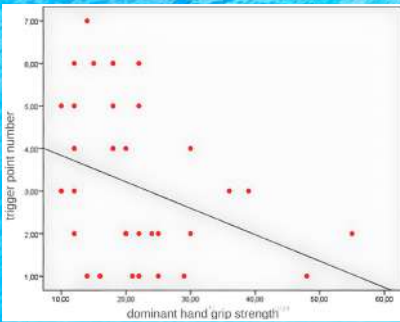


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Boğaziçi Tıp Dergisi



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Bosphorus Med J

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the process must be specified.

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Journal Article:

Matsukawa Y, Kato K, Hatta Y, Iwamoto M, Mizuno S, Kurihara R, et al. Helicobacter pylori eradication reduces platelet count in patients without idiopathic thrombocytopenic purpura. *Platelets* 2007;18:52-5.

Book Chapter Reference

Author. Title. In: Editor, 'Ed.'.^'Eds.'. Book Title. ed. Edition, Place Published: Publisher; Year: p. Pages. Lal G, Clark OH. Thyroid, parathyroid, and adrenal. In: Brunicaudi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Eds. *Schwartz's Principles of Surgery*. ed.10th, New York; Mc-Graw Hill; 2015: p.1521-96.

Book Reference

Author. Title. ed. Edition, Place Published: Publisher; Year. Walsh P. *Physiology and Pharmacology of the Bladder and Urethra*. *Campbell's Urology*. ed. 10th, Philadelphia: Saunders; 2014.

Conference Proceedings:

Author. Title. In: Editor, 'editor'.^'editors'. Conference Name; Year of Conference Date; Conference Location: Publisher; Year of Conference |. p. Pages.

Bengissson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. *MED-INFO 92. Proceedings of the 7th World Congress on Medical Informatics*; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report:

Author. Title. Type. Place Published: Institution; Year Date. Report No.: Report Number.

Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis:

Author. Title. Type. Place Published: Institution; Year Date. Report No.: Report Number.

Kaplan SI. Post-hospital home health care: elderly access and utilization (dissertation). St Louis (MO): Washington Univ; 1995.

Epub Ahead of Print Articles:

Author. Title. Alternate Title Year Date Accessed. doi: DOI. [Epub ahead of print].

Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. *Diagn Interv Radiol*. 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

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Author. Title. Available from: URL. Accessed Access Date, Access Year. Fox S. Pew Research Center. The social life of health information. 2014. Available from: <http://www.pewresearch.com>.

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The Effect of 25-OH Vitamin D Levels on Grip Strength in Myofascial Pain Syndrome

Miyofasiyal Ağrı Sendromunda 25-OH Vitamin D Seviyelerinin Kavrama Gücüne Etkisi

Yunus Emre Doğan, Gülcan Öztürk

ABSTRACT

Objectives: Vitamin D plays an important regulatory role in skeletal muscle through receptor-dependent pathways, and its deficiency has been associated with several chronic pain disorders. Although handgrip strength is frequently used as a proxy for overall muscular performance, the link between circulating 25-hydroxyvitamin D (25(OH)D) and muscle strength in individuals diagnosed with myofascial pain syndrome (MPS) has not been clearly established. This study investigated whether serum 25(OH)D concentrations are related to handgrip strength in patients with MPS.

Methods: This cross-sectional analysis included 39 individuals meeting the diagnostic criteria for MPS according to Travell and Simons and who had documented serum 25(OH)D values obtained within the previous six months. Participants were stratified into two groups based on vitamin D status: <20 ng/mL (Group 1, n=23) and ≥20 ng/mL (Group 2, n=16). Demographic features, duration of symptoms, body mass index, occupational status, number of trigger points, visual analog scale (VAS) pain scores, and grip strength of both hands were assessed.

Results: The mean 25(OH)D level of the cohort was 18.67±10.99 ng/mL. Dominant-hand and nondominant-hand grip strength averaged 21±9.98 kg and 17.33±9.31 kg, respectively. No significant differences were identified between the two vitamin D groups regarding clinical parameters, trigger point counts, VAS scores, or grip strength (p>0.05). While BMI, VAS score, and vitamin D concentrations showed no association with grip strength, an inverse correlation was observed between grip strength and the number of trigger points (p<0.05).

Conclusion: Serum 25(OH)D concentrations did not appear to influence handgrip strength in individuals with myofascial pain syndrome. Larger-scale, prospective, and interventional research is needed to clarify whether vitamin D supplementation may have a role in improving muscle function or clinical outcomes in this patient population.

Keywords: Hand strength; muscle strength; myofascial pain syndromes; vitamin D; vitamin D deficiency.

ÖZET

Amaç: Vitamin D, reseptör bağımlı yollar aracılığıyla iskelet kaslarında önemli bir düzenleyici rol oynar ve eksikliği çeşitli kronik ağrı bozukluklarıyla ilişkilendirilmiştir. El kavrama gücü, genellikle genel kas performansının bir göstergesi olarak kullanılır, ancak miyofasiyal ağrı sendromu (MPS) tanısı konmuş bireylerde dolaşımdaki 25-hidroksivitamin D (25(OH)D) ile kas gücü arasındaki bağlantı henüz net olarak belirlenmemiştir. Bu çalışma, serum 25(OH)D konsantrasyonlarının MPS hastalarında el kavrama gücü ile ilişkili olup olmadığını araştırmıştır.

Yöntem: Bu kesitsel analiz, Travell ve Simons'a göre MPS tanı kriterlerini karşılayan ve önceki altı ay içinde elde edilen serum 25(OH)D değerleri belgelenmiş 39 kişiyi içermektedir. Katılımcılar, vitamin D durumuna göre iki gruba ayrılmıştır: <20 ng/mL (Grup 1, n=23) ve ≥20 ng/mL (Grup 2, n=16). Demografik özellikler, semptomların süresi, vü-

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cut kitle indeksi, mesleki durum, tetik noktalarının sayısı, görsel analog skala (VAS) ağrı skorları ve her iki elin kavrama gücü değerlendirilmiştir.

Bulgular: Kohortun ortalama 25(OH)D seviyesi $18,67 \pm 10,99$ ng/mL idi. Dominant el ve non-dominant el kavrama gücü sırasıyla ortalama $21 \pm 9,98$ kg ve $17,33 \pm 9,31$ kg idi. İki vitamin D grubu arasında klinik parametreler, tetik nokta sayısı, VAS skorları veya kavrama gücü açısından anlamlı bir fark saptanmadı ($p > 0,05$). BMI, VAS skoru ve vitamin D konsantrasyonları kavrama gücü ile ilişkili bulunmazken, kavrama gücü ile tetik nokta sayısı arasında ters bir korelasyon gözlemlendi ($p < 0,05$).

Sonuç: Serum 25(OH)D konsantrasyonlarının, miyofasiyal ağrı sendromu olan bireylerde el kavrama gücünü etkilediği görülmemiştir. Vitamin D takviyesinin bu hasta popülasyonunda kas fonksiyonunu veya klinik sonuçları iyileştirmede bir rolü olup olmadığını açıklığa kavuşturmak için daha geniş ölçekli, prospektif ve müdahaleli araştırmalar gereklidir.

Anahtar sözcükler: El gücü; kas gücü; miyofasiyal ağrı sendromları; Vitamin D; Vitamin D eksikliği.

Myofascial pain syndrome (MPS) is a persistent or intermittently recurring musculoskeletal disorder characterized by pain and tenderness originating from affected muscles and their surrounding fascia. A hallmark of the condition is the presence of myofascial trigger points (MTrPs)—palpable, hyperirritable nodules situated within taut muscle fibers—that can provoke local discomfort as well as referred pain patterns.^[1] Individuals with MPS may experience limitations in joint mobility, reductions in muscle strength, and accompanying motor or autonomic manifestations.^[2] Numerous intrinsic and extrinsic factors have been proposed to contribute to the development of MPS,^[3] and systemic abnormalities, including nutritional deficiencies and metabolic disturbances, have been increasingly recognized as potential contributors.^[4] Among these, vitamin D insufficiency has received growing attention. Cross-sectional investigations suggest that a substantial proportion of patients with MPS present with low serum vitamin D levels,^[5] which may interfere with normal muscle function and facilitate the persistence of MTrPs.^[6]

MPS is frequently implicated in otherwise unexplained pain conditions affecting the cervical, shoulder, thoracic, and lumbar regions, and may also involve less common sites such as the pelvic girdle, abdomen, or chest wall. The contractile dysfunction induced by taut muscle bands can lead to muscle shortening and strength reduction even in the absence of observable muscle atrophy.^[7] Handgrip strength, although dependent primarily on upper-extremity musculature, is widely regarded as a reliable estimate of general muscle strength and overall physical performance.^[8,9]

Growing interest has emerged regarding the potential role of vitamin D in muscle health. The biological mechanisms through which vitamin D influences muscular function appear to involve both genomic pathways—affecting muscle cell proliferation and differentiation—and rapid non-genomic signaling mechanisms that regulate calcium dynamics within the muscle cell. Insufficient levels of 25-hy-

droxyvitamin D have been associated with proximal muscle weakness, often described as vitamin D-related myopathy.^[10,11] Several studies among athletes and dancers have suggested that inadequate vitamin D status may compromise muscle strength and performance.^[12,13] Conversely, other research has reported no meaningful association between vitamin D levels and indices of muscle strength or physical capability.^[14,15]

Given these conflicting findings and the paucity of research addressing this question specifically in individuals with MPS, the present study aimed to investigate whether serum 25-hydroxyvitamin D concentrations are associated with handgrip strength in patients diagnosed with myofascial pain syndrome.

Methods

The research protocol received approval from the Scientific Research Ethics Committee of Fatih Sultan Mehmet Training and Research Hospital on January 26, 2023 (Decision No: 2023/16). All study procedures complied with the ethical principles outlined in the Declaration of Helsinki and its later amendments. Written informed consent was obtained from all eligible participants prior to enrollment.

Study Design and Participant Selection

This observational cross-sectional study enrolled 39 individuals who presented to the Physical Therapy and Rehabilitation outpatient clinic of Fatih Sultan Mehmet Training and Research Hospital between February 1 and March 1, 2023, with complaints of neck or upper back pain. To be included, participants had to meet the diagnostic criteria for myofascial pain syndrome (MPS) as defined by Simons and colleagues and have a recorded serum 25-hydroxyvitamin D value obtained within the preceding six months.

The diagnostic framework required the presence of major criteria such as localized or spontaneous pain, typical

patterns of referred pain, a detectable taut band within the muscle, tenderness over myofascial trigger points (MTrPs), and restricted joint motion. Minor criteria consisted of reproduction of the patient's usual pain upon compression of the MTrP, a local twitch response, and symptom relief after stretching or trigger point-targeted treatment.^[7,16]

Participants were excluded if they had fibromyalgia, cervical disc pathology, cervical radiculopathy or myelopathy, were aged 60 years or older, had undergone treatment for MPS within the previous six months, had a history of surgery involving the cervical spine or shoulder region, or had inflammatory, infectious, malignant, or pregnancy-related conditions.

Participants were separated into two groups based on their serum 25(OH)D concentrations:

- Group 1: <20 ng/mL (vitamin D deficient; n=23)
- Group 2: ≥20 ng/mL (vitamin D sufficient/non-deficient; n=16)

Data collected included age, sex, occupation, symptom duration, anthropometric measurements (height, weight, BMI), number of trigger points, pain severity, bilateral grip strength, and serum vitamin D level.

Pain Assessment

Pain intensity was quantified using the Visual Analog Scale (VAS), a 10-cm line where 0 signifies the absence of pain and 10 represents intolerable pain. Participants were asked to place a mark on the scale that best represented their pain at the time of evaluation.^[17]

Grip Strength Evaluation

Handgrip strength was measured using a Jamar hydraulic dynamometer, which is widely regarded as the reference device for assessing grip force because of its established accuracy and reliability. Testing adhered to the standardized protocol endorsed by the American Society of Hand Therapists (ASHT). Participants were seated with the shoulder adducted and neutrally rotated, elbow flexed at a right angle, forearm in neutral orientation, and wrist positioned between 0–30° of extension and 0–15° of ulnar deviation. Each participant completed three consecutive trials, and the mean of these values was used for statistical analysis. Results were recorded in kilograms (kg).^[18,19]

Statistical Analysis

All analyses were conducted using IBM SPSS Statistics version 22. Distributional assumptions were checked with the Kolmogorov–Smirnov and Shapiro–Wilk tests, indicating non-normal distributions. Descriptive statistics were presented as means, standard deviations, medians, ranges, and frequencies where appropriate.

Between-group comparisons for continuous variables were performed using the Mann–Whitney U test, whereas categorical data were evaluated using Fisher's Exact Chi-square test or the Fisher–Freeman–Halton Exact Chi-square test, depending on the number of categories. Associations between continuous variables were assessed using Spearman's rho correlation coefficient. Statistical significance was set at $p < 0.05$.

Results

A total of 39 individuals participated in the study, of whom 36 were female (92.3%) and 3 were male (7.7%). The descriptive features of the sample are summarized in Table 1.

Participants in Group 2 were significantly older than those in Group 1 ($p = 0.050$; $p < 0.05$). No significant group differences were observed for sex, anthropometric variables (height, weight, BMI), educational background, duration of symptoms, number of myofascial trigger points, VAS pain intensity, hand dominance, or grip strength of either the dominant or non-dominant hand (all $p > 0.05$) (Table 2).

Correlation analyses indicated a moderate, statistically significant negative association between the number of trigger points and grip strength on both sides (dominant: $r = -0.380$, $p = 0.017$; non-dominant: $r = -0.393$, $p = 0.013$). In contrast, neither dominant nor non-dominant grip strength showed a significant relationship with serum 25(OH)D concentrations, BMI, or VAS pain scores (all $p > 0.05$) (Table 3; Figs. 1 and 2).

To address the potential confounding influences of age and sex, multivariable linear regression analyses were conducted for each outcome variable. After adjusting for age and sex, 25-OH vitamin D levels were not significantly related to dominant hand grip strength ($\beta = -0.083$, $p = 0.478$), non-dominant hand grip strength ($\beta = -0.099$, $p = 0.287$), VAS pain scores ($\beta = 0.005$, $p = 0.830$), or trigger point count ($\beta = -0.003$, $p = 0.906$). Sex was a very important factor in predicting grip strength in both the dominant ($\beta = 25.791$, $p < 0.001$) and non-dominant hands ($\beta = 27.123$, $p < 0.001$). Males had grip

Table 1. Characteristics of participants

	Min	Max	Mean±SD	Median
Age (year)	16	56	37.87±9.47	38
Height (cm)	150	197	164.08±9.61	162
Weight (kg)	40	120	68.67±15.08	66
BMI (kg/m ²)	16.2	41.8	25.55±5.42	24.4
<30	33	84.6		
≥30	6	15.4		
Gender (n, %)				
Female	36	92.3		
Male	3	7.7		
Education level (n, %)				
Literate	2	5.1		
Primary School	12	30.8		
Secondary School	2	5.1		
High School	8	20.5		
Associate Degree	3	7.7		
University	12	30.8		
Number of trigger points	1	7	3.15±1.83	3
Symptom duration (months)	1	6	3.1±1.8	3
VAS	5	10	7.38±1.6	8
Dominant hand (n, %)				
Right	37	94.9		
Left	2	5.1		
Dominant hand grip strength (kg)	10	55	21±9.98	20
Nondominant hand grip strength (kg)	8	50	17.33±9.31	15
Serum 25 OH D (ng/mL) level	4	58	18.67±10.99	17
<20 (Grup 1)	23	59.0		
>20 (Grup 2)	16	41.0		

SD: Standart deviation; BMI: Body mass index; cm: centimeter; kg: kilogram; m: meter; VAS: Visual analog scale.

strength that was about 26-27 kg higher than females. The only significant predictor of trigger point count was body mass index (BMI) ($\beta=0.126$, $p=0.032$), with each 1-unit increase in BMI associated with 0.13 additional trigger points. The explanatory power of the models increased substantially when age and sex were included for grip strength outcomes ($R^2=0.476$ for dominant hand, $R^2=0.618$ for non-dominant hand) compared to unadjusted models containing only vitamin D ($R^2=0.005$ and 0.004 , respectively), primarily due to the sex variable. Age showed no significant associations

with any outcome (all $p>0.05$). These findings suggest that the observed lack of association between vitamin D and clinical outcomes is not due to confounding by age or sex.

Discussion

In this study, serum vitamin D concentrations were not associated with either dominant or nondominant handgrip strength, nor with BMI or VAS pain severity. Although most patients with MPS exhibited inadequate vitamin D levels, these deficiencies did not translate into measurable differences in grip performance. The only significant functional relationship identified was a moderate inverse correlation between grip strength and the number of myofascial trigger points, suggesting that a higher burden of MTrPs may contribute to diminished muscle function. To date, no published work has focused specifically on the link between vitamin D status and grip strength in individuals with clinically diagnosed MPS, highlighting the originality and potential importance of the present findings.

Experimental research has long demonstrated that vitamin D engages multiple pathways to regulate skeletal muscle structure and function. Through activation of vitamin D receptors (VDRs) expressed on muscle precursor cells, the hormone participates in genomic processes that support myoblast proliferation, differentiation, and subsequent muscle fiber development. In parallel, vitamin D also exerts rapid, non-genomic effects by modulating intracellular and extracellular calcium balance—an essential component of effective muscle contraction.^[10,11]

Despite these mechanistic foundations, clinical research examining the vitamin D–muscle strength relationship has yielded conflicting results. Several investigations have reported higher grip strength among individuals with adequate 25(OH)D levels, whereas others have been unable to confirm such an association.^[20–23] These inconsistencies likely stem from substantial variation across study samples in demographic factors, baseline physical fitness, dietary habits, sun exposure, and comorbid health conditions.

For instance, Granlund et al.^[24] reported weaker grip performance in vitamin D–deficient immigrant adults aged 25–65 years, and Iolascon et al.^[20] observed similar findings in postmenopausal women. Beaudart et al.^[25] also documented improvements in limb strength following vitamin D supplementation. Conversely, Kim et al.^[26] reported no meaningful relationship in older Asian men and postmenopausal wom-

Table 2. Distribution of characteristic features

	Group 1		Group 2		p
	Min-Max	Mean±SD (median)	Min-Max	Mean±SD (median)	
Age (year)	16-56	35.3±10.81 (36)	33-51	41.56±5.57 (41)	¹ 0.050*
Height (cm)	150-197	164.87±11.49 (162)	150-170	162.94±6.18 (163,5)	¹ 0.886
Weight (kg)	40-102	68.78±14.26 (70)	50-120	68.5±16.67 (64,5)	¹ 0.679
BMI (kg/m ²)	16.2-41.8	25.4±5.38 (24.9)	19-41.5	25.76±5.65 (24.2)	¹ 0.977
Number of trigger points	1-6	2.96±1.77 (2)	1-7	3.44±1.93 (3.5)	0.459
Symptom duration (months)	1-6	3.09±1.86 (3)	1-6	3.13±1.78 (3)	0.907
VAS	5-10	7.52±1.68 (8)	5-10	7.19±1.52 (7)	0.476
Dominant hand grip strength	10-55	22.65±11.15 (20)	10-39	18.63±7.74 (17)	0.228
Nondominant hand grip strength	8-50	19±10.66 (18)	8-30	14.94±6.5 (12)	0.195
	n	%	n	%	
BMI group					
<30	19	82.6	14	87.5	² 1.000
≥30	4	17.4	2	12.5	
Gender					
Female	21	91.3	15	93.8	² 1.000
Male	2	8.7	1	6.3	
Education level					
Literate	2	8.7	0	0	³ 0.683
Primary School	6	26.1	6	37.5	
Secondary School	1	4.3	1	6.2	
High School	6	26.1	2	12.5	
Associate Degree	1	4.3	2	12.5	
University	7	30.4	5	31.3	
Dominant hand					
Right	22	95.7	15	93.8	² 1.000
Left	1	4.3	1	6.3	

¹Mann Whitney U test, ²Fisher's Exact Test, ³Fisher Freeman Halton Exact Test *p≤0.05; SD: Standart deviation; BMI: Body mass index; cm: centimeter; kg: kilogram; m: meter; VAS: Visual analog scale.

en. Wang et al.^[27] found a positive association only in men aged 50 years or older, with no comparable effect in younger adults. Likewise, Güloğlu et al.^[28] detected no correlation in premenopausal women aged 40–50 years. In our study, no correlation was found between vitamin D levels and grip strength. However, the absence of a statistically significant correlation should not be interpreted as an absolute lack of clinical relevance. This is because the relatively small sample size may have led to a risk of Type 2 error (false negatives).

These divergent outcomes underscore the challenges of isolating vitamin D's contribution to muscle performance. Li et al.^[29] proposed that muscle-related effects may depend

more directly on circulating 1,25-dihydroxyvitamin D—the hormonally active metabolite—rather than on 25(OH)D concentrations alone. Given that 1,25(OH)₂D plays a direct regulatory role in calcium-handling proteins and VDRs are present in human skeletal muscle, future studies incorporating measurements of both metabolites may offer a more refined understanding of vitamin D–muscle interactions.

Study Limitations

This study has several limitations that should be considered. The relatively small sample size and the fact that the sample consisted mostly of women may affect the applicability of

Table 3. Vitamin D, BMI, trigger point count and VAS correlation with grip strength

		Grip strength	
		Dominant hand	Nondominant hand
Dvit	r	0.012	0.020
	p	0.941	0.903
BMI	r	-0.135	-0.074
	p	0.414	0.652
Number of trigger points	r	-0.380	-0.393
	p	0.017*	0.013*
VAS	r	-0.214	-0.174
	p	0.191	0.291

Spearman's rho korelasyon, *p<0.05; BMI: Body mass index; VAS: Visual analog scale.

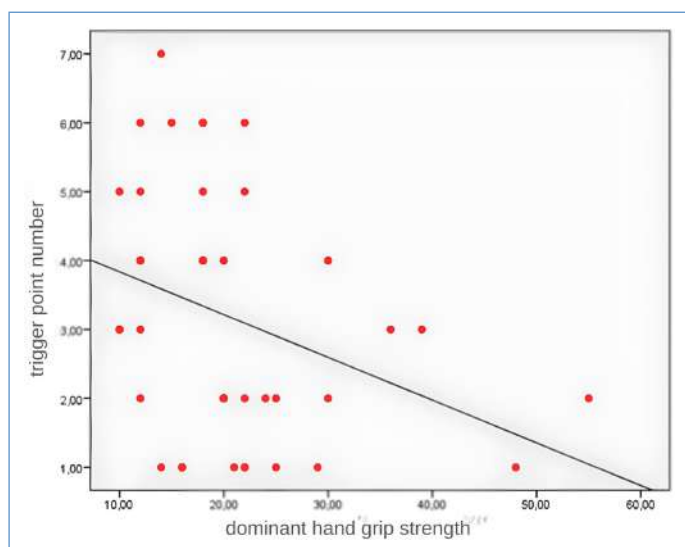


Figure 1. Correlation between dominant hand grip strength and number of trigger points.

the findings to men and broader populations. Additionally, there was an age difference between the two vitamin D groups, and age is a known determinant of muscle strength and vitamin D metabolism. Finally, since serum 25(OH)D measurements were obtained over the previous six months rather than on the day of assessment, they may not fully reflect participants' current vitamin D status.

Conclusion

In the present study, serum 25-hydroxyvitamin D concentrations did not demonstrate a measurable effect on handgrip strength among individuals diagnosed with myofascial pain syndrome. Ongoing inconsistencies in the existing literature—largely attrib-

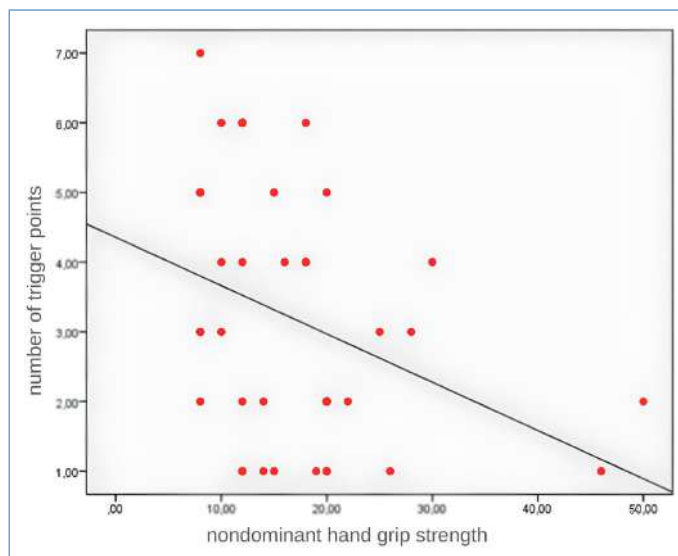


Figure 2. Correlation of trigger point number with nondominant hand grip strength.

utable to methodological differences and heterogeneity across study populations—make it difficult to establish a definitive relationship between vitamin D status and muscle strength. Consequently, well-designed studies with larger sample sizes and more homogeneous patient groups are warranted to better elucidate whether 25-hydroxyvitamin D plays a meaningful role in determining grip strength in this patient population.

Disclosures

Ethics Committee Approval: The study was approved by Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (No: 2023/16, Date: 26.01.2023).

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Clinical and Histopathological Findings in Breast Cancer Patients Undergoing Endometrial Sampling: A Retrospective Study

Endometrial Örnekleme Yapılan Meme Kanseri Tanılı Hastaların Klinik ve Histopatolojik Sonuçlarının Retrospektif Olarak Değerlendirilmesi

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ABSTRACT

Objectives: To evaluate the clinical and histopathological findings of breast cancer patients who underwent endometrial sampling and to determine the relationship between endocrine therapy type and abnormal endometrial pathology.

Methods: This retrospective study included 48 breast cancer patients who underwent endometrial sampling between 2010 and 2021. Clinical data such as age, menopausal status, symptoms, and type/duration of endocrine therapy were recorded. Histopathological results were categorized as normal, benign, premalignant, or malignant. Statistical analyses were performed using SPSS 22.0, and a p value <0.05 was considered significant.

Results: The mean age was 55±8.16 years, and 50% of patients were postmenopausal. Tamoxifen was used in 75%, and aromatase inhibitors in 8.3% of patients. Abnormal uterine bleeding was the leading indication for biopsy (85.4%). Benign polyps were the most common abnormality (39.6%), followed by hyperplasia (6.3%) and carcinoma (4.2%). No significant differences in abnormal endometrial pathology were observed between tamoxifen and aromatase inhibitor users (p>0.05). Treatment duration, menopausal status, and receptor profile were not associated with endometrial pathology.

Conclusion: Benign polyps were the most frequent abnormal endometrial findings among breast cancer patients undergoing endometrial sampling, while premalignant and malignant lesions were rare. The type or duration of endocrine therapy did not significantly affect the risk of endometrial pathology. Invasive evaluation should be guided by symptoms rather than routine screening.

Keywords: Aromatase inhibitor; breast cancer; endometrial biopsy; endometrial pathology; tamoxifen.

ÖZET

Amaç: Endometrial örnekleme yapılan meme kanseri tanılı hastaların klinik ve histopatolojik sonuçlarını değerlendirmek ve endokrin tedavi türü ile endometrial patoloji arasındaki ilişkiyi incelemektir.

Yöntem: Bu retrospektif çalışmaya, 2010–2021 yılları arasında endometrial örnekleme uygulanan 48 meme kanseri hastası dahil edilmiştir. Hastaların demografik özellikleri, menopozal durumları, klinik semptomları ve endokrin tedavi türü/süresi kaydedildi. Histopatolojik bulgular normal, benign, premalign ve malign olarak sınıflandırıldı. İstatistiksel analizler SPSS 22.0 kullanılarak yapıldı ve p<0,05 anlamlı kabul edildi.

Bulgular: Hastaların ortalama yaşı 55±8,16 yıl olup, %50'si postmenopozal dönemdeydi. Hastaların %75'i tamoksifen, %8,3'ü aromataz inhibitörü kullanmaktaydı. Endometrial biyopsi için en sık endikasyon anormal uterin kanamaydı (%85,4). En sık saptanan patoloji benign polipler (%39,6) olup, endometrial hiperplazi (%6,3) ve karsinom (%4,2) daha nadir görüldü. Endokrin tedavi türü ile anormal endometrial patoloji arasında anlamlı bir ilişki saptanmadı (p>0,05).

Sonuç: Endometrial örnekleme yapılan meme kanseri hastalarında en sık benign polipler izlenirken, premalign ve malign patolojiler nadirdir. Endokrin tedavi türü ve süresinin endometrial patoloji riskini anlamlı olarak artırmadığı görülmüştür. İnvaziv değerlendirme, semptom varlığında planlanmalıdır.

Anahtar sözcükler: Aromataz inhibitörü; meme kanseri; endometrial biyopsi; endometrial patoloji; tamoksifen.

Breast cancer, the most common malignancy in women, affects approximately one in eight in developed countries and represents the second leading cause of cancer-related death among women.^[1] Its incidence increases with age, and family history, obesity, and nulliparity are well-established risk factors.^[2] Despite these risks, survival outcomes remain favorable, with 5- and 10-year survival rates of about 73% and 61%, respectively.^[3]

Hormone therapy plays a central role in breast cancer management, with selective estrogen receptor modulators (SERMs), aromatase inhibitors (AIs), fulvestrant, and luteinizing hormone-releasing hormone (LHRH) agonists being commonly employed. Among these, tamoxifen remains the most extensively utilized SERM for estrogen receptor–positive tumors.^[4] However, its estrogenic activity on the endometrium has been associated with an increased risk of endometrial pathology.^[5] Documented endometrial abnormalities include polyps, hyperplasia, and carcinoma, and evidence suggests that the risk of endometrial cancer is approximately threefold higher in tamoxifen users compared with non-users, particularly with higher cumulative doses and prolonged treatment.^[6] By contrast, AIs appear to confer a lower risk of endometrial pathology and cancer compared with tamoxifen.^[7]

In this study, we retrospectively evaluated breast cancer patients who underwent endometrial sampling (biopsy or curettage) at our institution. The objectives were: (1) to determine the prevalence and spectrum of endometrial histopathological findings in these patients, and (2) to assess associations between clinical factors—such as menopausal status, symptoms, and duration/type of endocrine therapy—and the likelihood of abnormal pathology. Our aim is to provide evidence to guide the gynecological management of breast cancer patients receiving tamoxifen or aromatase inhibitors (AIs), particularly in determining when an invasive evaluation is necessary.

Methods

Study Design and Patient Population

This retrospective observational study was conducted at a single tertiary care hospital. A total of 48 breast cancer pa-

tients who underwent endometrial sampling between 2010 and 2021 were identified from the institutional pathology database. Eligible patients had a history of breast cancer at any stage and had undergone endometrial biopsy or dilatation and curettage during or after adjuvant endocrine therapy (tamoxifen and/or aromatase inhibitors). Both premenopausal and postmenopausal women were included. Patients with a prior diagnosis of endometrial cancer or those who underwent biopsy for reasons unrelated to breast cancer follow-up were excluded.

Data Collection and Variables

Clinical and demographic data were retrieved from electronic medical records. Variables included age, reproductive history, menopausal status, presenting symptoms, indication for endometrial sampling, type and duration of endocrine therapy, and receipt of chemotherapy or radiotherapy. Missing data were managed using a complete-case (listwise deletion) approach; patients with unavailable information for essential variables were excluded from the analyses.

Histopathologic Evaluation

Endometrial specimens were obtained by dilatation and curettage, pipelle biopsy, or hysteroscopic-guided biopsy. Histopathological findings were categorized as proliferative, secretory, or atrophic/inactive endometrium, as well as pathological entities such as polyps, hyperplasia, and carcinoma. All pathological diagnoses were classified according to the World Health Organization (WHO) and European Society of Gynaecological Oncology (ESGO) guidelines to ensure standardized terminology and reproducibility.

Statistical Analysis

Data are presented as mean±standard deviation (SD), median with range, or number (percentage), as appropriate. Continuous variables were compared using the Student's t-test or Mann–Whitney U test, and categorical variables were analyzed with the chi-square test or Fisher's exact test, where appropriate. Multivariate logistic regression analysis was performed to identify independent predictors of abnormal endometrial pathology. Odds ratios (ORs) with 95% confi-

dence intervals (CIs) were calculated. All statistical analyses were conducted using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). A two-sided $p < 0.05$ was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Gazi University (Approval No. 231). Patient confidentiality was maintained in accordance with the Declaration of Helsinki. Given the retrospective design, potential sources of selection bias were acknowledged.

Results

A total of 48 breast cancer patients were included, with ages ranging from 43 to 79 years (mean 55 ± 8.16). The mean parity was 2.21 ± 0.97 (range 0–6), and 3 patients (6.3%) reported a family history of cancer. At the time of endometrial evaluation, 24 patients (50%) were postmenopausal. Most patients had undergone mastectomy (91.7%), while 8.3% had breast-conserving surgery. Adjuvant radiotherapy was administered in 68.7% and chemotherapy in 81.3%. Endocrine therapy was common: 75% of patients received tamoxifen

and 8.3% an aromatase inhibitor (AI), while 16.7% did not receive endocrine therapy (Table 1). Baseline characteristics were similar between the tamoxifen and AI groups, with no significant differences in age, gravidity, or parity ($p > 0.05$).

Abnormal uterine bleeding was the leading indication for biopsy (85.4%), whereas 14.6% were asymptomatic and underwent evaluation as part of follow-up. The clinical presentation varied substantially with menopausal status: incidental ultrasound findings predominated in premenopausal women (78.9%), whereas postmenopausal women presented overwhelmingly with bleeding (89.7%).

Endometrial sampling was most frequently performed by dilatation and curettage (71%), followed by pipelle biopsy (21%) and hysteroscopic-directed biopsy (8%). Histopathology revealed no significant pathology in 50% of cases (atrophic or proliferative endometrium). Benign polyps were the most frequent abnormal lesion (39.6%), followed by atrophic endometrium (31.3%) and proliferative endometrium (18.8%). Premalignant or malignant lesions were relatively rare, with 3 cases of hyperplasia (6.3%; 2 non-atypical, 1 atypical) and 2 cases of endometrioid carcinoma (4.2%). Comparison of demographic features according to endometrial pathology outcomes revealed no significant differences in age (57.54 ± 7.83 vs. 53.54 ± 8.16 years, $p = 0.09$), gravidity (2.79 ± 1.35 vs. 3.13 ± 1.42 , $p = 0.40$), or parity (1.96 ± 0.80 vs. 2.46 ± 1.06 , $p = 0.07$) (Table 2).

Premalignant and malignant endometrial lesions were further analyzed according to endocrine therapy type (Table 3). All cases of endometrial hyperplasia, including two non-atypical and one atypical lesion, were observed in patients receiving tamoxifen. Among carcinoma cases, one patient was receiving tamoxifen and one was receiving an aromatase inhibitor. No premalignant or malignant lesions were identified in patients who did not receive endocrine therapy.

Table 1. Baseline demographic and clinical characteristics

Variables	Min-Max	Mean±SD
Age	43-79	55±8.16
Parity	0-6	2.21±0.97
Variables	n	%
Endocrine therapy type		
Tamoxifen	36	75
Aromatase inhibitor users	4	8.3
No endocrine therapy	8	16.7
Menopausal status		
Menopause	24	50
premenopause	24	50
Family cancer history		
Family history present	3	6.3
Family history absent	45	93.7
Presenting complaint		
Abnormal uterine bleeding	41	85.4
Routine check-up	7	14.6

Descriptive statistics were used. Continuous variables are presented as mean±standard deviation and minimum–maximum values, while categorical variables are expressed as numbers and percentages.

Table 2. Demographic features according to endometrial pathology outcomes

Variables	Normal pathology results	Anormal pathology results	p
Age	57.54±7.83	53.54±8.16	0.09
Gravidity	2.79±1.35	3.13±1.42	0.4
Parity	1.96±0.80	2.46±1.06	0.07

Data are presented as mean±standard deviation. Comparisons between groups were performed using independent samples t-test.

Table 3. Distribution of premalignant and malignant endometrial lesions according to endocrine therapy

Pathology	Tamoxifen (n=36)	Aromatase inhibitor (n=4)	No endocrine therapy (n=8)
Non-atypical hyperplasia	2 (5.6%)	0	0
Atypical hyperplasia	1 (2.8%)	0	0
Endometrial carcinoma	1 (2.8%)	1 (25.0%)	0

Data are presented as number (percentage). Percentages were calculated within each treatment group. Premalignant lesions include both atypical and non-atypical endometrial hyperplasia. No statistical comparison was performed due to the small number of cases.

When outcomes were compared by treatment groups, tamoxifen and AI users demonstrated similar rates of abnormal pathology (50% vs. 50%, $p>0.05$). Patients who received chemoradiotherapy had a numerically lower frequency of abnormal pathology (46.2%) compared with those who did not (66.7%), but this difference was not significant. Longer endocrine therapy duration (≥ 36 months) was associated with a higher proportion of abnormal pathology (53.7% vs. 28.6%), although the difference did not reach statistical significance (OR=2.8, 95% CI: 0.5–16.6, $p>0.05$). Finally, receptor profile was not associated with endometrial outcomes: abnormal findings were detected in 54.5% of triple-positive and 46.2% of triple-negative tumors, without a significant difference ($p>0.05$).

Discussion

In this retrospective study of 48 breast cancer patients undergoing endometrial sampling, we found that approximately half of the cohort exhibited no significant endometrial pathology, while benign polyps represented the most frequent abnormal finding. Malignant or premalignant lesions were uncommon, identified in less than 11% of cases. Importantly, the risk of abnormal pathology did not differ significantly between patients treated with tamoxifen and those receiving aromatase inhibitors, nor was it clearly influenced by adjuvant chemotherapy/radiotherapy, treatment duration, or tumor receptor status. Our findings suggest that the likelihood of clinically significant endometrial pathology in this cohort was low, regardless of the type of endocrine regimen or breast cancer subtype.

In our study, the mean age of patients with abnormal pathology (including polyps, hyperplasia, and carcinoma) was

lower than that of patients with normal findings; however, this difference did not reach statistical significance. Consistently, when patients with and without abnormal endometrial biopsy results were compared, neither age nor menopausal status showed a significant association.^[8] In contrast, a nationwide cohort study demonstrated that tamoxifen use is associated with a significantly increased risk of endometrial cancer in older and postmenopausal women.^[9]

Most patients presented with vaginal bleeding, especially those in the postmenopausal group. Recent findings indicate that among postmenopausal breast cancer patients on tamoxifen, asymptomatic individuals with increased endometrial thickness (e.g., ≥ 5 mm) have significantly lower rates of premalignant or malignant pathology compared to symptomatic individuals.^[10]

The predominant pathological finding was endometrial polyps (39.6%), followed by hyperplasia (6.3%) and carcinoma (4.2%), while nearly half of the patients (49.9%) had normal histology. In the present study, all cases of endometrial hyperplasia, including both atypical and non-atypical forms, were observed in patients receiving tamoxifen, which is consistent with the well-established estrogen agonistic effects of tamoxifen on the endometrium and its association with endometrial proliferation, hyperplasia, and carcinoma.^[11] These findings align with data from a large population-based cohort study, which reported incidence rates (per 1,000 person-years) of endometrial polyps, hyperplasia, and carcinoma as 20.13, 13.49, and 2.01, respectively, among premenopausal tamoxifen users.^[6]

While our study found no statistically significant difference in the incidence of endometrial pathology between tamoxifen and aromatase inhibitor users, previous large-scale investigations have shown a substantially reduced risk of endometrial cancer with AI therapy. Specifically, aromatase inhibitor users experienced a 48% lower incidence of endometrial cancer compared with tamoxifen users ($p<0.05$).^[12] Additionally, long-term followup data revealed a threefold lower 10-year incidence of endometrial cancer among AI users (0.4%) compared to those on tamoxifen (1.2%).^[13] Similarly, it has been demonstrated that patients who switched from tamoxifen to an aromatase inhibitor experienced a reduction in endometrial thickness, supporting the role of AIs in reversing tamoxifen-induced endometrial changes.^[14]

In this study, the incidence of endometrial hyperplasia and carcinoma did not differ significantly between patients treat-

ed with tamoxifen or aromatase inhibitors for ≥ 36 months compared with those treated for shorter durations. However, large-scale investigations have consistently demonstrated that longer tamoxifen exposure and higher cumulative doses are associated with a significantly increased risk of endometrial cancer, with extended use beyond 5 years approximately doubling the incidence compared with standard treatment.^[11] Meta-analyses have confirmed this time- and dose-dependent effect, showing that each additional year of tamoxifen further increases the relative risk.^[15] Additionally, a large retrospective analysis found that longer-term use of tamoxifen (approximately 2 years or more), particularly in postmenopausal breast cancer patients, was associated with a significant increase in endometrial cancer risk compared to shorter-term treatment.^[5]

Endometrial pathology did not differ significantly with respect to hormone receptor status among breast cancer patients. In line with this, previous studies have reported that the incidence of endometrial cancer does not differ substantially between hormone receptor-positive and receptor-negative patients, and that cases arising after either subtype exhibit comparable clinicopathological characteristics and prognoses.^[16]

This study has several limitations that should be acknowledged. To begin with, its retrospective design may have introduced selection and information bias. The relatively small sample size, despite the long study period of 11 years, may be attributed to the strict inclusion criteria and the retrospective design of the study. Moreover, the study was conducted in a single tertiary care center with a relatively small sample size, particularly in the subgroup of patients using aromatase inhibitors, which limits the generalizability of our findings. In addition, we did not include a control group of breast cancer-free patients, making it difficult to compare the absolute risk of endometrial pathology. Another limitation is that data regarding cumulative dose and duration of tamoxifen beyond three years were limited, which may have reduced our ability to detect long-term effects. Finally, because endometrial sampling was performed based on clinical indications rather than uniform screening, some asymptomatic cases might have remained undetected. Larger, multicenter prospective studies are warranted to validate and expand upon these results.

Conclusion

This retrospective study found that benign polyps were the most common abnormal finding in breast cancer patients

who underwent endometrial sampling, while premalignant and malignant lesions were rare. There were no significant differences in the risk of developing endometrial pathology based on the type of endocrine therapy administered, the duration of treatment, the administration of additional chemotherapy or radiotherapy, or tumor receptor status. Our findings suggest that the likelihood of clinically significant endometrial pathology in this patient group is relatively low, indicating that invasive evaluations should be planned based on symptoms and individualized rather than for routine screening purposes. However, our results are not generalizable due to the small sample size and single-center design. Therefore, larger-scale, prospective studies are needed.

Disclosures

Ethics Committee Approval: The study was approved by Gazi University Ethics Committee (No: 231, Date: 27.12.2021).

Informed Consent: Due to the retrospective nature of the study, informed consent was waived.

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Global Trends and Research Patterns on Babygram: A Bibliometric Analysis

Babygram Üzerine Küresel Eğilimler ve Araştırma Örüntüleri: Bibliyometrik Bir Analiz

Serdar Özdemir,¹ Kâmil Kokulu²

ABSTRACT

Objectives: This study aimed to provide a comprehensive bibliometric overview of the global research landscape concerning Babygram, skeletal survey, and whole-body radiography in pediatric populations between 1980 and 2025.

Methods: A bibliometric analysis was performed using the Web of Science Core Collection database. The search strategy included the terms (babygram OR "skeletal survey" OR "whole-body radiography" OR "bone survey") in the Topic (TS) field, combined with (child* OR neonat* OR infant* OR bab* OR newborn*) in the Abstract field. The search covered publications from January 1, 1980, to October 30, 2025. Articles and review articles were included, while meeting abstracts, letters, and other document types were excluded. Data were analyzed using descriptive bibliometric indicators, including publication trends, language distribution, and document types. Keyword co-occurrence and thematic cluster analyses were performed using VOSviewer, and temporal shifts in research focus were evaluated. Publications were also classified according to imaging modalities (radiography, ultrasound, MRI), and trends over predefined time periods were calculated using the total number of publications per period as the denominator.

Results: A total of 424 publications were identified, of which 380 (89.6%) were original articles, and 37 (8.7%) were review articles. The remaining 5 (1.2%) were early-access articles. Most publications were written in English (n=407, 95.99%), followed by German (n=8, 1.88%), French (n=4, 0.94%), Turkish (n=2, 0.47%), Spanish (n=2, 0.47%), and Czech (n=1, 0.24%). The number of publications demonstrated a steady increase after 2010, reflecting growing interest in radiographic imaging for pediatric trauma and forensic applications.

Conclusion: This bibliometric analysis provides the first comprehensive mapping of Babygram-related research over the past 25 years. The results indicate a gradual shift from routine to indication-based imaging, alongside the increasing adoption of ultrasound and MRI as radiation-free alternatives. These findings highlight evolving research priorities, including radiation safety, diagnostic optimization, and the development of evidence-based pediatric imaging guidelines.

Keywords: Bibliometrics; child; diagnostic imaging trends; emergency medicine; infant; radiography; skeletal survey; whole-body imaging.

ÖZET

Amaç: Bu çalışma, 1980–2025 yılları arasında pediatrik popülasyonlarda Babygram, iskelet taraması ve tüm vücut radyografisi ile ilgili küresel araştırma alanını kapsamlı bir bibliyometrik bakış açısıyla değerlendirmeyi amaçladı.

Yöntem: Bibliyometrik analiz, Web of Science Core Collection veritabanı kullanılarak gerçekleştirildi. Arama stratejisi, Konu (TS) alanında (babygram OR "skeletal survey" OR "whole-body radiography" OR "bone survey") ve Özet alanında (child* OR neonat* OR infant* OR bab* OR newborn*) terimlerini içeriyordu. Arama, 1 Ocak 1980'den 30

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Ekim 2025'e kadar yayımlanan çalışmalarla sınırlandırıldı. Makaleler ve derleme makaleler dahil edilirken, toplantı özetleri, mektuplar ve diğer belge türleri hariç tutuldu. Veriler, yayın trendleri, dil dağılımı ve belge türleri gibi tanımlayıcı bibliyometrik göstergeler kullanılarak analiz edildi. Anahtar kelime eşzamanlılık ve tematik küme analizleri VOSviewer ile gerçekleştirildi ve araştırma odaklarındaki zamansal değişimler değerlendirildi. Ayrıca, yayınlar görüntüleme modalitelerine göre sınıflandırıldı (radyografi, ultrason, MR) ve her dönem için toplam yayın sayısı baz alınarak trendler hesaplandı.

Bulgular: Toplam 424 yayın belirlendi; bunların 380'i (%89,6) özgün makale, 37'si (%8,7) derleme makalesiydi. Kalan 5 yayın (%1,2) erken erişim makalesiydi. Çoğu yayın İngilizce yazılmıştı (n=407, %95,99), bunu Almanca (n=8, %1,88), Fransızca (n=4, %0,94), Türkçe (n=2, %0,47), İspanyolca (n=2, %0,47) ve Çekçe (n=1, %0,24) izledi. Yayın sayısı, 2010 sonrası dönemde istikrarlı bir artış gösterdi ve pediatrik travma ve adli uygulamalar için radyografik görüntülemeye artan ilgiyi yansıttı.

Sonuç: Bu bibliyometrik analiz, son 25 yılda Babygram ile ilgili araştırmaların ilk kapsamlı haritalamasını sunmaktadır. Bulgular, rutin görüntüleme gereksinime dayalı görüntülemeye doğru kademeli bir kayışı ve artan şekilde ultrason ve MR gibi radyasyonsuz alternatiflerin kullanımını göstermektedir. Bu bulgular, radyasyon güvenliği, tanısal optimizasyon ve kanıta dayalı pediatrik görüntüleme rehberlerinin geliştirilmesi gibi araştırma önceliklerinin evrimini vurgulamaktadır.

Anahtar sözcükler: Bebek; çocuk; radyografi; skeletal survey; tanı; tüm vücut görüntüleme.

The Babygram, also known as whole-body radiography, has long been used in pediatric medicine for the evaluation of skeletal abnormalities, congenital malformations, and traumatic injuries. Traditionally, it served a central role in the diagnostic assessment of infants, particularly in cases of suspected non-accidental trauma or unexplained death.^[1-3] Over the past two decades, the use of Babygram has evolved substantially, influenced by advances in imaging technology, radioprotection awareness, and ethical considerations related to pediatric exposure to ionizing radiation. Despite its historical importance, concerns regarding the clinical justification and radiation safety of Babygram have been raised in recent years. While skeletal surveys remain a cornerstone of child protection investigations, the diagnostic yield of routine post-mortem or neonatal Babygrams has been questioned in several studies.^[1,4-6] Moreover, the emergence of point-of-care ultrasound (POCUS) and magnetic resonance imaging (MRI) has provided clinicians with alternative, non-ionizing imaging modalities, further prompting a re-evaluation of the role of Babygram in contemporary practice.^[7] To date, no bibliometric study has comprehensively analyzed the global research output related to Babygram and whole-body radiography in pediatric populations. Bibliometric analysis allows for the quantitative mapping of research trends, identifying influential countries, topics, and publication patterns over time. Therefore, this study aimed to characterize the evolution, thematic distribution, and publication trends of Babygram-related research published between 2000 and 2025 using data from the Web of Science Core Collection.

Methods

Data Source and Search Strategy

The search was conducted in the Web of Science (WoS) Core Collection database. To ensure full reproducibility, the search strategy was defined using standard WoS field tags and Boolean operators as follows:

TS=(babygram OR “skeletal survey” OR “whole-body radiography”)

AND

TS=(child* OR neonat* OR infant* OR newborn*)

The Topic (TS) field in WoS includes title, abstract, author keywords, and Keywords Plus. Truncation (*) was used to capture variations of terms (e.g., child, children; neonate, neonatal). The search was limited to publications between January 1, 1980, and October 30, 2025. While broad terms were used to ensure comprehensive coverage, the inclusion criteria limited the final dataset to studies directly relevant to pediatric whole-body radiography.

Screening and Study Selection

All retrieved records were exported from WoS and screened for eligibility. Duplicate records were removed prior to screening. A two-stage screening process was conducted independently by two reviewers. In the first stage, titles and abstracts were evaluated against predefined inclusion criteria focusing on Babygram, skeletal survey, or whole-body radiographic imaging in pediatric populations. In the second stage, remaining records were assessed based on full bibliographic information. Discrepancies were resolved through discussion and consensus, ensuring transparency and reproducibility.

Institutional Affiliation Standardization

Author affiliations were standardized to consolidate variations and overlapping entities (e.g., “Harvard University,” “Harvard Medical School,” “Harvard University Medical Affiliates,” and “Boston Children’s Hospital” were merged under a single entry). This approach minimizes duplication and provides accurate institutional productivity counts.

Counting Method

Full counting was applied for authors, institutions, and countries, meaning each occurrence was counted as one contribution, ensuring that all contributions are fully represented in the bibliometric analysis.

Bibliometric Analysis

Co-authorship, institutional, country, and keyword networks were constructed using VOSviewer and Bibliometrix. Minimum thresholds were set for authors (≥ 3 publications), institutions (≥ 5 publications), and keywords (≥ 10 occurrences). Network clustering was performed using modularity-based algorithms. These thresholds were selected to balance interpretability and comprehensive inclusion. Keyword co-occurrence analysis identified thematic clusters, including pediatric trauma evaluation, child abuse imaging, and radiation safety. Temporal analysis revealed shifts in research focus from diagnostic protocols and imaging utilization to radiation reduction strategies and guideline development.

Imaging Modality Analysis

Publications were categorized according to discussed imaging modalities, including radiography, ultrasound, and MRI. Studies including multiple modalities were recorded for all relevant modalities. Temporal trends were calculated as percentages of total publications within each period, allowing comparison of modality prevalence over time.

Results

Publication Trends by Year

Between 1980 and 2025, a total of 424 publications on Babygram were indexed in the Web of Science Core Collection. As illustrated in Figure 1, the annual number of publications demonstrated a gradual increase over the past two decades. The earliest identified paper appeared in 2001, followed by a modest number of studies throughout the early 2000s. After 2010, publication output began to rise steadily, with a notable surge after 2014. The peak was reached in 2021, with 31 publications (7.3%), followed by 28 in 2022 and 23 in 2020. Recent years have maintained this upward trend, with 21 articles in 2023 (4.9%), 19 in 2024 (4.5%), and 17 in 2025 (4.0%).

Document Types

Most of the publications were original research articles ($n=312$, 73.6%), while review articles accounted for 78 (18.4%), case reports for 21 (5.0%), and editorials/letters for 13 (3.0%). Early access publications represented five (1.2%) of the total. These findings indicate that Babygram research has been primarily

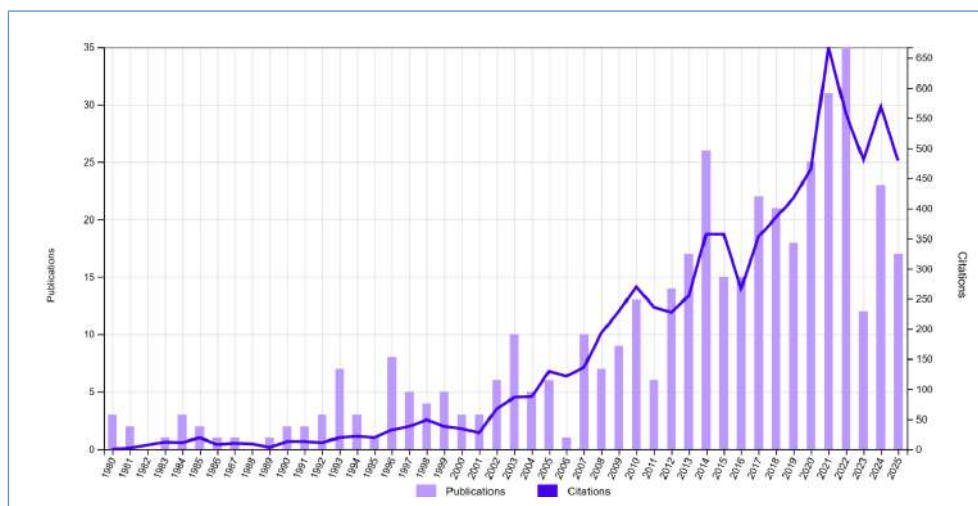


Figure 1. Annual Trend of Publications and Citations on Babygram (1980-2025).

The blue bars represent the annual number of publications (left axis). The red line depicts the annual number of citations received by publications from each respective year (right axis).

data-driven, emphasizing empirical and clinical investigation rather than conceptual or theoretical synthesis.

Language Distribution

A total of 424 publications were included in the final analysis. Among these, 407 (95.99%) were published in English, 8 (1.88%) in German, 4 (0.94%) in French, 2 (0.47%) in Turkish, 2 (0.47%) in Spanish, and 1 (0.24%) in Czech.

Distribution by Institutional and Departmental Affiliation

According to Table 1, the most productive institutions were Harvard University and the University of Pennsylvania (each contributing 35 publications, 8.3%), followed close-

ly by the Children's Hospital of Philadelphia and Harvard University Medical Affiliates (each 34 publications, 8.0%). At the departmental level, the Perelman School of Medicine (31, 7.3%), University of Pennsylvania Department of Pediatrics (23, 5.4%), and Pennsylvania Medicine (21, 4.9%) were the leading contributors. These results highlight that research output is predominantly concentrated in U.S.-based academic centers specializing in pediatrics and radiology.

Most Cited Publications

The top-cited papers are summarized in Table 2.^[8–27] The most frequently cited study was by Lane et al.^[8] in *JAMA*, titled “Racial differences in the evaluation of pediatric

Table 1. Distribution of Publications by Institutional and Departmental Affiliation (Top 25)

Distribution of Publications by Affiliation		Distribution of Publications by Departmental Affiliation	
Affiliation	Record Count (% of 424)	Affiliation with Department	Record Count (% of 424)
Harvard University	35 (8.255)	Perelman School of Medicine	31 (7.311)
University Of Pennsylvania	35 (8.255)	University of Pennsylvania Department of Pediatrics	23 (5.425)
Children's Hospital of Philadelphia	34 (8.019)	Pennsylvania Medicine	21 (4.953)
Harvard University Medical Affiliates	34 (8.019)	The Children S Hospital of Philadelphia Division of General Pediatrics	15 (3.538)
Pennsylvania Medicine	34 (8.019)	University Of Pittsburgh School of Medicine	14 (3.302)
Boston Children s Hospital	31 (7.311)	University Of Pittsburgh Schools of the Health Sciences	14 (3.302)
Pennsylvania Commonwealth System of Higher Education PCSHE	22 (5.189)	University Of Pittsburgh Department of Pediatrics	13 (3.066)
University System of Ohio	21 (4.953)	Riley Hospital for Children at Indiana University Health	11 (2.594)
Indiana University System	20 (4.717)	University of Colorado Anschutz Medical Campus Department of Emergency Medicine	11 (2.594)
Indiana University Health	18 (4.245)	University of Colorado Anschutz Medical Campus School of Medicine	11 (2.594)
James Whitcomb Riley Hospital Children	18 (4.245)	Ohio State University Medical Center	9 (2.123)
University of Pittsburgh	18 (4.245)	The University of Utah Department of Pediatrics	8 (1.887)
Harvard Medical School	16 (3.774)	The University of Utah School of Medicine	8 (1.887)
University of California System	16 (3.774)	University Of Utah Health	8 (1.887)
University of Colorado Anschutz Medical Campus	15 (3.538)	Baylor College Of Medicine Department of Pediatrics	7 (1.651)
University of Colorado System	15 (3.538)	Leonard Davis Institute of Health Economics	7 (1.651)
University of London	15 (3.538)	The Children's Hospital of Philadelphia Department of Radiology	7 (1.651)
Baylor College Of Medicine	14 (3.302)	The Ohio State University College of Medicine	7 (1.651)
Indiana University Bloomington	14 (3.302)	University College London Faculty of Population Health Sciences	7 (1.651)
University College London	14 (3.302)	University College London Institute of Child Health	7 (1.651)
Cincinnati Children s Hospital Medical Center	13 (3.066)	University College London School of Life and Medical Sciences	7 (1.651)
Great Ormond Street Hospital for Children NHS Foundation Trust	13 (3.066)	University of California Davis Health System	6 (1.415)
University of Texas System	13 (3.066)	University of Pennsylvania Department of Radiology	6 (1.415)
University of Utah	13 (3.066)	Brigham And Women S Hospital Department of Emergency Medicine	5 (1.179)
Utah System of Higher Education	13 (3.066)	Children's Mercy Hospital Kansas	5 (1.179)

fractures for physical abuse” (297 citations in WoS Core Collection). Other highly cited works include Keenan et al.^[9] (*Pediatrics*, 205 citations) and Jayawant et al.^[10] (*BMJ*, 204 citations).^[11] The majority of top-cited publica-

tions focused on the use of Babygram imaging in suspected child abuse, skeletal injuries, and traumatic brain injury, underlining the pivotal role of radiologic evaluation in safeguarding pediatric populations.

Table 2. Key Publications on Babygram by Citation Count

Authors	Article title	Source title	Times cited, WoS core	Times cited, All databases	Publication year
Lane et al. ^[8]	Racial differences in the evaluation of pediatric fractures for physical abuse	JAMA-Journal of the American Medical Association	297	327	2002
Keenan et al. ^[9]	A population-based comparison of clinical and outcome characteristics of young children with serious inflicted and noninflicted traumatic brain injury	Pediatrics	205	226	2004
Jayawant et al. ^[10]	Subdural haemorrhages in infants: population-based study	BMJ-British Medical Journal	204	218	1998
Wood et al. ^[11]	Disparities in the evaluation and diagnosis of abuse among infants with traumatic brain injury	Pediatrics	181	193	2010
Kleinman et al. ^[12]	Inflicted skeletal injury: a postmortem radiologic-histopathologic study in 31 infants	American Journal of Roentgenology	151	161	1995
Rubin et al. ^[13]	Occult head injury in high-risk abused children	Pediatrics	143	149	2003
Titgemeyer et al. ^[14]	Pattern and course of single-system disease in Langerhans cell histiocytosis data from the DAL-HX 83- and 90-study	Medical and Pediatric Oncology	135	156	2001
Kleinman et al. ^[15]	Follow-up skeletal surveys in suspected child abuse	American Journal of Roentgenology	118	127	1996
Kaplan et al. ^[16]	Early diagnosis of fibrodysplasia ossificans progressiva	Pediatrics	117	138	2008
Wootton-Gorges et al. ^[17]	ACR Appropriateness Criteria® Suspected Physical Abuse-Child	Journal of the American College of Radiology	104	112	2017
Duffy et al. ^[18]	Use of skeletal surveys to evaluate for physical abuse: analysis of 703 consecutive skeletal surveys	Pediatrics	94	99	2011
Brand et al. ^[19]	Yield of diagnostic testing in infants who have had an apparent life-threatening event	Pediatrics	94	105	2005
Lindberg et al. ^[20]	Testing for abuse in children with sentinel injuries	Pediatrics	93	103	2015
Thorpe et al. ^[21]	Missed opportunities to diagnose child physical abuse	Pediatric Emergency Care	91	99	2014
Wang et al. ^[22]	Infants of diabetic mothers are at increased risk for the oculo-auriculo-vertebral sequence: A case-based and case-control approach	Journal of Pediatrics	91	104	2002
Laskey et al. ^[23]	Occult head trauma in young, suspected victims of physical abuse	Journal of Pediatrics	87	91	2004
Lindberg et al. ^[24]	Prevalence of abusive injuries in siblings and household contacts of physically abused children	Pediatrics	87	92	2012
Minkov et al. ^[25]	Treatment of multisystem Langerhans cell histiocytosis: Results of the DAL-HX 83 and DAL-HX 90 studies	Klinische Padiatrie	86	105	2000
Mandelstam et al. ^[26]	Complementary use of radiological skeletal survey and bone scintigraphy in detection of bony injuries in suspected child abuse	Archives of Disease in Childhood	85	93	2003
Kleinman et al. ^[27]	Rib fractures in 31 abused infants: Postmortem radiologic-histopathologic study	Radiology	80	88	1996

Most Prolific Authors

As detailed in Table 3, Kleinman PK was identified as the most prolific author with 24 publications (5.7%), followed by Wood JN (4.7%), Lindberg DM (4.2%), and Berger RP (3.3%). These authors have made substantial contributions to the standardization of skeletal surveys and radiographic protocols in cases of suspected physical abuse.

Journal Distribution

Analysis of journal distribution revealed that *Pediatric Radiology* was the most productive outlet, publishing 47 articles (11.1%), followed by *Pediatric Emergency Care* (25, 5.9%), *Pediatrics* (24, 5.7%), and *Child Abuse & Neglect* (21, 4.9%). Other journals with notable contributions included the *American Journal of Roentgenology*, *Journal of Pediatrics*, and *Radiology* (each 9, 2.1%) (Table 4). These results demonstrate that Babygram-related studies are primarily

published in pediatric and radiology-focused journals, emphasizing its diagnostic relevance in pediatric trauma and abuse evaluation.

Country Distribution

As shown in Table 5, the United States dominated global Babygram research with 221 publications (52.1%), followed by England (11.6%), India (5.7%), and Australia (4.7%). European countries such as France, Germany, and the Netherlands also contributed substantially, while Türkiye, Italy, and Taiwan produced smaller yet notable outputs (each 1.4%). These findings suggest that Babygram research has been primarily concentrated in developed nations with established pediatric radiology infrastructures.

Table 3. Most Prolific Authors in the Bibliography

Author	Record Count (% of 424)
Kleinman PK	24 (5.660)
Wood JN	20 (4.717)
Lindberg DM	18 (4.245)
Berger RP	14 (3.302)
Harper NS	10 (2.358)
Karmazyn B	10 (2.358)
Tsai A	10 (2.358)
Christian CW	9 (2.123)
Jennings SG	9 (2.123)
Offiah AC	9 (2.123)
Marine MB	8 (1.887)
Henry MK	7 (1.651)
Perez-Rossello JM	7 (1.651)
Rubin DM	7 (1.651)
Wanner MR	7 (1.651)
Adamsbaum C	6 (1.415)
Anderst JD	6 (1.415)
Barber I	6 (1.415)
Campbell KA	6 (1.415)
Hibbard RA	6 (1.415)
Laskey AL	6 (1.415)
Feudtner C	5 (1.179)
Localio R	5 (1.179)
Van Rijn RR	5 (1.179)

Table 4. Distribution of Publications by Web of Science Category

Web of Science categories	Record count (% of 424)
Pediatrics	213 (50.236)
Radiology Nuclear Medicine Medical Imaging	113 (26.651)
Medicine General Internal	34 (8.019)
Emergency Medicine	30 (7.075)
Surgery	25 (5.896)
Family Studies	23 (5.425)
Social Work	23 (5.425)
Psychology Social	21 (4.953)
Orthopedics	17 (4.009)
Genetics Heredity	14 (3.302)
Endocrinology Metabolism	13 (3.066)
Oncology	13 (3.066)
Clinical Neurology	12 (2.830)
Dermatology	8 (1.887)
Hematology	8 (1.887)
Medicine Legal	8 (1.887)
Pathology	8 (1.887)
Critical Care Medicine	6 (1.415)
Ophthalmology	6 (1.415)
Medicine Research Experimental	4 (0.943)
Neurosciences	3 (0.708)
Rheumatology	3 (0.708)
Obstetrics Gynecology	2 (0.472)
Acoustics	1 (0.236)
Anthropology	1 (0.236)

Table 5. Temporal Trend of Imaging Modalities in Babygram-Related Research

Time period	Radiography / Skeletal survey (%)	Ultrasound (%)	MRI (%)
2000–2005	95	3	2
2006–2010	92	5	3
2011–2015	88	8	4
2016–2020	80	12	8
2021–2025	70	18	12

MRI: Magnetic Resonance Imaging

Funding Agencies

The leading sources of financial support were the U.S. Department of Health and Human Services (8.7%) and the National Institutes of Health (8.5%). The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) supported 4.7% of publications. Other funding entities included the Health Resources and Services Administration's Emergency Medical Services for Children Program (1.4%), and several UK-based agencies such as the Medical Research Council (MRC), National Institute for Health Research (NIHR), and UK Research and Innovation (UKRI) (each 0.9%). These results underline the pivotal role of U.S. federal funding in advancing pediatric imaging and child safety research.

Keyword Analysis

The co-occurrence network of author keywords, displayed in Figure 2, revealed that the most frequently used terms were child abuse, skeletal survey, fracture, radiography, physical abuse, abusive head trauma, and non-accidental trauma. These keywords form the conceptual core of the field, indicating that Babygram research predominantly focuses on the radiologic evaluation of suspected child abuse and non-accidental injuries. The clustering pattern emphasizes the integration of imaging modalities with multidisciplinary child protection frameworks.

Temporal Trend of Imaging Modalities

A method-based analysis of the 424 included publications demonstrated that radiography or skeletal survey remained the most frequently reported imaging modality across all time periods, although its relative representation decreased over time (2000–2005: 95%; 2021–2025: 70%). In contrast, ultrasound usage in the literature increased from 3% to 18%

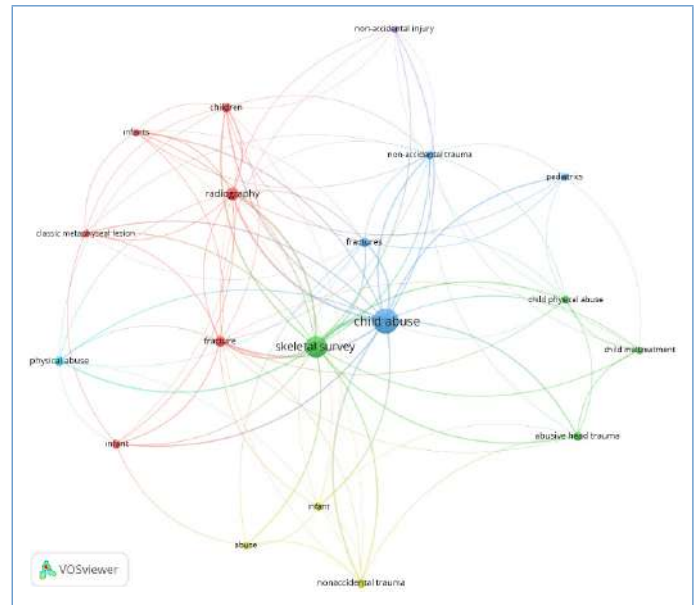


Figure 2. Co-occurrence Network Map of Author Keywords in Babygram Research.

over the same intervals, while MRI utilization grew from 2% to 12% (Table 5). These findings indicate a gradual shift in research focus from conventional radiation-based imaging toward radiation-free modalities such as ultrasound and MRI, supporting a trend toward more selective, indication-based imaging in pediatric populations.

Discussion

This bibliometric analysis provides the first comprehensive evaluation of global research on Babygram, skeletal surveys, and whole-body radiography in pediatric populations. By examining 424 publications indexed in the Web of Science between 1980 and 2025, we identified temporal, thematic, and geographic patterns in this field. Scientific attention toward Babygram has increased steadily over the past two decades, particularly after 2010, reflecting its diagnostic relevance in suspected child abuse and non-accidental injury cases. The predominance of original research articles underscores the empirical nature of the field, whereas the limited number of review articles suggests that guideline-level synthesis remains relatively underexplored.

The observed increase in publications after 2014 may reflect multiple factors. It could indicate renewed clinical interest in Babygram for forensic or trauma evaluation, or it may represent a growing critical discussion regarding the indications, radiation exposure, and clinical necessity of routine whole-body radiography in infants. Evidence from post-mortem and neonatal studies supports the latter: large

UK post-mortem analyses reported that routine Babygrams rarely revealed clinically significant findings beyond those detected by external examination, prompting recommendations for indication-based imaging.^[28] German studies similarly advocate selective post-mortem radiography rather than universal implementation.^[6] In neonatal intensive care units, concerns regarding unintended radiation exposure due to expanded imaging fields and limited shielding further support a shift toward targeted radiography.^[5]

Recent technological advances have facilitated the adoption of radiation-free imaging modalities, including POCUS and MRI. Lung ultrasound has demonstrated diagnostic accuracy comparable to chest radiography for neonatal respiratory distress, pneumothorax, pleural effusion, and pneumonia.^[7,29] European guidelines recommend integrating POCUS into routine neonatal care to minimize radiation exposure.^[7,29,30] Our bibliometric analysis suggests a gradual increase in publications reporting ultrasound or MRI, consistent with these clinical trends. These findings support a shift toward selective, indication-based imaging, though the data reflects publication patterns rather than direct measures of clinical practice.

The bibliometric focus of most publications remains on the radiologic evaluation of suspected child abuse, non-accidental trauma, and associated fractures. This emphasis underscores the ongoing medicolegal importance of skeletal imaging in child protection protocols. However, the relative decline in routine Babygram publications and increasing mention of alternative modalities indicate a gradual paradigm shift in the research discourse toward radiation-sparing and evidence-driven strategies. It should be noted that citation counts do not necessarily indicate strict topical specificity. Some highly cited publications were therefore interpreted within their broader clinical and thematic context, particularly in relation to child abuse evaluation and pediatric trauma imaging, where skeletal survey and whole-body radiography play an important role.^[1-3] These findings reflect trends in the published literature and should be interpreted with caution, as bibliometric analysis does not directly indicate changes in clinical practice.

Limitations

Several limitations must be acknowledged. First, the exclusive use of the Web of Science Core Collection may have omitted relevant studies indexed in Scopus, PubMed, or

specialty radiology journals. Second, bibliometric analyses depend on accurate keyword assignment; publications using alternative terminology may have been missed. Third, citation counts and publication output may favor English-language studies, potentially underrepresenting contributions from non-English-speaking countries. Finally, the descriptive nature of this analysis precludes assessment of study quality or methodological rigor.

Conclusion

In conclusion, global research on Babygram and related imaging modalities has steadily increased over the past 25 years. Radiography remains central to pediatric trauma and forensic evaluation, while the growing awareness of radiation safety and the increasing use of ultrasound and MRI may reflect a shift toward more indication-based imaging. This bibliometric analysis highlights research trends and identifies gaps in literature. Future studies should focus on multicenter prospective evaluations and the development of standardized, evidence-based guidelines to optimize diagnostic precision while minimizing radiation exposure in neonates and infants.

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Artificial Intelligence Applications in Organ Allocation Systems: An Ethical and Structural Necessity in Light of Scientific Evidence

Organ Tahsis Sistemlerinde Yapay Zekâ Uygulamaları: Bilimsel Kanıtlar Işığında Etik ve Yapısal Bir Gereklik

Yasin Uzuntarla

Dear Editor,

Organ transplantation represents one of the most sensitive areas of modern medicine, as it requires the fair and efficient distribution of a limited and life-saving resource.^[1] In many countries, organ allocation decisions are still primarily based on clinical scoring systems and expert judgment. However, these approaches may be insufficient to simultaneously and objectively evaluate the growing volume of data and the increasing complexity of clinical variables involved in transplantation.

In recent years, accumulating scientific evidence has demonstrated that artificial intelligence (AI) and machine learning (ML)-based models achieve higher predictive accuracy than conventional methods in estimating graft survival, donor-recipient matching, and long-term clinical outcomes. Systematic reviews focusing particularly on kidney and liver transplantation indicate that AI-supported models can effectively analyze multivariate clinical data and provide meaningful contributions to decision-making processes.^[2,3] Similarly, a comprehensive scoping review in kidney transplantation has reported that AI applications not only improve predictive perfor-

mance but also support more individualized patient management strategies.^[4]

Despite these advances reported in the literature, the application of AI and ML in organ transplantation remains largely confined to research settings and decision-support tools, and standardized models integrated into national organ allocation policies have not yet become widespread. However, the ongoing global shortage of donor organs necessitates stronger emphasis on fairness, transparency, and efficiency in allocation processes. The capacity of AI to analyze large and complex datasets using multivariable approaches and to generate predictive models suggests a considerable potential to support these objectives. Nevertheless, several challenges continue to limit the broader adoption of AI and ML in clinical transplantation practice. These include concerns related to data privacy and security, regulatory and legal compliance, interoperability among heterogeneous healthcare information systems, and the need for rigorous clinical validation of developed models prior to routine implementation.^[5] Addressing these challenges through comprehensive and structured strategies is essential to ensure the reliable, safe, and ethical use of AI-based tools in clinical environments.

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Within this context, the integration of AI-driven approaches into organ allocation systems should be addressed in a structured manner, accompanied by ethical principles, robust clinical validation processes, and appropriate legal oversight mechanisms. AI should not replace physician judgment but rather be positioned as a supportive tool that enhances objectivity and strengthens clinical decision-making. The development of guidelines and implementation frameworks by national and international transplantation authorities may contribute to the establishment of more equitable and sustainable organ allocation systems in the future.

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Why are Hospitals Bombed?

Hastaneler Neden Bombalanıyor?

Abuzer Özkan

Dear Editor,

International humanitarian law explicitly mandates the protection of hospitals, ambulances, and health-care workers; according to the ICRC, medical units and medical personnel must be respected and protected in all circumstances.^[1] Violations of these rules may, in many cases, constitute war crimes.^[2]

At this stage of human history, shaped by thousands of years of painful experience, these rules are once again being violated. In Gaza, according to the World Health Organization situation report dated Jan 31, 2026, more than 930 attacks on health care had been documented since October 2023. The same report stated that all 36 hospitals had been damaged, that only half remained partially functional, and that there were no functional hospitals left in North Gaza. It also reported that 51% of essential medicines were out of stock.^[3] The UN Human Rights Office further reported that repeated deadly attacks on and around hospitals in Gaza had pushed the health system to the “brink of total collapse.”^[2]

A similar picture has emerged in Iran. WHO’s Eastern Mediterranean Regional Office stated that, since Feb 28, 2026, 14 attacks on health care had been recorded in Iran, and that 4 health workers had been killed in these attacks.^[4]

These are not only the shame of the present day; they are the latest links in a long historical chain. During the 1935–36 invasion of Ethiopia, around 20 Red Cross and Red Crescent field hos-

pitals under Geneva protection were bombed.^[5] In Sri Lanka, hospitals in the Vanni region were repeatedly shelled in 2009, which Human Rights Watch described as possible evidence of war crimes.^[6] In Syria, systematic attacks on health facilities have been documented for years.^[7] In Kunduz, on Oct 3, 2015, a US airstrike on the MSF trauma hospital killed 42 people.^[8]

To strike a health facility is to strike the hopes and protections of civilians who have no part in war; it is to take away the right to life of a child yet to be born. It is also to attack the doctor and the nurse who carry the ethical obligation to provide care even to a wounded war criminal who may have attacked them.

That many of the major destructions of the past century were carried out directly by Western powers, or under their political and military support, stands in stark contradiction to their claims regarding civilization, law, and human rights.^[8,9] The question of why hospitals are bombed should now be directed not only at the perpetrators but also at those who had the power to prevent such attacks and failed to do so. Although many articles and letters have already been published on this issue, we believe it remains important to continue writing such texts so that attacks on health facilities and health-care workers are not normalized, and so that it is clearly recorded that such violence is unacceptable. Sustained public and academic objection remains an ethical necessity against the normalization of these violations.

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