obtained overlap with the results in the literature. Ang vd, revealed that phubbing leads to social disconnection and undermines communication skills.[28] Al-Saggaf & O'Donnell reported that phubbing increases depression, decreases relationship satisfaction, negatively affects empathic care and weakens the relationship bond.[27] Ergün et al, reported that individuals exposed to phubbing may have anxiety, depression and negative self-perception.[60]

## CONCLUSION

There may be an increase in contributing actions due to the differentiation of the individual's self. However, the presence of attitudes and behaviors that will affect the individual negatively, such as phubbing, may cause the process to be shaped negatively. It would be useful to include topics such as self-regulation, regulation of emotions, differentiation of the self and contribution in the life of the individual in intervention and prevention studies to be carried out for situations that will negatively affect the individual such as technology addiction. In addition, directing adolescents to semantically rich, process-oriented actions that they will personally participate in will help them both shape their selves in a healthy way and increase their well-being by interacting with different people. Participating in volunteer activities, taking part in social responsibility activities and participating in club activities will help individuals develop these aspects.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Tokat Gaziosmanpaşa University Ethics Committee (Date: 30.01.2024, Decision No: 01-65).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1502013
J Contemp Med 2024;14(4):204-209

Original Article / Orijinal Araştırma


# Relationship Between Electrocardiography and Electrolytes Before and After Dialysis in Hemodialysis Patients

## Hemodiyaliz Hastalarında Diyaliz Öncesi ve Sonrası Elektrokardiyografi ile Elektrolitler Arası İlişki

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## Abstract

**Aim**: Cardiovascular events are the most important cause of mortality in hemodialysis patients. Rapid volume changes and electrolyte shifts during dialysis lead to arrhythmias. The study aims to determine whether there is a relationship between before and after hemodialysis electrocardiographic (ECG) whole wave and interval changes and electrolyte levels in hemodialysis patients.

**Material and Method**: A total of 112 patients undergoing maintenance hemodialysis treatment three times a week for four hours for more than six months were included in the study. Before and after hemodialysis, 12-lead ECG, weight, arterial blood pressure, before hemodialysis hemogram and biochemistry, and demographic data were recorded. Waves and intervals were calculated from the 12-lead ECG taken before and immediately after dialysis, and the relationship with serum electrolyte levels was evaluated. P<.05 was considered significant.

**Results**: Among the patients, 51.8% were female, and the mean age was 49.83(±18.69) years. Post-dialysis RR interval showed a significant negative correlation with phosphorus (p=.007) and uric acid (p=.013). A moderate negative correlation was found between the pre-dialysis QTc interval and uric acid (p=.008), and between the post-dialysis QTc interval and sodium (p=.016). Linear regression analysis revealed that phosphorus (p=.007) and uric acid (p=.013) significantly affected the post-dialysis RR interval, uric acid (p=.008) was significant on pre-dialysis QTc interval. Again sodium (p=.016) and calcium (p=.027) were significant for the post-dialysis QTc interval.

**Conclusion**: The negative correlation between post-dialysis RR interval and phosphorus and uric acid, between pre-dialysis QTc and uric acid, and between post-dialysis QTc and sodium makes ECG interpretation and arrhythmia risk assessment difficult as a result of volume and electrolyte shifts.

**Keywords**: Hemodialysis, electrocardiography, electrolytes

## Öz

**Amaç**: Hemodiyaliz hastalarında kardiyovasküler olaylar en önemli mortalite nedenidir. Diyaliz esnasındaki hızlı volüm değişiklikleri ve elektrolit şiftleri aritmilere önderlik eder. Bu çalışma hemodiyaliz hastalarında hemodiyaliz öncesi ve sonrası elektrokardiyografik (ECG) tüm dalga ve interval değişiklikleri ile elektrolit düzeyleri arasında ilişki olup olmadığının belirlenmesini amaçlamaktadır.

**Gereç ve Yöntem**: Çalışmaya altı aydan uzun süre, haftada üç gün dört saat süreyle hemodiyaliz tedavisi gören 112 hasta dahil edildi. Hemodiyaliz öncesi ve sonrası 12-derivasyonlu EKG, kilo, tansiyon arteriyel, hemodiyaliz öncesi hemogram ve biyokimya ile demografik verileri kaydedildi. Diyaliz öncesi ve hemen sonrası çekilen 12-derivasyonlu EKG'den dalga ve intervalleri hesaplanarak serum elektrolit düzeyleri ile arasındaki ilişki değerlendirildi. P<.05 anlamlı kabul edildi.

**Bulgular**: Hastaların %51.8 kadın, ortalama yaş 49.83(±18.69) idi. Diyaliz sonrası RR intervali, fosfor (p=.007) ve ürik asit (p=.013) ile anlamlı negatif korelasyon gösterdi. Diyaliz öncesi QTc intervali ile ürik asit (p=.008) arasında, diyaliz sonrası QTc intervali ile sodyum arasında negatif yönde (p=.016) orta derecede korelasyon bulundu. Lineer regresyon analizinde, fosfor (p=.007) ve ürik asitin (p=.013) diyaliz sonrası RR intervalini, ürik asitin (p=.008) diyaliz öncesi QTc intervalini anlamlı düzeyde etkilediği görüldü. Yine diyaliz sonrası QTc intervali için sodyum (p=.016) ve kalsiyum (p=.027) etkileri anlamlıydı.

**Sonuç**: Diyaliz sonrası RR intervali ile fosfor ve ürik asit arasında negatif yönde, öncesi QTc ile ürik asit arasında ve sonrası QTc ile sodyum arasında negatif yönde bulunan korelasyon, volüm ve elektrolit şiftleri sonucu EKG yorumunu ve aritmi risk değerlendirmesini zorlaştırmaktadır.

**Anahtar Kelimeler**: Hemodiyaliz, elektrokardiyografi, elektrolitler

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**Received *(Geliş Tarihi)*:** 16.06.2024 **Accepted *(Kabul Tarihi)*:** 28.07.2024

## INTRODUCTION

Cardiovascular problems are the most important cause of morbidity and mortality in hemodialysis patients.[1,2] Decreased renal function is associated with an increased incidence of arrhythmia and coronary artery disease.[3] The American renal data system reports that arrhythmia and cardiac arrest are the leading causes of death and account for 40% of deaths in hemodialysis. This rate is 50% in the first three months of starting hemodialysis.

Mortality is expected to be higher given the increasing prevalence of left ventricular hypertrophy and arteriosclerotic disease on hemodialysis.[3] KDIGO practice guidelines recommend ECG at the beginning and follow-up of renal replacement therapy.[4]

Unlike the general population, the main cause of acute cardiac death in dialysis patients is not coronary artery disease, and arrhythmias such as bradycardia, ventricular arrhythmia, and asystole have drawn attention.[5] Ventricular arrhythmias are expected to occur because chronic uremia causes diffuse myocardial fibrosis, coronary calcification, endothelial and autonomic dysfunction, and left ventricular hypertrophy.[6]

The fact that electrocardiography, which is used as a diagnostic tool in cardiovascular diseases, may be affected by volume and electrolyte changes makes ECG interpretation difficult. Metabolic and structural changes in hemodialysis patients are factors in cardiac events.[5]

The P wave, indicating atrial repolarization, is followed by the QRS wave, indicating ventricular depolarization. The QT interval is an indicator of ventricular depolarization and repolarization. Dynamic and variable QT repolarization is especially affected by potassium, magnesium, calcium, and acidosis. Prolonged QT has been linked to acute cardiac deaths and ventricular arrhythmias, with over 480 milliseconds associated with death.[6] Again, longer duration of stay in hemodialysis treatment was associated with QT prolongation.[5] QTc is obtained by correcting the heart rate effect. This study aimed to evaluate the relationship between ECG waves and intervals and electrolytes levels in hemodialysis patients to better understand the potential for arrhythmia risk.

## MATERIAL AND METHOD

The study included 112 patients undergoing hemodialysis three times a week for four hours for more than six months. Electrocardiography (ECG) (MAC 2000 device), weight, systolic and diastolic blood pressure measurements were recorded before and after hemodialysis at the beginning of the week before and after two days of dialysis. White cell count, hemoglobin, C-reactive protein (CRP), sodium, potassium, calcium, phosphorus, magnesium, albumin, intact parathormone (iPTH), thyroid stimulating hormone (TSH), and bicarbonate levels were also recorded before dialysis. Before hemodialysis, electrolytes were measured with the Siemens ADVIA Centour XPT immunoassay system after transferring the blood into a plain tube to the laboratory at room temperature. An automatic 12-lead ECG was taken before dialysis, after resting in the supine position for five minutes before starting the weekly session and before vascular access was made for dialysis. Post-dialysis ECG was obtained with the same device five minutes after leaving the dialysis machine, without changing the supine position. P wave duration, PR interval, RR interval, QRS duration, QT interval, and QTc interval were calculated from the automatic ECG device. All patients were receiving hemodialysis with standard dialysate containing 2.0 mEq/L potassium, 1.25 mEq/L calcium, and 1 mEq/L magnesium.

Exclusion criteria consisted of patients on hemodialysis for less than four hours, patients on hemodialysis for less than six months, patients with hyperkalemia above 6.5 mEq/L, and patients with signs of acute coronary syndrome, significant rhythm disturbance, pacemaker, and malignancy. Since it is known that the risk is high in patients who have just started hemodialysis, patients who completed six months were included in the study. Acute coronary syndrome, known arrhythmia and paced patients were not included in the study because ECG waves and intervals would be affected. Hemodialysis patients are resistant to potassium levels above normal ranges and were not included in the study due to the expected effects on ECG waves and intervals above 6.5 mEq/L.

This study was conducted with the decision of Mardin Artuklu University Non-Interventional Clinical Research Ethics Committee dated 03.05.2023 and numbered 2023/5-10. Informed consent was obtained from all subjects involved in the study.

### Statistical Analysis

Analyses were conducted using UN Statistical Package for Windows 22.0 version (IBM SPSS Statistic, Armonk, NY, IBM Corp.2013). Categorical variable gender was presented as frequency (n) and percentage (%). The conformity of continuous variables to normal distribution was tested with Skewness and Kurtosis and expressed as arithmetic mean, standard deviation values. Values that do not show normal distribution are presented as median and interquartile range. Paired sample t test was applied to P, RR, QT, QTc, systolic, diastolic and weight variables that showed normal distribution before and after dialysis. Two related sample test (Wilcoxon) was applied for PR and QRS that did not show normal distribution. Pearson correlation was applied for the relationship between ECG waves and intervals of normally distributed sodium, potassium, calcium, phosphorus, magnesium electrolytes and uric acid. Correlated parameters were evaluated by univariate and multivariate regression analysis. $p<.05$ was accepted as a significance level.

## RESULTS

The mean age was 49.83 (±18.69) years, and 51.8% of the patients were female (**Table 1**). There was no significant correlation between ECG waves and intervals and CRP, TSH, iPTH, and bicarbonate measured in blood gas, which may have clinical effects. Again, there was no relationship between albumin and electrolytes.

**Table 1. Demographic characteristic of the Group and Laboratory Results**

| | |
|---|---|
| Age | 49.83±18.69 |
| Male/Female | 51.8% / 48.2% |
| Dialysis time (year) | 4 (4.75) |
| KT/V | 1.6 (.45) |
| WBC ($10^3$/uL) | 7.50 ±2.32 |
| Hemoglobin (g/dL) | 10.84 (±1.67) |
| CRP (mg/dL) | 7.9 (15.58) |
| Sodium (mEq/L) | 137.59 (±3.74) |
| Potassium (mEq/L) | 5.09 (±.82) |
| Calcium (mg/dL) | 8.47 (±.95) |
| Phosphorus (mg/dL) | 4.62 (±1.54) |
| Magnesium (mg/dL) | 2.26 (±.56) |
| Uric Acid (mg/dL) | 6.44 (±1.46) |
| Albumin (g/dL) | 3.75 (±.42) |
| PTH (IU/mL) | 437.2 (532.8) |
| TSH (IU/mL) | 1.86 (2.16) |
| Bicarbonate (mmol/L) | 22 (3.78) |
| Before weight (kg) | 65.54 (±16.37) |
| After weight (kg) | 63.09 (±15.95) |

Mean (±sd), median (IQR)

### ECG wave and interval relationship before and after hemodialysis

There was a significant difference in P wave duration (p=.000), RR interval was significantly shorter after dialysis (p=.000), and there was no significant difference in PR interval (p=.151). QT interval showed a significant shortening after dialysis (p=.000). There was a statistically significant difference in QTc interval (p=.000). There were significant differences in weight (p=.000), systolic blood pressure (p=.000), and diastolic blood pressure (p=.000) before and after dialysis (**Table 2**).

### Relationship between ECG waves and intervals and electrolytes and hemodialysis patient follow-ups

There was no correlation between pre- and post-dialysis P, pre- and post-dialysis PR, pre- and post-dialysis RR, pre- and post-dialysis QRS, and pre-and post-dialysis QT waves, and normally distributed and non-normally distributed laboratory parameters. Post-dialysis RR interval was negatively correlated with phosphorus (p=.007) and moderately correlated with uric acid (p=.013).

**Table 2. Comparison of electrocardiographic parameters before and after hemodialysis**

| Parameters | Total | t, z | p |
|---|---|---|---|
| Before P<br>After P | 108 (±18.7)<br>108.1 (±16.7) | -.61 | .000 |
| Before PR<br>After PR | 157 (33.5)<br>152 (28) | -1.43 | .151 |
| Before RR<br>After RR | 717.7 (±99.13)<br>691.2 (±95.11) | -3.63 | .000 |
| Before QRS<br>After QRS | 89.7 (±14.5)<br>88 (14) | -.114 | .909 |
| Before QT<br>After QT | 394 (±31.8)<br>391 (±43.8) | -2.70 | .000 |
| Before QTc<br>After QTc | 443.9 (±31.78)<br>443.2 (±30.57) | -.075 | .000 |
| Before Systolic<br>After Systolic | 143.2 (±26.8)<br>121.1 (±25.5) | -7.96 | .000 |
| Before Diastolic<br>After Diastolic | 85.9 (±13.8)<br>73.1 (±13.5) | -7.31 | .000 |
| Before Weight<br>After Weight | 65.4 (±16.3)<br>63.1 (±15.9) | 8.26 | .000 |

Mean (± sd), median (IQR) P, PR, RR, QRS, QT, QTc: millisecond Weight: Kg

Post-QTc correlated negatively with pre-weight (p=.007) and positively with post-weight (p=.006). Pre-QRS was negatively correlated with age at dialysis (p=.007), and pre-QT was negatively correlated with age at dialysis (p=.039). Pre-systolic blood pressure was positively correlated with pre-PR (p=.028) and post-PR (p=.043), and post-systolic blood pressure was positively correlated with pre-PR (p=.004) and post-PR (p=.000).

Pre-dialysis weight was positively correlated with post-dialysis QRS (p=.044) and post-QTc (p=.007), and post-dialysis weight was positively correlated with post-dialysis QRS (p=.020) and post-QTc (p=.006).

Pre-QTc was negatively (p=.008) moderately correlated with uric acid. Post QTc was negatively (p=.016) moderately correlated with sodium. Phosphorus (p=.007) and uric acid (p=.013) with RR, were found significant in univariate linear regression analysis (**Table 3**).

**Table 3. Univariate linear regression analysis**

| Dependent | Independent | R2 | B | F | t | p |
|---|---|---|---|---|---|---|
| After RR | Phosphorus | .065 | -15.77 | 7.685 | -2.772 | .007 |
| | Uric acid | .055 | -15.20 | 6.422 | -2.534 | .013 |
| Before QTc | Uric acid | .062 | -5.36 | 7.213 | -2.686 | .008 |
| After QTc | Sodium | .052 | -2.07 | 6.016 | -2.453 | .016 |

In multivariate regression analysis for the effects of serum electrolyte levels on ECG waves, uric acid had a significant effect on pre-QTc (p=.019) and sodium (p=.013) and calcium (p=.027) on post-QTc (**Table 4**).

**Table 4. Multivariate regression analysis of electrolytes affecting ECG waves**

| After QTc | Standardized Coefficients | t | p | Correlations | | | Collinearity Statistics | |
|---|---|---|---|---|---|---|---|---|
| | Beta | | | Zero-order | Partial | Part | Tolerance | VIF |
| Sodium | -.240 | -2.516 | .013 | -.228 | -.237 | -.228 | .906 | 1.104 |
| Calcium | -.205 | -2.239 | .027 | -.175 | -.212 | -.203 | .983 | 1.017 |
| Phosphorus | .029 | .300 | .765 | -.075 | .029 | .027 | .862 | 1.160 |
| Magnesium | .116 | 1.244 | .216 | .035 | .120 | .113 | .942 | 1.061 |
| Uric Acid | -.181 | -1.861 | .065 | -.201 | -.178 | -.169 | .865 | 1.156 |
| Before QTc Uric Acid | -.236 | -2.388 | .019 | -.248 | -.226 | -.220 | .865 | 1.156 |

## DISCUSSION

Cardiac events, which are the most important cause of mortality and morbidity in hemodialysis patients, are most frequent in the last 24 hours of a two-day interval without dialysis and the twelve hours after dialysis at the beginning of the week. In addition to the increased incidence of coronary artery disease, ventricular arrhythmias, asystole, and bradycardia have been noted. Uremic environment, volume overload, and electrolyte shifts may cause dangerous arrhythmias during and immediately after dialysis.[5] Due to volume and electrolyte shifts, more arrhythmias are expected during hemodialysis and in the hours following its completion.[3]

Publications comparing all electrolytes with ECG waves are scarce in the literature. In this study in which we examined the relationship between ECG waves and intervals and electrolytes, no significant relationship was found between pre- and post-dialysis PR intervals and pre- and post-dialysis QRS intervals and electrolytes, and there was no significant difference in PR intervals and QRS intervals before and after dialysis. Marano et al. reported that P wave prolongation was associated with interatrial block and atrial fibrillation, and in addition, electrolyte changes during dialysis, especially potassium decrease, further slowed down interatrial conduction.[7] In this study, no relation was found between potassium and P wave and PR interval. The fact that patients with potassium levels above 6.5 mEq/L were not included in the study may not have shown the rapid change effect.

Nishi et al. pointed out that the incidence of atrial fibrillation increased in hemodialysis patients.[8] Yamaguchi et al. reported that QRS amplitude decreased with volume load, PR prolongation, QRS interval, and QT shortening occurred with hyperkalemia, QT prolongation could be masked by hyperkalemia, and the effects of hyperphosphatemia on ECG were not reported. They interpreted that electrolytes were risk factors for noncardiac cardiovascular disease and that low magnesium was the most effective factor.[9] They reported that prolonged QT due to hypocalcemia may not be an indicator of cardiac tissue damage but may be an effect of transient electrolyte abnormalities.[9] In this study, post-RR was negatively correlated with phosphorus and uric acid. Tsampasian et al. stated that high ATP turnover for normal functioning of the heart depends on efficient energy substrate utilization and that heart diseases can be evaluated noninvasively with phosphorus magnetic resonance.[10] The relationship between RR and phosphorus was found to be compatible with the effects of phosphorus in the metabolic process. Jebali et al. found significant changes in heart rate, R wave, T wave, and T wave/R wave (T/R) before and after dialysis only between QTc and serum potassium in multiple regression. They reported that the effects of hyperkalemia were less pronounced in hemodialysis patients.[11] Our potassium data were consistent with this view. Poulikakos et al. also reported that the increase in P wave duration in hemodialysis was inversely associated with potassium and magnesium and positively associated with calcium, and the increase in QRS duration was associated with a decrease in potassium.[12] In this study, no relation was found between potassium, magnesium and ECG waves. Only sodium and calcium were found to be effective in post-dialysis QTc. The reason may be that only preliminary magnesium, sodium and calcium levels were measured in the study, and serial follow-up was not performed.

The relationship between QTc interval and arrhythmias in hemodialysis patients has been shown in many studies. In the present study, a negative correlation was found between post-dialysis QTc and sodium, calcium. Poulikakos et al. reported that low calcium and potassium concentrations in dialysate prolonged QTc.[12] Covic et al. reported that hemodialysis prolongs QTc with rapid electrolyte changes, especially in calcium, and is not significant in the absence of cardiac disease.[13] In this study, the negative effect of calcium on post-dialysis QTc was consistent with the results of this study.

Octavia et al. reported that QT dispersion before and after dialysis was significant but not correlated with clinical factors.[14] Korkmaz et al. also found that hemodialysis did not cause a change in the QRS axis in their study, which suggested that rapid volume and electrolyte concentration changes in hemodialysis would cause ECG changes and arrhythmias.[15] The absence of QT dispersion and QRS prolongation in this study was consistent with the above study.

Watt et al. found that long QTc intervals were associated with prolonged post-dialysis recovery independent of serum electrolytes.[16] They stated that efforts to shorten QTc would contribute positively to the quality of life in hemodialysis patients. In this study, post-dialysis QTc was negatively correlated with sodium. Astan et al. interpreted QRS and QTc prolongation after hemodialysis as a noninvasive marker for ventricular arrhythmias.[17] Matsumoto et al. reported that the

QTc interval was prolonged as the duration of life on dialysis increased.[5] The negative correlation between QTc and sodium after hemodialysis may help shorten QTc with the increase in serum sodium as a result of dialysis output volume withdrawal. Post-dialysis QTc correlation with calcium may constitute a risk for arrhythmias. This problem can be prevented by standardizing the dialysate calcium level.

Poulikakos et al. reported the appropriateness of creating a person-specific dynamic profile with continuous ECG recording during hemodialysis in determining the risk for sudden cardiac death in hemodialysis patients.[12] They found that PTH was effective in myocardial repolarization. In our study, ECG was performed before and after hemodialysis, and there was no relation with pre-PTH. Kalantzi et al. evaluated the arrhythmogenic potential of hemodialysis sessions and found no significant findings in QRS, QTc interval, and QT dispersion.[18] No effect of electrolytes on QT dispersion and QRS were observed in this study. Calcium and sodium were found to be negatively correlated with post-QTc. Ozportakal et al. examined the effects of serum electrolytes and pH changes on ECG parameters before and after hemodialysis. They emphasized that Tpe, the time between the peak and end of QRS and T wave, increased after hemodialysis and the effect of hypocalcemic patients on the increase in Tpe. They stated that ultrafiltration was associated with mean QTc, and these two parameters were important in repolarization abnormalities.[19] In this study, there was no relationship between calcium and ECG waves, but post-dialysis QTc was found to be negatively significant in multiple regression analysis; its negative correlation with pre-weight and positive correlation with post-weight in volume evaluation was compatible with this study.

Chen et al. reported that the decreasing effect of hyperuricemia on heart rate developed in hemodialysis patients with autonomic dysfunction due to insulin resistance. They also mentioned that it reflects the impaired sympathovagal balance in hemodialysis patients and the potential effects of lowering uric acid levels in lowering heart rate.[20] In this study, the negative correlation of post-RR and pre-QTc with uric acid and the significant effect in univariate linear regression was found to be compatible with the mentioned studies.

Wenjing et al. reported that QTc prolongation was not observed in peritoneal dialysis in contrast to hemodialysis. This suggests that ECG wave change is less in treatment modalities without volume load and short-term shifts of electrolytes.[21] In this study, the correlation of pre- and post-dialysis weights with pre- and post-dialysis QTc suggests the effect of volume load.

Bukhari et al. reported that serum potassium and calcium levels and heart rate strongly affected the T wave.[22] In our study, no correlation was found between RR, which is an expression of heart rate, and serum potassium and calcium. Tarif et al. did not find a relationship between potassium and calcium and ECG after hemodialysis in multiple regression.[23] They reported that a decrease in serum potassium after hemodialysis caused a decrease in the T/R wave ratio on ECG, which was arrhythmogenic. In this study, we did not observe any effect of serum potassium level on post-dialysis RR and found that sodium was negatively correlated with post-dialysis QTc. Szewieczek et al. reported that QRS voltage was positively correlated with various hemodynamic, metabolic, and inflammatory factors, including systolic blood pressure, vitamin B12, sodium, calcium, phosphorus, and e-GFR.[24] In their circadian modeling study of heart rhythm, Wisniowska et al reported that sodium, potassium, calcium electrolyte balance and circadian change were factors affecting the QT circadian change.[25] Fluctuations in sodium during dialysis may cause this effect due to the effect of circadian change of electrolytes on OTc. The negative correlation between sodium and QTc found in this study may be attributed to volume overload in patients receiving end-stage renal replacement therapy.

In this study, the negative correlation between post QTc and sodium and calcium indicate the potential for ventricular arrhythmia, as seen in other studies. Considering that QT prolongation is a non-invasive indicator showing increased susceptibility to ventricular arrhythmias, monitoring and evaluation of electrolytes are important in the prediction of arrhythmia.

### Limitations

This study has several limitations. This study is limited by its retrospective design and single-center setting, which may limit the generalizability of the findings. Additionally, the sample size was relatively small, and not all electrolytes were measured at multiple time points during dialysis. Future studies should consider a larger, multicenter design to enhance generalizability and include continuous ECG monitoring throughout the dialysis session to capture transient changes in cardiac function.

## CONCLUSION

It is known that volume changes and electrolyte shift during hemodialysis have effects on ECG waves and intervals that cannot be determined with precise limits. Chronic exposure renders hemodialysis patients resistant to the cardiac effects of hyperkalemia. Phosphate appears to be affected by its role in energy metabolism. The negative association of sodium with post-QTc appears to affect heart rate through the effect of volume load. The positive correlation of post-dialysis weight with post-dialysis QRS and QTc supports this. In this study, phosphorus had an effect on heart rate, and sodium had an effect on post-dialysis QTc, but statistically, the effects were not very strong. Multifactorial factors on ECG waves and intervals in hemodialysis patients make arrhythmia prediction difficult. This study found significant correlations between post-dialysis ECG changes and serum phosphorus, sodium, calcium and uric acid levels, suggesting that careful monitoring of these electrolytes could help predict arrythmia risk in hemodialysis patients.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Mardin Artuklu University Non-invasive Clinical Research Ethics Committee (Date: 03.05.2023, Decision No: 2023/5-10).

**Informed Consent:** Informed consent was obtained from all subjects involved in the study.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Acknowledgement**: I would like to thank the Mardin dialysis team and my teacher, Prof. Dr. Mehmet Fatih Bulucu, for reading my article.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1087851
J Contemp Med 2024;14(4):210-212

Case Report / Olgu sunumu

# A Giant Hepatic Hydatid Cyst: Case Report

## Karaciğer Yerleşimli Dev Kist Hidatik: Olgu Sunumu

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## Abstract

Hydatid cyst is a general health problem that can be seen in every country, with a higher prevalence in some certain areas. Liver is the most involved organ. The disease is usually asymptomatic. The cyst may enlarge and lead to compressive symptoms or complications through opening to THE biliary system. Although medical agents and surgical interventions have long been used in the treatment of hydatid cyst, minimally invasive percutaneous interventions and laparoscopic surgical interventions are also safely applied in selected patients. In this paper, we presented a case of a giant hepatic hydatid cyst for which we preferred open surgery.

**Keywords**: Hydatid cyst, liver, giant, surgery

## Öz

Kist hidatik dünya üzerinde belli bölgelerde yoğun olmakla beraber her ülkede görülebilen genel bir sağlık sorunudur. En sık görülen organ tutulumu karaciğerdir. Genellikle asemptomatik seyretmektedir. Kist boyutları büyüyerek bası semptomlarına veya biliyer sisteme açılarak komplikasyon gelişimine neden olabilir. Kist hidatik tedavisinde medikal ajanlar ve cerrahi girişimler kullanılmakla beraber, son dönemde minimal invaziv özelliğe sahip olan perkutan girişimler ve laparoskopik cerrahi girişimler seçilmiş hastalarda güvenle uygulanmaktadır. Biz bu yazımızda açık cerrahi prodedür tercih ettiğimiz dev boyuta ulaşan, karaciğer kist hidatik olgusunu sunduk.

**Anahtar Kelimeler**: Kist hidatik, karaciğer, dev, cerrahi

## INTRODUCTION

Hydatid cyst is a parasitic disease caused by a cestode known as echinococcus.[1] Four out of 12 types of the parasite cause human disease. These include Echinococcus granulosus, Echinococcus multilocularis (alveolar hydatid cyst), Echinococcus vogeli (polycystic echinococcus) and Echinococcus oligarthrus.[2,3] The first two have clinical importance. Echinococcus granulosus is the most common type. Dogs, foxes and wolves are the main host of Echinococcus granulosus, and cattle, sheep and goats are the intermediate host. The disease is prevalent in the Middle East, Middle Europe, Australia and South America where intermediate hosts are commonly bred. The parasite egg, which is ingested by mouth, reaches the liver through the portal system and located there or causes disease in other organs by passing to the systemic circulation. Internal organ involvement is frequently observed, mainly involving the liver (70%) and the lungs (10-15%).

## CASE

A 19-year-old female patient was admitted to the General Surgery Clinic of Hatay Research and Training Hospital with complaints of abdominal distention, loss of appetite, intermittent vomiting and weight loss. On physical examination, a mass lesion extending from the right subcostal space to the pelvic region and leading to swelling in the abdomen was palpated. On laboratory examination, aspartate aminotransferase (AST) was 23 IU/L, alanine aminotransferase (ALT) was 51 IU/L and alkaline phosphatase (ALP) was 112 IU/L. Computed tomography of the abdomen revealed a cystic mass lesion measuring 236 mm in the cranio-caudal plain and 109x90 mm in the transverse plain, showing an intra-abdominal extension in the left lobe of the liver and consistent with Type III hydatid cyst (**Figure 1**).

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**Received *(Geliş Tarihi)*:** 15.03.2022 **Accepted *(Kabul Tarihi)*:** 05.06.2024

The patient underwent surgery under general anesthesia after having obtained approval for anesthesia. The abbdomen was entered through a midline incision. The cyst was seen to extend from the left lobe of the liver to the pelvic region and omental and intestinal loop adhesions were observed (**Figure 2**). To prevent contamination, the intra-abdominal organs and the vicinity of the cyst were washed with hypertonic solution (10% NaCl). The cyst content was aspirated and it was seen to be cyst hydatid rockwater(?). Cystotomy was applied and the germinative membrane and the daughter vesicles were evacuated (**Figure 3**). The inner surface of the cyst was washed with hypertonic solution and 10 minutes were awaited. After cystectomy had been applied to the hepatic margin, omentoplasty was applied to the cavity. Drains were placed into the pelvic region and the subhepatic region and the operation was terminated. On post-operative follow-ups, hemorrhagic material was drained and 2 units of erythrocytes were transfused. The control hemoglobin and hematocrit values were seen to be stable on the follow-ups. The drainage content was observed to convert to sero-hemorrhage. The patient's vital signs and laboratory parameters were stable, and hence, she was discharged with per-oral albendazole on the post-operative 9$^{th}$ day. Written informed consent was obtained from the patient to publish this case report and accompanying images.

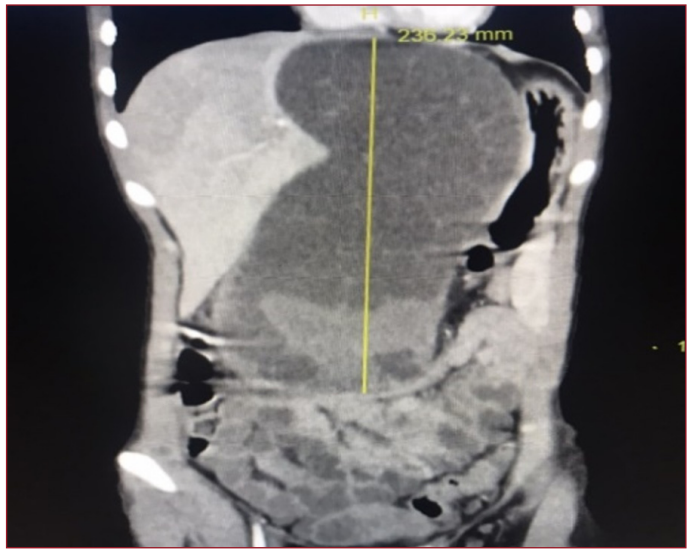

**Figure 1.** CT image of the lesion

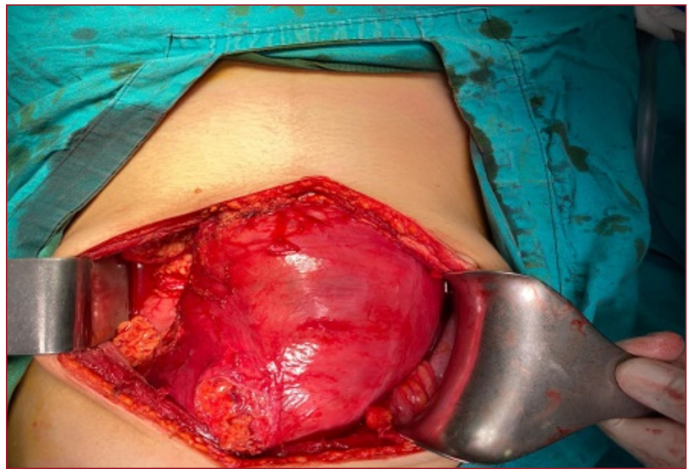

**Figure 2.** The incision and appearance of the cyst (?)

**Figure 3.** Intra-operative appearance (?)

## DISCUSSION

Most hydatid cysts do not cause symptoms. The disease is usually asymptomatic; however, clinical symptoms may be seen depending on the size or the location of the cyst or due to the compression caused by the enlarged cyst.[5] Our patient had symptoms such as abdominal distention, vomiting and loss of appetite due to compression onto the gastrointestinal organs.

Rupture into the bile ducts is the most common complication of hydatid cyst and seen in 5-17% of the patients.[6] In our patient, the cyst was not in connection with the biliary system. Intra-peritoneal free rupture may be spontaneous or due to trauma, and in these cases, the rate of anaphylaxis and death has been reported as 25%.[7] In our case, the cyst was not ruptured although it extended to the pelvic region.

Diagnosis of hydatid cyst is made by imaging methods and may be confirmed with serological tests; however, negative test results do not exclude the disease.[8] IHA was found to be 1/2560 positive in our case.

There are some laboratory tests in the differential diagnosis between liver hydatid cyst and simple cyst. Blood eosinophilia values may be 39 percent higher in liver hydatid cyst.

Other serological indicator tests, such as EgAg5, EgAgBs, endophilin B1, and rEgAgB2, whose applicability has been studied, are among the tests that will be used in differential diagnosis in the future.[9]

Some studies report that the recurrence rate of liver hydatid cyst after primary surgery is between 6% and 30%, and that there is no significant difference in postoperative complications between laparoscopic surgery and open surgery . However, open surgery is still the main method of surgical treatment today, and an increasing number of studies hope to achieve therapeutic goals with more minimally invasive methods such as piercing-grinder-aspirator-apparatus (PGAA) and nanosecond pulsed electric field (nsPEF). However, laparoscopic surgery also has some shortcomings, such as difficulty in exposing partial cysts and an increased risk of fluid leakage.[10]

Surgical procedures may be divided to two as conservative and radical. While the cyst is totally removed in radical interventions (regular hepatotectomy, total pericystectomy, etc.), residual cyst cavity remains in conservative interventions. In hepatic hydatid cyst disease, unroofing and drainage operations that are deemed conservative are preferred more often and radical resections are performed in selected patients.[11] It should be kept in mind that intra-operative complications may develop more frequently in radical approaches.[12] The aim of surgical interventions is to inactivate the cyst, to prevent the spread of the cyst content in the abdomen, to clear cyst content and to reduce the cyst cavity as much as possible. In our case, we performed subtotal cystectomy-omentoplasty up to the hepatic margin.

## CONCLUSION

In endemic regions for hydatid cyst, the importance of evaluating the suspected patients for hydatid cyst disease, which may lead to liver and other intra-abdominal organ involvement, should be considered. The primary treatment is interventional and the spectrum lies between percutaneous drainage and open radical surgery. The lesion should be evaluated with radiological methods before any intervention. Individualized treatment plans should be made. Surgical treatment should be supported by albendazole treatment.

## ETHICAL DECLARATIONS

**Informed Consent**: All patients signed the free and informed consent form.

**Referee Evaluation Process**: Externally peer-reviewed.

**Conflict of Interest Statement**: The authors have no conflicts of interest to declare.

**Financial Disclosure**: No financial support was received from any organisation in this study.

**Author Contributions**: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1502845
J Contemp Med 2024;14(4):213-214

Letter to the Editor / Editöre Mektup

# A Case of Pediatric Brain Abscess Secondary to Rhinosinusitis

## Rinosinüzite Sekonder Gelişen Pediatrik Beyin Absesi Olgusu

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**Dear Editor,**

Acute bacterial rhinosinusitis is a common childhood infection and a frequent complication of viral infections or allergic inflammations of the upper respiratory tract. Untreated cases may have serious complications such as meningitis, orbital cellulitis, epidural, and brain abscesses.[1,2] Brain abscesses rarely seen in pediatric infections with high mortality and morbidity rates, are mostly observed secondary to extrasinus spread of rhinosinusitis and acute otitis media, hematogenous spread, and penetrating trauma.[3] The most common predisposing factors are immunodeficiencies, cyanotic heart, and hematologic diseases.

A 16-year-old boy was admitted to the emergency service due to seizure. It was learned from his history that he was admitted to the hospital 10 days ago due to a headache and high fever. With the diagnosis of acute sinusitis, azithromycin, and ornidazole treatment was started, but there was no improvement in his complaints. On physical examination, clouding of consciousness and postnasal purulent discharge were detected. Remarkable laboratory test results: WBC: 22.500/mm³, platelets 156.000/mm³, C-reactive protein 226 mg/L. Brain tomography revealed a 4-cm suspicious abscess or mass lesion in the right frontal region of the brain compatible with right frontal and ethmoid sinusitis. Upon consultation with pediatric neurology and neurosurgery departments, cranial MRI and MR spectrometry were performed which revealed a lesion compatible with a 4-cm brain abscess, brain edema, shift, and acute sinusitis in the right frontal region (**Figure 1**).

Treatment with cefotaxime, vancomycin, and metronidazole was started for acute sinusitis, and hypertonic sodium infusion and leveteresitam treatment for brain edema. Surgical drainage of the abscess >2 cm was performed by neurosurgery. Gram staining and culture of the abscess material were unremarkable.

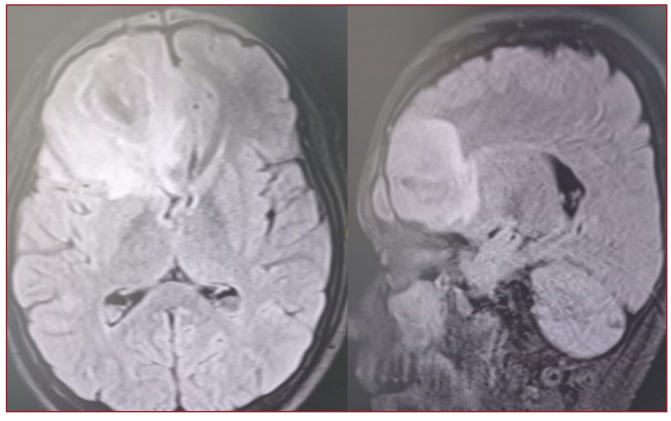

**Figure 1.** MRI Image of the Case

Upon evaluation by pediatric immunology, cardiology, and hematology departments, immunodeficiency, cyanotic heart disease, and hematologic disease were not detected. The lesion was evaluated as an inappropriately treated brain abscess secondary to acute sinusitis. In the 2nd week of treatment, edema surrounding the abscess, shift, and pressure regressed, but the abscess did not shrink, so the treatment with meropenem, vancomycin, and metronidazole was initiated. Antiedema therapy was discontinued, and antibiotherapy was maintained for 9 weeks until the abscess size was <2 cm. When the abscess shrinked below 1 cm in the control cranial images he was discharged with follow-up recommendations.

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**Received *(Geliş Tarihi)*:** 20.06.2024 **Accepted *(Kabul Tarihi)*:** 21.07.2024

Acute bacterial sinusitis is one of the most common and clinically diagnosed infectious diseases of childhood. And current guidelines recommend amoxicillin, amoxicillin-clavulanic acid, and cephalosporins (ie. cefdinir) as the first-line treatment. Considering the high drug resistance in our country, macrolides are not the first choice in patients without a history of penicillin allergy.[2] If not treated appropriately, serious cranial complications preventable with timely appropriate antibiotherapy may develop. Brain abscesses are rare but mortal infectious diseases in childhood. The most common cause is the extrasinus spread of infections such as acute rhinosinusitis.[3] A combination of medical and surgical treatment is usually recommended for abscesses >2 cm. For abscesses <2 cm and inoperable multiple abscesses only medical treatment is an option. Although the duration of treatment depends on the size, location, causative agent, and treatment response, medical treatment is recommended for approximately 6-12 weeks until the abscess is <2 cm.[4]

## ETHICAL DECLARATIONS

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1504990
J Contemp Med 2024;14(4):215-221

Review / Derleme

# Reverse Shoulder Arthroplasty in the Treatment of Cuff Tear Arthropathy: Systematic Review

## Omuz Rotator Manşet Yırtığı Artropatisi Tedavisinde Ters Omuz Artroplastisi: Sistematik Derleme

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## Abstract

**Aim**: In our study, we aimed to examine the results and complications of reverse shoulder prosthesis (RSA) applied after rotator cuff tear arthropathy (CTA) in the light of the current literature.

**Material and Method:** The literature search was conducted simultaneously on 1 April 2024 in the Medline, Cochrane, EMBASE, Google Scholar and Ovid databases using the "reverse total shoulder arthroplasty", "reverse total shoulder prosthesis", "cuff tear arthropathy", "outcomes" and "complications" keywords. Only clinical review published in English in peer-reviewed journals was evaluated. The comparison between preoperative and postoperative clinical scores, as well as range of motion (ROM), was performed using the Wilcoxon–Mann–Whitney test. P values lower than 0.05 were considered statistically significant.

**Results**: 12 articles were included in our study. When comparing the results of the pre- and postoperative examinations, a statistically significant improvement in the range of motion and the functional score was found. It was found that various complications occurred in 21.1% of patients. The most common complication is scapular notching, which occurred in 13.8% of patients. Revision surgery was required in 1.57% of patients. The most common cause of revision was a periprosthetic joint infection.

**Conclusion**: In CTA patients, RSA can achieve both freedom from pain in the shoulder joint and an increase in function. Despite positive results, complications of varying degrees of severity can occur in around one fifth of patients. The lack of Level I studies limits a true understanding of the possibilities and limitations of RSA in the treatment of CTA patients.

**Keywords**: Reverse total shoulder arthroplasty, cuff tear arthropaty, outcomes, complications

## Öz

**Amaç**: Çalışmamızda güncel literatür eşliğinde rotator manşet yırtığı artropatisi (CTA) sonrasında uygulanan ters omuz protezinin (RSA) sonuçlarını ve komplikasyonlarını incelemeyi amaçladık.

**Gereç ve Yöntem**: Yöntemler Literatür taraması 1 Nisan 2024 tarihinde Medline, Cochrane, EMBASE, Google Scholar ve Ovid veritabanlarında "ters total omuz artroplastisi", "ters total omuz protezi", "manşet yırtığı artropatisi", "sonuçlar" ve "komplikasyonlar" anahtar kelimeleri kullanılarak eş zamanlı olarak yapılmıştır. Yalnızca hakemli dergilerde İngilizce olarak yayınlanan klinik araştırmalar değerlendirildi. Preoperatif ve postoperatif klinik skorların yanı sıra eklem hareket açıklığı (ROM) arasındaki karşılaştırma Wilcoxon-Mann-Whitney testi kullanılarak yapıldı. 0,05'in altındaki P değerleri istatistiksel olarak anlamlı kabul edildi

**Bulgular**: Çalışmamıza 12 makale dahil edildi. Ameliyat öncesi ve ameliyat sonrasında yapılan muayenelerde elde edilen sonuçlar karşılaştırıldığında eklem hareket açıklıklarında ve fonksiyonel skorlamalarda istatistiksel olarak anlamlı bir iyileşme olduğu görüldü. Hastaların %21.1'inde çeşitli komplikasyonlar geliştiği gözlendi. Komplikasyonların en sık görüleni hastaların %13,8'inde meydana gelen skapular çentiklenmedir. Hastaların %1.57'sinde revizyon ameliyatı gerekti. Revizyonun sık nedeninin periprostetik eklem enfeksiyonu olduğu görüldü.

**Sonuç**: CTA hastalarında RSA ile hem ağrısız omuz eklemi hem de fonksiyonel olarak artış sağlanabilmektedir. Olumlu sonuçlarına karşın hastaların yaklaşık beşte birinde çeşitli şiddetlerde komplikasyon görülebilemektedir. Level I çalışmalarının olmayışı, CTA hastalarının tedavisinde RSA'nın potansiyelleri ve sınırlamalarının gerçek anlamda anlaşılmasını sınırlamaktadır.

**Anahtarı Kelimeler**: Ters omuz artroplastisi, manşet yırtığı artropatisi, sonuçlar, komplikasyonlar

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**Received *(Geliş Tarihi)*:** 25.06.2024 **Accepted *(Kabul Tarihi)*:** 26.07.2024

## INTRODUCTION

Rotator cuff tear arthropathy (CTA) was first defined by Neer et al. in 1983 as a set of symptoms including proximal migration of the humeral head, degeneration in the glenohumeral joint and rotator cuff failure.[1]

After the identification of CTA, treatment methods against this challenging problem continue to develop over the years.[2] Total shoulder arthroplasty (TSA) was initially used in CTA treatment but was abandoned due to high rates of implant failure, instability and poor functional outcomes.[3,4] Nowadays, the presence of CTA is considered a contraindication for TSA.[2,5,6] After the poor results observed in the early period following the use of TSA in CTA treatment, hemiarthroplasty began to be used, but the need to develop new implants persisted due to instability, bone loss and failure to achieve the desired results in joint range of motion.[7,8]

Reverse shoulder arthroplasty (RSA), developed by Grammont, is now used in the treatment of CTA to improve patients' quality of life, allow pain-free range of motion (ROM) and improve shoulder function and strength.[9,10] This method increases the stability and range of motion of the shoulder by tensing the deltoid muscle more by distalising and medialising the joint rotation centre.[10-12] Following the introduction of RSA in the treatment of CTA, its use has gradually increased after promising early results in functional outcomes and patient pain levels.[13-16] Despite positive clinical results, as with all shoulder prosthesis surgery, patients undergoing RSA may experience various complications such as instability, periprosthetic fractures, infections and component loosening.[17,18]

The aim of this review is to evaluate the clinical and functional outcomes of RSA in CTA patients as well as the complication and revision rates.

## MATERIAL AND METHOD

We conducted a systematic review of the literature according to the PRISMA guidelines. Two independent reviewers (M.G. and U.S.) conducted a blind search The literature search was conducted simultaneously on 1 April 2024 in the Medline, Cochrane, EMBASE, Google Scholar and Ovid databases using the "reverse total shoulder arthroplasty", "reverse total shoulder prosthesis", "cuff tear arthropathy", "outcomes" and "complications" keywords. Only clinical review published in English in peer-reviewed journals was evaluated

First, the abstracts of the publications retrieved from the databases were reviewed. Publications without abstracts were excluded from the study. The selected publications were then analysed in detail using the inclusion and exclusion criteria listed in **Table 1**. All clinical studies reporting on the outcomes and complications of RSA administered for the treatment of CTA were included.

**Table 1: Inclusion and exclusion criteria**

| | |
|---|---|
| Databases screened | Medline, Cochrane, EMBASE, Google Scholar and Ovid |
| Date of source | April 1, 2024 |
| Language accepted | English |
| Key words matched | "Reverse total shoulder arthroplasty", "Reverse total shoulder prosthesis", "Cuff tear arthropathy", "Outcomes" and "Complications" |
| Type of articles excluded | Reviews, case reports, animal studies, cadavers studies, biomechanical studies, tumoral studies |
| Inclusion criteria | RSA implanted as primary surgery; description of the surgical approach; description of the version of the humeral stem of RSA; preoperative and postoperative information on clinical condition of the patients (using outcomes scores, measuring ROM); description of the follow-up period; detailed information of the complications and their management |
| Exclusion criteria | Studies on RSA for revision surgery of failed RC repair; failed RSA, RSA in fractures, RSA in instability or failed RSA; follow-up period shorter than 12 months; no information on surgical intervention, complications, clinical outcomes, radiographic outcomes and statistical analysis pf the relative results |

### Statistical Analysis

All the statistical analyses were performed using SPSS for Mac (IBM SPSS Statistics version 22.0; Chicago, Illinois). The comparison between preoperative and postoperative clinical scores as well as the degrees of anterior elevation, abduction, external rotation and internal rotation ROM was carried out using the Wilcoxon–Mann–Whitney test. P values lower than 0.05 were considered statistically significant.

In all studies, P values <0.5 were considered statistically significant.

## RESULTS

Fourty-six articles were eligible for the present study.[2,13,19-62] 12 studies that met the inclusion and exclusion criteria were included in our study.[19-30] (**Figure 1**). The exclusion reasons of the other 17 articles are explained in **Table 2**.

It was noted that there were no Level I studies among the included studies. There were two Level IV studies[21,26] nine Level III studies[19,20,22,24,25,27-30] and only one prospective Level II study.[23]

### Demographic Data

In the 12 articles we reviewed in our study, 634 shoulders from a total of 623 patients underwent surgery for CTA. Considering the gender distribution, we found that 437 patients were female (70.2%) and 186 patients were male (29.8%). The male to female ratio was 0.42. The involvement of the dominant limb was investigated in five studies, and in these studies 137 of the 193 shoulders operated on were found to be the dominant side.[19,20,22,23,25]

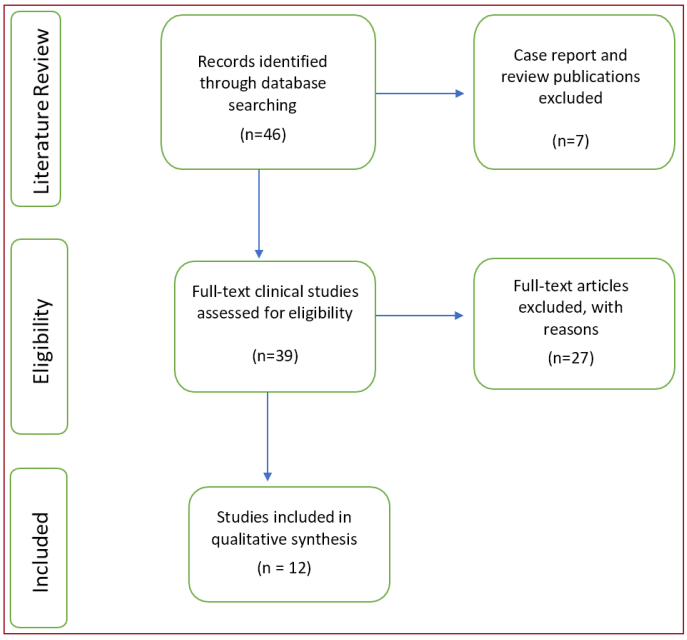


**Figure 1**

**Table 2: Reasons of exclusion of the studies**

| Reference | Reason of exclusion |
|---|---|
| Paszicsnyek[31] | The study includes includes fractures |
| Baram[32] | The study not reports functional outcomes and information on surgical approach; |
| Lindbloom[34] | The study includes includes fractures |
| Cabarcas[35] | The study not describes the surgical technique |
| Waterman[36] | The study included patients who underwent revision arthroplasty. |
| Silva[38] | The study includes fracture and tendon transfer associated with RTSA. |
| Testa[39] | The study includes rheumatoid arthritis. |
| Freislederer[41] | The study not evaluates clinical outcomes |
| İlyas[42] | The study not describes the surgical technique, ROM and clinical outcomes |
| İlyas[43] | The study not describes the surgical technique and ROM |
| Bacle[44] | The study not evaluates ROM |
| Tornberg[45] | The study not describes the surgical technique, ROM and clinical outcomes |
| DeLaSelle[46] | The study not evaluates ROM |
| Stenson[47] | The study not evaluates ROM |
| Imiolczyk[48] | The study not evaluates ROM |
| Yoon[50] | The study not evaluates clinical outcomes |
| Huber[51] | The study not describes the surgical technique and ROM |
| Kim[53] | The study includes rheumatoid arthritis. |
| Lehtimäki[13] | The study not describes the surgical technique, ROM and clinical outcomes |
| Nielsen[2] | The study not describes the surgical technique and ROM |
| Wanga[54] | The study not describes the surgical technique, ROM and clinical outcomes |
| Frankle[55] | The study not evaluates clinical outcomes |
| Ammitzboell[56] | The study not describes the surgical technique and ROM |
| Shah[73] | The study not describes the surgical technique and ROM, also includes revisions of previous arthroplasty |
| Sadoghi[58] | The study not evaluates clinical outcomes |
| Valenti[59] | The study not evaluates clinical outcomes |
| Chawla[60] | The study not describes the surgical technique and ROM |

While the average age at the time of surgery was 72.2±3 years (47-95), the average follow-up time after surgery was 25.9±8.3 months.

### Radiological Examinations

All patients included in the study underwent standard antero-posterior (AP) radiographs of the shoulder before surgery and at the last follow-up examination. In addition to the AP radiographs of the shoulder, radiographs in the Y and Grashey views of the shoulder were also taken in 111 patients who were examined in two articles.[21-23]

In the preoperative evaluation phase, magnetic resonance imaging (MRI) was available in addition to radiographs of the shoulder in a total of 181 patients who were examined in the studies by Lee et al. and Saini et al.[25,29] It was observed that 314 patients were examined with preoperative Computed Tomography (CT) in five studies.[20,23,24,29,30]

### Surgical Approach, Implant Types and Humeral Stem Retroversion

In all patients analysed in the publications included in our study, RSA implantation was performed via the deltopectoral approach.

A single brand of implant was used in the five studies analysed. In these studies: SMR Modular Shoulder System (Systema Multiplana Randelli; Lima-LTO, San Daniele del Friuli, Italy) in 31 patients,[31] Equinoxe from Exactech (Exactech, Inc., Gainesville, FL, USA) in 89 shoulders of 88 patients[20,25] 59 shoulders in 57 patients Aequalis Reverse Prostheses (Houston, TX, USA.[24] at the shoulder, Tornier Ascend Flex in 61 patients; (Tornier, Memphis, TN, USA).[27] In the studies by Barlow et al. and Nolan et al. no information was provided on implant brand and implant type.[21,26] In the other five studies, more than one brand of implant was used and the exact numbers of use were not reported in the studies.[22,23,28-30]

In the four articles that we reviewed in our study, no information was provided on the degree of retroversion of the humerus.[19,24,26,29] In the other eight studies, detailed information on retroversion of the humeral shaft was provided. Implantation of the humeral shaft was performed in 59 shoulders with a retroversion of 10°[23,28] and in 351 shoulders of 342 patients with a retroversion of 20°.[20-22,25,27,28,30]

### Rehabilitation

The rehabilitation programme applied in the postoperative phase was not specified in two studies,[23,29] and 484 shoulders of 473 patients included in the study were observed in an abduction-supported arm sling for 3.3±0.8 weeks. Passive exercises were started 1.8±0.9 days after surgery, while active range-of-motion exercises were started 4±1.7 weeks after surgery.

### Clinical outcome assessment

Many different scoring systems were used to assess the functional outcome of patients in the pre- and postoperative

phase: Visual Analogue Scale (VAS)[19-21,24-26,29] the American Shoulder and Elbow Surgeons Score (ASES)[21,23-25,29,30] the Constant–Murley Shoulder Score[19,21,24,25,27,28,30] the Subjective Shoulder Value (SSV)[21,27,28] the University of California Los Angeles Shoulder Score (UCLA)[19,20] the Simple Shoulder Test (SST)[23,26] the Shoulder Pain and Disability Index (SPADI)[22] and the Disability of Arm Shoulder and Hand Score (DASH).[20]

The ROM measurements of the patients were performed before and after the operation and were used to evaluate the functional results. Active forward flexion and external rotation measurements were taken and recorded in all patients. Active abduction measurements were performed in 474 shoulders of 472 patients in five studies.[19,24,25,28,30] Patient internal rotation measurements were performed in 502 shoulders of 495 patients, except in the studies by Nolan et al. and Adam et al.

A statistically significant improvement in functional results was observed in the postoperative period in all patients examined in our study (**Table 3**). At the same time as the improvement in functional results, a significant improvement was observed in all joint ranges of motion (**Table 4**).

**Table 3:Comparison between preoperative and postoperative clinical scores**

| Clinical score | N shoulders | Preoperative | Postoperative | p |
|---|---|---|---|---|
| VAS | 363 | 6.9±0.7 | 1.3±0.4 | <0.005 |
| ASES | 422 | 30.8±15.7 | 75.2±23.8 | <0.005 |
| CMS | 317 | 32.1±23.4 | 65.3±18.6 | <0.005 |
| SSV | 174 | 34.4±16.3 | 75.9±24.1 | <0.005 |
| UCLA | 52 | 12.9±6.3 | 29±11.3 | <0.005 |

VAS visual analogue scale, ASES American shoulder and elbow surgeons score, CMS Constant–Murley shoulder score, SSV subjective shoulder value, UCLA University of California, Los Angeles shoulder score. P value: result of the Wilcoxon–Mann– Whitney test

**Table 4: Comparison between preoperative and postoperative range of motion**

| Range of Motion | N shoulders | Preoperative | Postoperative | p |
|---|---|---|---|---|
| Forward flexion | 634 | 72.3±30.1 | 132.8±16.1 | <0.005 |
| Abduction | 295 | 52.9±19.7 | 106.1±37.8 | <0.005 |
| External Rotation | 571 | 21.7±6.7 | 30.9±9.3 | <0.005 |

P value: result of the Wilcoxon–Mann–Whitney test; Mean±SD

### Complications

All of the studies we analysed described complications as part of our inclusion criteria. Various complications occurred in 126 of 634 operated shoulders (19.8%). The most common complication was scapular notching, which was observed in 88 patients (13.8%). The second most common complication was acromion fracture, which was observed in 12 patients (1.8%). Revision surgery was performed in 10 (1.57%) of the patients involved in the study. Five patients underwent revision surgery due to infection, two patients due to dislocation, one patient due to failed humeral baseplate, one patient due to failed glenosphere and one patient due to loosening of the glenoid component (**Table 5**).

**Table 5: Complications and revision rate**

| Complications | n (%) | Revision (%) |
|---|---|---|
| Scapular notching | 88 (13.88) | 0 |
| Deep vein thrombosis | 3 (0.47) | 0 |
| Hematoma | 2 (0.31) | 0 |
| Infection | 6 (0.94) | 5 (83.3%) |
| Wound healing problems | 3 (0.47) | 0 |
| Transitory nerve palsies | 2 (0.31) | 0 |
| Humerus fracture | 1 (0.15) | 0 |
| Acromion fracture | 11 (1.73) | 0 |
| Coracoid process fracture | 1 (0.15) | 0 |
| Glenoid fracture | 1 (0.15) | 0 |
| Drill bit breakage | 1 (0.15) | 0 |
| Central screw breakage | 1 (0.15) | 0 |
| Failed Baseplate | 1 (0.15) | 1 (100%) |
| Metaglene loosening | 3 (0.47) | 1 (33%) |
| Failed glenosphere | 1 (0.15) | 1 (100%) |
| Dislocation | 3 (0.47) | 2 (66%) |
| Heterotopic ossification | 2 (0.31) | 0 |

## DISCUSSION

In this systematic review study, we analysed the outcomes of CTA patients treated with RSA. Due to the rather restrictive inclusion and exclusion criteria at the beginning of the study, 12 articles were included in our study.

When analysing the demographic data of the patients, it can be seen that the number of female patients is more than twice as high as that of male patients (70.2% vs. 29.8%). The mean age of patients was 72.7±3 years, and it was found that surgery was frequently performed in the seventh and eighth decades of life. Although dominant limb involvement was not assessed in all studies, the fact that 137 of 193 shoulders examined in the studies in which it was assessed had dominant limb involvement indicates that CTA negatively affects patients' daily lives.

We found that active forward flexion and external rotation were measured in the preoperative and postoperative phases and increased significantly in all articles included in our study. According to the results of the studies, active forward flexion increased from 72.3±30.1° to 132.8±16.1° and active external rotation increased from 21.7±6.7° to 30.9±9.3°. Active abduction was measured in half of the included studies, but increased approximately twofold at postoperative follow-up compared to before (52.9±19.7 vs. 106.1±37.8). The ability to internally rotate also increases in the postoperative phase. In contrast to other movements, however, it could not be statistically analysed as it was measured as the maximum vertebral height that the hand could reach.

As is well known, RSA was first developed by Grammont for the treatment of CTA.[9] Over the past 20 years, with the approval of RSA by the Food and Drug Administration (FDA), it has been used for other indications and has become

increasingly popular.[63] Our patients were evaluated using ROM, VAS, and various functional scores. When examining the results, we found that the CTA patients with RSA performed according to the technique were pain-free, had increased ROM and thus significantly increased their functional capacity.

The external rotation movement of the patients included in our study increased from 21.7±6.7° to 30.9±9.3°. However, in some publications we evaluated, it was observed that external rotation did not improve at a statistically significant level.[21,22,27] Loss of external rotation or inability to gain it sufficiently creates a limitation in the functions of the arm, especially in abduction.[10] While the deltoid muscle can provide abduction and forward flexion after RSA, it cannot have an effect on external rotation. In CTA patients treated with RSA, the external rotation movement is performed by the teres minor (TM) muscle, and this muscle may be torn and retracted like other muscles forming the postero-superior part of the rotator cuff, especially in elderly patients.[64,65] Therefore, postoperatively in CTA patients planned to undergo RSA. It is important to carefully evaluate the TM muscle in the preoperative MRI examination to determine the external rotation function and to be prepared for muscle transfer in the presence of a retracted tear that will prevent healing.[10,66,67]

The amount of retroversion of the humeral component also affects the shoulder's ability to rotate internally and externally. Some authors have suggested a more retroverted implantation of the humeral component may increase the capacity of external rotation. Biomechanical studies have shown that implantation of the humeral stem in retroversion up to 40° increases external rotation without impigment.[9,12,68-70] However, it is also known that the ability to internal rotation increases with decreasing humeral retroversion.[9,12,68] In more recent studies on this topic, Rhee et al. found that implantation in 0° retroversion was associated with less difficulty in activities of daily living that required internal rotation.[71] Similarly, Oh et al. found that the functional scores and range of motion of patients with individualised stems were better than those implanted at 20° retroversion.[72] Jassim et al. concluded in a systematic review study that although better external rotation and forward flexion can be achieved after implantation at a retroversion of 20° or more, internal rotation is limited.[70]

The incidence of complications is also increasing due to the increase in RSA used for various indications. It is reported that complications can occur in around a quarter of patients.[44,73-75] Scapular notch is the most common complication after RSA, it is specific to RSA and has no negative impact on clinical outcomes.[76,77] Studies analysing the results of RSA report that it can develop between 10% and 96%.[76,78,79] In our study, scapular scarring occurred in 88 of 634 shoulders and was the most common complication. In a study by Zumstein et al, one of the first studies on this topic, the most common reason for revision was instability, but over the years, as prosthesis designs have evolved and surgical experience has increased, instability has become less common and infection has become the most common complication.[74] However, the complications and reasons for revision vary over the years. A total of ten patients underwent revision, and the most common cause was infection, similar to the literature.

The strengths of our study are that it was conducted according to the PRISMA criteria and that it standardised the selection of articles, the data extraction and the evaluation of the results. Another strength is that it was blindly analysed by two independent orthopaedic and traumatology surgeons who were not involved in the study. Finally, the fact that only patients with a follow-up of at least 12 months who underwent RSA due to a CTA were included strengthens our study.

The most important limiting aspect of our study is the lack of high-quality clinical studies due to the absence of Level I studies. Secondly, the fact that only one of the 12 articles included in our study was prospectively designed increases the risk of bias. Another weakness is the inclusion of studies reporting the results of RSA performed both as primary surgery and as revision surgery after cuff repair failure. Finally; 634 shoulders of 623 patients were examined in 12 studies, and it is obvious that larger patient series will be needed for more definitive results.

## CONCLUSION

RSA continues to be used successfully as a safe and effective treatment method for CTA. After the procedure, there is not only a significant reduction in patients' pain levels, but also a significant increase in outcomes in terms of joint range of motion, activities of daily living and functional scores. RSA was developed by Grammont in 1985 for the treatment of CTA and is now used for many indications. Its frequency is increasing, but it should not be forgotten that intra- and perioperative complications can occur, which are associated with high revision rates.

## ETHICAL DECLARATIONS

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Acknowledgement**: I would like to thank Mete Gedikbaş, Ass. Prof. and Utkan Sobay M.D. for their efforts in researching the literature for this study.

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JOURNAL OF
CONTEMPORARY MEDICINE
J Contemp Med 2024;14(4): 222

Erratum / Düzeltme

# Erratum to:
# The Prognostic Value of Systemic Immune Inflammation Index in Children with Carbon Monoxide Poisoning

# Düzeltme:
## Karbon Monoksit Zehirlenmesi Olan Çocuklarda Sistemik İmmün İnflamasyon İndeksinin Prognostik Değeri

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The author forwarded the following statement to the Editorial Board of the Journal of Contemporary Medicine and requested a correction to be published. "In the article titled 'The Prognostic Value of Systemic Immune Inflammation Index in Children with Carbon Monoxide Poisoning' with DOI number 16899/jcm.1347034, which was published in the 13 Volume 5 Issue of your journal in 2023, the dates of collection of patient data were mistakenly written as January 2018 - January 2023 instead of January 2018 - January 2021. In order to correct this inadvertent error, I request that the dates in the English and Turkish abstract and in the study design section in the main text be rearranged as January 2018 to January 2021.r."

Wrong Sentence:
"We conducted a retrospective observational study involving pediatric patients (age <18 years) diagnosed with CO poisoning and treated at Aksaray University Training and Research Hospital, a tertiary medical center, from January 2018 to January 2023.."

Corrected Sentence:
"We conducted a retrospective observational study involving pediatric patients (age <18 years) diagnosed with CO poisoning and treated at Aksaray University Training and Research Hospital, a tertiary medical center, from January 2018 to January 2021."

DOI of original article: https://doi.org/16899/jcm.1347034

**Özdemir Kaçer E. The Prognostic Value of Systemic Immune Inflammation Index in Children with Carbon Monoxide Poisoning. J Contemp Med. Eylül 2023;13(5):879-884. doi:10.16899/jcm.1347034**

**Journal of Contemporary Medicine**; Journal homepage: https://dergipark.org.tr/tr/pub/jcm

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