

## D Vitamini Reseptörü Rs1544410 Polimorfizminin Diş Çürüğü Oluşumuna Etkisi

### Effect of Vitamin D Receptor rs1544410 Polymorphism on Tooth Decays

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#### Öz

D vitamininin kas ve kemik gelişimindeki etkilerinden dolayı ağız ve diş sağlığı açısından önemli etkileri bulunmaktadır. Ağız hijyenini belirten en önemli ölçeklerden biri DMF-T (Çürük, kayıp, dolgululu dişler) indeksidir. Çalışmamızda D vitamini reseptörü (VDR) üzerinde bulunan rs1544410 polimorfizmi ile oral hijyen indeksi olan DMF-T arasındaki ilişkisi araştırılmıştır. Çalışmamızda 11'i kız, 13'ü erkek, toplamda 24 sporcuda katılmıştır. Çalışmamıza gönüllü olarak katılan atletlerin DNA eldesi periferik kandan ticari kit kullanılarak elde edilmiştir. Sporcuların genotiplerinin belirlenmesi için gerçek zamanlı polimeraz zincir reaksiyonu (GZ-PZR) metodu kullanılmıştır. Bireylerin diş çürük analizlerinin değerlendirilmesinde de DMF-T indeksinden yararlanılmıştır. rs1544410 polimorfizmi için elde edilen bulgulara göre çalışmaya katılan atletlerin AA, AG, GG genotipleri sırasıyla 8 (%33), 13 (%54), 3(%12) GG olarak bulunmuştur. Allelik dağılımlar incelendiğinde A alleli çalışma grubunda %60, G alleli %40 oranında bulunmuştur. rs1544410 polimorfizminde DMFT analizi ile genotipler karşılaştırıldığında AA genotipli bireylerde 0-1 arası 2 sporcu (%25), 2-4 arası 4 sporcu (%50), 5-10 arası 2 sporcu (%25) bulunurken, 10 ve üzeri değerde hiçbir sporcuya rastlanılmamıştır. AG genotipli bireylerde ise 0-1, 2-4, 5-10, 10 ve üzeri değerlere sahip birey sayıları ve yüzdeleri; sırasıyla; 3 (%23), 3(%23), 5 (%38), 2 (%16) şeklinde bulunmuştur. GG genotipli bireylerde DMFT indeksi 0-1 arası değere sahip olan 2 sporcu (%67), 2-4 arası

değere sahip olan 1 sporcuda (%33) tespit edilmiş olup, 5-10 ile 10 ve üzeri değere hiçbir bireylerde rastlanılmamıştır. Bu çalışmanın, VDR geninin rs1544410 polimorfizmlerinin diş çürüğü oluşumuna etkisinin araştırılacağı diğer çalışmalara veri kaynağı olabileceğini düşünmekteyiz.

**Anahtar Kelimeler:** D vitamini, polimorfizm, diş çürüğü, DMFT indeksi

#### Abstract

Due to the effects of vitamin D on muscle and bone development, there are significant effects on oral and dental health. One of the important markers of oral health is the index (DMF-T), which reports the number of caries, missing filled teeth. In our study, the relationship between rs1544410 polymorphism on D vitamini reseptör (VDR) and the number of teeth affected by caries and results was investigated. A total of 24 athletes, 11 girls and 13 boys, participated in the study. The DNA samples of the athletes were isolated from buccal cells by using a commercially available DNA isolation Kit. The real-time polymerase chain reaction (RT-PCR) method was used to determine the genotypes of the athletes. The DMF-T index was used to identify individuals with caries, missing filled teeth. Respective number and percentages of AA, AG, GG genotypes were found as 8 (33%), 13 (54%) and 3 (12%) GG, for rs1544410 polymorphism. When allele distributions were examined, A allele was found to be as 60%, and G allele as 40%. When genotypes were compared with DMF-T, 2 athletes were (25%) between 0-1, 4 athletes (50%) between 2-4, 2 athletes (25%) were between 5-10, and none of the athletes had above 10 for the individuals with AA genotypes. For AG genotypes, the respective numbers and percentages of individuals with values 0-1, 2-4, 5-10, 10 and above are 3 (23%), 3 (23%), 5 (38%) and 2 (16%). For GG genotypes, the DMFT index was found in 2 athletes with a score of 0-1 (67%) and in 1 (33%) with a score of 2-4. None of the athletes with GG genotypes had 5-10 or 10 and above score for DMF-T. We suggest that this study may be an informative data for further studies to investigate the effect of rs1544410 polymorphisms on the formation of tooth decays.

**Keywords:** Vitamin D, polymorphism, tooth decay, DMF-T

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## Giriş

İnsan Genom Projesi'nin sonuçlarının oral biyoloji ve tıp alanında kullanılmaya başlanmasıyla birlikte, diş çürüğü ile ilişkili genomik bölgelerin tespiti için genom taraması gerçekleştirilerek düşük ve yüksek çürük yatkınlığıyla ilgili gen bölgeleri tespit edilmeye başlanmıştır. Diş çürüklerinin genetik temelleri monozigotik ve dizigotik ikizleri de kapsayan geniş popülasyon çalışmaları ile araştırılmıştır. Yapılan ilk önemli ve kapsamlı çalışma Bachrach ve Young (1) tarafından tek ve çift yumurta ikizleri üzerinde yapılmış ve normal popülasyona ve çift yumurta ikizlerine göre tek yumurta ikizlerinde çürük oluşum insidansının daha yüksek olduğu bildirilmiştir. Bireylerde enfeksiyöz bir hastalık olarak belirtilen, diş çürük oluşumuna yatkınlığına neden olduğu düşünülen bazı genetik faktörlerin varlığı ve diş çürüklerine neden olan mikroorganizmaların da birtakım genetik belirteçlere sahip olduğu düşünülmektedir. Genetik faktörlerin çürük oluşumu üzerindeki etkisi günümüze kadar mine ve dentin mineralizasyonu, tükürük proteinleri, muhtemel gen bölgeleri incelenerek araştırılmıştır. Ayrıca çalışılan genler *HLA* genleri, *AMELX* geni, *CD14* geni, vitamin D reseptör (VDR) genleri ve tükürük bileşenlerini oluşturan genleri de içine almaktadır (2).

Diş, mine ve dentin yapısında mineraller ve vitaminlerin oldukça önemli bir yeri bulunmaktadır. D vitamini, bireylerin kemik ve kas gelişimini indükleyerek kemik ve kas büyümesini, bağırsak ve böbrekte kalsiyum ve fosforun emilimini sağlayarak vücutta mineral dengesinin korunmasını sağlayarak vücutta birçok mekanizmada direkt veya indirekt rol oynayan, yağda çözünen sterol yapılı bir moleküldür (3).

D vitamini hücre içindeki biyolojik fonksiyonunu reseptörüne bağlanarak gerçekleştirilmektedir. D vitamini reseptör geni (VDR) 12q13.11'de lokalizedir, 100 kb uzunluğunda ve üzerinde 100'den fazla polimorfizm tanımlanmıştır (4,5). D vitamini reseptör geni fonksiyonuna etki eden *FokI*, *BsmI*, *Apal* ve *TaqI* polimorfizmleri saptanmış ve belirlenen bu polimorfizmler ile çeşitli metabolik sorunlar, diş çürüğü ve periodontitis gibi oral sorunlar ile reseptör polimorfizmleri arasındaki ilişkiler araştırılmıştır (6).

VDR geninin 8. intronunda ve genin 3'-UTR bölgesine yakın bir lokasyonunda *BsmI* polimorfizmi (rs1544410) yer almaktadır (7). Bu polimorfizm A>G baz değişikliği sonucu oluşmaktadır. VDR *BsmI* polimorfizminde A allelinin mRNA aktivitesinin düşük olduğu belirtilmektedir (8). VDR geninin G alleli taşıyıcıları daha kısa formda olduklarından

dolayı transkripsiyonel aktiviteyi uyardığı düşünülmektedir (9). *BsmI* polimorfizmi mRNA stabilitesini düzenleyerek gen ekspresyonunu etkileyebilmektedir (10).

Bu çalışmanın amacı ağız ve diş sağlığı açısından önemli olan D vitamini metabolizmasına etki eden D vitamini reseptör genindeki *BsmI* (rs1544410) polimorfizminin Türk atletlerdeki dağılımının incelenmesidir.

## Materyal ve Metot

### Atletler:

Çalışmamıza gönüllü olarak 11 kız ve 13 erkek olmak üzere 24 atlet katılmıştır. Çalışmamız ve çalışma protokolümüz, Helsinki Deklarasyonu-2 (2015) yönergelerine uygun olarak hazırlanmış ve Üsküdar Üniversitesi Girişimsel Olmayan Etik Kurulu tarafından onanmıştır. Çalışmaya gönüllü katılan sporculara, çalışma öncesi yapılan analizler ve çıktıları hakkında detaylı bilgi verilmiş, kendilerinden onam formu alınmıştır.

### DNA Genotipleme:

#### DNA İzolasyonu:

Çalışmamıza gönüllü olarak katılan sporculardan 1 cc periferik kan eldesi sonrasında lökosit DNA'ları PureLink DNA izolasyon kiti (Invitrogen, Van Allen Way Carlsbad, CA, USA) kullanıcı protokolleri izlenerek kullanılmış ve DNA izolasyonları tamamlanmıştır. Kısaca, 200 µL periferik kan üzerine 20 µL proteinaz K, 10µL RNAaz eklenerek vortekslendi. 2 dk oda sıcaklığında bekledikten sonra 200µL bağlanma tamponu eklendi ve karıştırılarak homojen hale getirildi. 55°C su banyosunda 10 dk inkübe edildikten sonra 200 µL etanol ilavesinden sonra 5 sn vortekslendi. Filtreli tübe alındı ve 10000g 'de 1 dk santrifüj edildi. Süpernatant kısmı atılarak pellet kısmı üzerine 500 µL yıkama tamponu eklendi ve 10000g'de 1,15 dk santrifüj edildi ve yine süpernatant kısmı alınarak üzerine 2. yıkama tamponu eklendi ve maksimum hızda 3 dk santrifüj edildi. 80 µL elüsyon tamponu eklenerek inkübe edildi ve maksimum hızda 1 dk santrifüj edildi. İlgili gen bölgelerinin analizlerinin tamamlanmasına kadar, elde edilen DNA örnekleri – 20° C de saklanmıştır.

### VDR rs1544410 Genotiplemesi

*BsmI* (rs1544410) genotipleri izole edilen DNA materyalinden "7500 Fast Real-Time PCR System"

(Applied Biosystems) cihazı ile Taqman Genotyping Assays (Applied Biosystems Foster City, CA, USA) genotipleme kiti kullanılarak gerçekleştirilmiştir. Totalde 10uL olacak şekilde 5 µL master mix, 3,75µL H<sub>2</sub>O, 0,25µL assay ve 1µL (10 ng) DNA kullanılarak genotipleme işlemi tamamlanmıştır.

### DMFT Değerlendirilmesi

Çalışmamızda çürük değerlendirmesi DMFT indeksi ile tespit edilmiştir. DMF-T indeksi 0-1 arası iyi, 1-4 orta kabul edilebilir, 5-10 kötü, 10 ve üstü ise çok kötü şeklinde değerlendirilmiştir.

### Sonuçlar

Çalışmamıza 11'i kız, 13'ü erkek olmak üzere toplam 24 atlet katılmıştır. VDR *BsmI* (rs1544410) polimorfizminin genotip ve allelik dağılımları ve DMFT indeksi sırasıyla Tablo 1 ve Tablo 2'de özetlenmiştir. *BsmI* (rs1544410) polimorfizmi için elde edilen bulgulara göre çalışmaya katılan atletlerin AA, AG, GG genotipleri sırasıyla 8 (%33), 13 (%54), 3 (%12) GG olarak analiz edilmiştir. Allelik dağılımlar incelendiğinde *BsmI*'in A alleli çalışma grubunda (%60), G alleli (%40) olarak bulunmuştur (Tablo1).

**Tablo 1:** Analiz edilen *BsmI* rs (1544410) polimorfizminin atletlerdeki dağılımı

|            | Branş       |       | GENOTİP |       |       | ALLEL FREKANSI |       |
|------------|-------------|-------|---------|-------|-------|----------------|-------|
|            |             |       | AA      | AG    | GG    | A              | G     |
| Kız (11)   | Sprinter    | Sayı  | 2       | 2     | 1     | 6              | 4     |
|            |             | Yüzde | %8      | (%8)  | (%4)  | (%12,5)        | (%8)  |
|            | Uzun mesafe | Sayı  | -       | 5     | 1     | 5              | 7     |
|            |             | Yüzde | -       | (%21) | (%4)  | (%10)          | (%15) |
| Erkek (13) | Sprinter    | Sayı  | 3       | 6     | 1     | 12             | 8     |
|            |             | Yüzde | (%12,5) | (%25) | (%4)  | (%25)          | (%17) |
|            | Uzun mesafe | Sayı  | 3       | -     | -     | 6              | -     |
|            |             | Yüzde | (%12,5) | -     | -     | (%12,5)        | -     |
| Toplam     |             | Sayı  | 8       | 13    | 3     | 29             | 19    |
|            |             | Yüzde | (%33)   | (%54) | (%12) | (% 60)         | (%40) |

*BsmI* rs1544410 polimorfizminde DMFT analizi ile genotipler karşılaştırıldığında AA genotipli bireylerde 0-1 arası arası değere sahip olan 2 sporcu (%25) , 2-4 arası

değere sahip olan 4 sporcuda (%50), 5-10 arası değere sahip olan 2 sporcuda (%25) bulunurken, 10 ve üzeri değere hiçbir sporcuda rastlanılmamıştır. AG genotipli sporculara ise sırasıyla 0-1, 2-4, 5-10, 10 ve üzeri birey sayıları ve yüzdeleri; 3 (%23), 3(%23), 5 (%38), 2 (%16) şeklinde bulunmuştur. GG genotipli bireylerde DMFT indeksi 0-1 ve 2-4 arasında olan değerler sırasıyla 2 sporcu (%67) ve 1 bireyde (%33) tespit edilmiş olup 5-10 ve 10 ve üzeri değerlere bireylerde rastlanılmamıştır. Tablo 2'de genotip ve DMFT indeksi gösterilmiştir.

**Tablo 2:** rs1544410 genotipleri ve DMFT değerleri

| <i>BsmI</i><br>rs1544410 | DMFT İNDEKSİ |       |      |       |      |       |      |       |
|--------------------------|--------------|-------|------|-------|------|-------|------|-------|
|                          | 0-1          |       | 2-4  |       | 5-10 |       | >10  |       |
|                          | Sayı         | Yüzde | Sayı | Yüzde | Sayı | Yüzde | Sayı | Yüzde |
| AA                       | 2            | (%25) | 4    | (%50) | 2    | (%25) | -    | -     |
| AG                       | 3            | (%23) | 3    | (%23) | 5    | (%38) | 2    | (%16) |
| GG                       | 2            | (%67) | 1    | (%33) | -    | -     | -    | -     |

### Tartışma

D vitamininin sadece kemik mineral metabolizmasında değil vücudumuzdaki birçok metabolik süreçte görev olarak insan yaşamında önemli bir yerinin olduğu günümüze kadar yapılan çalışmalarla belirtilmiştir. D vitamini reseptör yapısında meydana polimorfizmler sonucunda diş çürüğü, periodontal hastalıklar gibi çeşitli ağız sağlığı sorunları ve çeşitli metabolik hastalıklar meydana gelmektedir. Ayrıca kemik metabolizmasının, monosit farklılaşması ve fagositozda rol oynayan D vitamini reseptörü ve *VDR* polimorfizmlerinin de periodontitise duyarlılık ile ilişki olabileceği öngörülmektedir.

Çalışma grubumuzda *BsmI* polimorfizmi incelendiğinde AG genotipinin ve A allelinin baskın olduğu gözlenmiştir. rs1544410 polimorfizminde AA genotipinde DMFT indeksi incelendiğinde çalışma kohortunda 0-1 arası değer 2 bireyde (%25) iyi düzeyde, 2-4 arası değer 4 bireyde (%50) orta derecede, 5-10 arası değer 2 bireyde (%25) kötü düzeyde olarak değerlendirilmektedir. DMFT değeri 10 ve üstü hiçbir bireyde gözlenmemiştir. AG genotipinde DMFT değerinin 0-1 arasında 3 bireyde (%23) iyi düzeyde, 2-4 arasında 3 bireyde (%23) orta derecede, 5-10 arasında 5 bireyde (%38) kötü düzeyde olduğu tespit edilmiş olup, 10 ve üstü değer ise 2 bireyde %16 oranında saptanmıştır. DMFT değeri %38 oranında görülmesi nedeniyle AG genotipine sahip olan bireylerin diş çürük oluşumuna daha yatkın olduğu sonucuna varılmıştır. GG genotipinde DMFT değeri 0-1 arası 2 bireyde (%67) iyi düzeyde, 2-4 arası 1

bireyde (%33) orta derecede tespit edilmiş olup, 5-10 ile 10 ve üstü değere hiçbir bireyde rastlanılmamıştır.

Sengün ve ark., (11) çalışmasında kemik ve dişlerin gelişiminde rol oynayan *VDR* genindeki *BsmI* ve *Apal* polimorfizmlerinin bireylerde diş çürüğü oluşumuna etkisini araştırmışlar ancak bu polimorfizmlerin diş çürüğü oluşumuna herhangi bir etkisinin olmadığını bildirmişlerdir.

Wang ve ark., (12) Çin popülasyonunda 107 hasta ve 121 kontrol grubunda *VDR* genlerinin *BsmI*, *TaqI*, *Apal* ve *FokI* polimorfizmleri ile kronik periodontitis (CP) arasındaki ilişkiyi incelemişlerdir. *VDR* genindeki *BsmI*, *Apal* veya *FokI* polimorfizmleri her iki grup arasında değerlendirilmiş genotip dağılımında veya allel frekanslarında anlamlı bir farklılık bulunamamıştır.

Ulucan ve ark., (7) D vitamini reseptörlerinden *FokI*, *BsmI*, *TaqI* polimorfizmleri ile dentinogenesis imperfekta tip II (DGI-II) arasındaki ilişkiyi bir Türk ailesinde araştırmışlardır. Çalışma sonucunda dentinogenesis imperfekta görülen anne ve kızlarında *BsmI* polimorfizminde GG, baba ve oğlunda aynı polimorfizm için AG genotipi görülürken, *TaqI* polimorfizminde etkilenen çocuklarda tt, ailenin geri kalan üyelerinde Tt, *FokI* polimorfizmi için ailenin tüm bireylerinde CC genotipi gözlenmiştir. Sonuç olarak *BsmI* polimorfizmindeki GG genotipinin DGI-II ile ilişkili olduğu belirlenmiştir.

Kong ve ark., (13) 4-7 yaş arasında gelişme çağındaki olan 380 Çin’li çocuk (203 kız ve 177 erkek) üzerinde *BsmI* rs1544410 ve *FokI* rs2228570 polimorfizmleri ile diş çürüğü oluşumu arasındaki ilişkiyi araştırmışlardır. Çalışma sonucunda %95 oranında AG frekansının olduğunu tespit etmişler ve *BsmI* polimorfizmi ile diş çürüğü oluşumunun ilişkili olduğunu belirtmişlerdir. Ancak *FokI* polimorfizmi ile diş çürüğü arasında herhangi bir ilişki olmadığını bildirmişlerdir. Bu çalışmada AG genotipinin yüksek oranda görülmesi bizim çalışmamız ile uygunluk göstermektedir. Çalışmada DMFT indeksi incelendiğinde ise yaş ortalaması 5.85 olan çocukların DMFT değeri 4.4 iken, yaş ortalaması 5.72 olan çocukların DMFT değeri 6.6 olarak saptanmıştır.

Genetik faktörlerin agresif periodontitis üzerinde güçlü bir etkisi olabileceğini ifade eden Li ve ark. (14) 51 Çinli agresif periodontitis ve 53 periodontal kontrol grubunda *VDR* geni *FokI*, *BsmI*, *Apal* ve *TaqI* polimorfizmlerinin yaygın agresif periodontitisle olan ilişkisini genotipik ve allelik frekansları ile karşılaştırmışlardır. *VDR FokI* rs 2228570 polimorfizminin CC genotip ve C alellerinin yüksek oranda görülmesi *FokI* polimorfizminin Çinli hastalarda yaygın

agresif periodontitis ile ilişkili olabileceğini göstermektedir. Ayrıca *FokI* polimorfizminde C alelinin yüksek oranda olması yaygın agresif periodontitis geliştirme riskini arttırmaktadır. Ancak *VDR* geni *BsmI*, *Apal* ve *TaqI* polimorfizmleri ile iki grup arasında genotip veya allel frekansları arasında anlamlı bir ilişki bulunamamıştır.

Sonuç olarak diş çürük oluşumuna yatkınlık oluşturan genetik faktörlerin saptanması ve oral hijyenin artırılması yoluyla da sağlıklı yaşam kalitesine sahip bireylerin yetişmesinin mümkün olabileceğini düşünmekteyiz. Ayrıca diş çürüklerinin oluşumunu engelleyen ya da diş çürüklerinin daha yüksek oranlarda oluşmasına neden olan genetik faktörlerin tanımlanması sayesinde hekimlerin daha etkili ve koruyucu tedaviler sunmalarına olanak sağlanacaktır.

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# A Preliminary Study of Prevalence and Characteristics of Pneumatization of Articular Eminence on Cone Beam Computed Tomography

Konik Işınlı Bilgisayarlı Tomografide Artiküler Eminens Pnömatizasyonunun Özelliklerinin ve Prevalansının İncelenmesi

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## Abstract

**Introduction:** The aim of this retrospective study was to identify the prevalence and properties of pneumatized articular eminence (PAT) in a group of Turkish population using CBCT.

**Material and Methods:** The subjects for this retrospective study consisted of all 300 adult patients who referred to the Department of Oral Diagnosis and Radiology, Marmara University Faculty of Dentistry, and underwent a single CBCT examination from 2016 to 2017. Age and gender were noted for all patients, and for the cases of pneumatization, sides and type were recorded.

**Results:** Of the 300 patients, 98 (32,0%) had PAT, of whom 43 were female and 55 were male. PAT was seen 14% on bilateral sides, 10% on the right side and 8.7% on the left side. 51% of those which had pneumatization were unilocular and 49% were multilocular

**Conclusion:** CBCT images are a true and confident tool for the exploration of the definite size and pattern of pneumatization and the relationship of pneumatization to the adjacent tissue. In case of surgical treatment is planned or for the differential diagnosis of suspected cases, panoramic radiographs should be supported with CBCT.

**Keywords:** Cone beam computed tomography; pneumatized articular eminence; temporomandibular joint

## Öz

**Giriş:** Bu retrospektif çalışmanın amacı bir grup Türk populasyonunda pnömatize artiküler eminens (PAT) prevalansını ve özelliklerini konik ışınli bilgisayarlı tomografide (KIBT) incelemektir.

**Materyal ve Metod:** Bu retrospektif çalışma, 2016'dan 2017'ye kadar KIBT incelemesi yapılan, Marmara Üniversitesi Dişhekimliği Fakültesi Oral Diagnoz ve Radyoloji Anabilim Dalı'na başvuran 300 yetişkin hastadan oluşmaktadır. Çalışmaya dahil edilen tüm hastaların yaş ve cinsiyetleri kaydedilmiş ve pnömatizasyon gözlemlenen durumlarda, pnömatizasyon tarafları ve tipler kaydedilmiştir.

**Bulgular:** 300 hastanın içinde; 43'ü kadın, 55'i erkek olan 98 vakada (% 32,0) PAT gözlenmiştir. PAT, bilateral % 14, sağda% 10, solda% 8.7 olarak saptanmıştır. Pnömatizasyon izlenenlerin % 51'i uniloküler,% 49'u multilokülerdir.

**Sonuç:** KIBT görüntüleri, boyutların tam olarak belirlenmesinde, pnömatizasyon paterninin incelenmesinde ve komşu dokular ile ilişkisinin araştırılması için doğru ve güvenilir bir araçtır. Cerrahi tedavi planlanmasında veya şüphelenilen vakaların ayırıcı tanısında panoramik radyografiler KIBT ile desteklenmelidir.

**Anahtar Kelimeler:** Konik Işınli Bilgisayarlı Tomografi, Pnömatize artiküler eminens, temporomandibular eklem

## Introduction

The bones of the skull includes multiple airfilled cavities, which are entitled as pneumatization also known as air cells. These pneumatic regions can emerge at different sites including the temporal bone. The best known of these are the mastoid air cells in the temporal bone (1,2) .

Ten locations of air cells may be present within the temporal bone, including the zygomatic process of the temporal bone, which is termed as pneumatized articular eminence (PAT) (3,4). The term PAT was used for the first time by Tyndall and Matteson to define air cells that

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arise in the roof of the zygomatic arch and in the articular eminence of the temporal bone, that is, similar to air cells in the mastoid process and ethmoid bone (5). Tyndall and Matteson also reported about the anatomical relationship of PAT with mastoid air cells. Accordingly, PAT can be thought of as prolongation of mastoid air cells, similar to the expansion of paranasal sinuses (6).

The common characteristics of the PAT of the temporal bone were identified and included: 1) an asymptomatic radiolucent defect in the zygomatic process of the temporal bone with the similar appearance to mastoid air cells, 2) extension of the defect anteriorly as far as the articular tubercle but not beyond the zygomaticotemporal suture and 3) no enlargement or cortical destruction of the zygoma. PATs may be unilateral or bilateral and have two pattern types; unilocular or multilocular (7,8)

Diagnosis of the pneumatization of the glenoid fossa and articular eminence is significant because it is a defect that makes easy the spread of various disease stages along the joint including inflammations, tumors, and the fractures owing to minimal resistance (7). Tumours of the mastoid process and ear may spread into the temporomandibular joint, while otitis or mastoiditis may include the TMJ and may result with ankylosis. All of them may be probable complications in TMJ surgery, therefore various researchers have suggested that imaging studies should be done before any surgical procedure (9,10).

The prevalence of PAT has been formerly evaluated in the literature using different imaging modalities. The utilization of conventional panoramic radiographs to examine PAT is suitable because the radiographs are acquired during routine examination of numerous patients. However, conventional panoramic radiographs, have inherent problems, including a wide focal region and superimposition of adjacent structures. High-resolution computerised tomography (CT) is assumed as the procedure of option for the evaluation of bony structures and air spaces in the base of the skull. Although the air cells adjacent to the temporomandibular joint may be visible on panoramic radiographs, a less superficially located region such as the medial portion of the articular eminence may be visible on only CT (4). Cone beam computed tomography (CBCT), a more recent three-dimensional imaging technique, provides detailed anatomical information of mineralized maxillofacial tissues with minimal distortion. With no superimposition on CBCT, it exceeds the diagnostic accuracy of panoramic radiographs in the evaluation of temporal air spaces.

The aim of this retrospective study is to determine the prevalence and characteristics of PAT in a group of Turkish population using CBCT.

## Materials and Method

### Patient Data

Subjects for this retrospective study consist of all 300 patients who visited Department of Oral Diagnosis and Radiology, Marmara University Faculty of Dentistry and CBCT images of these patients between 2016-2017 were retrieved from the PACS system. CBCT imaging was performed with Planmeca Promax 3D Mid (Planmeca Oy, Helsinki, Finland) and assessment of CBCT was performed directly on monitor screen (Monitor 23 inch Acer 1920x1080 pixel HP Reconstruction PC). The purpose of CBCT scans were for impacted third molar surgery, orthodontic purposes, dental implant treatment and Le Fort I osteotomy. Patients with systemic diseases influencing growth and development, history of trauma and/or surgery involving the maxillofacial region, developmental anomalies/pathologies affecting the maxillofacial region and previous sinus surgery were excluded from the study. The study was carried out according to the recommendations of the Helsinki declaration and the study protocol was approved by the Local Committee of Research and Ethics of Marmara University, Faculty of Medicine (Protocol No: 09.2017.008).

### Image Interpretation

Two oral and maxillofacial radiologist (AYS and GU) evaluated and interpreted PAT. Before starting the radiographic examination in the study, the researchers were calibrated to identify and agree on PAT anatomy. For such objectives, a series of 50 CBCT images (not included in this study) were examined. As part of the calibration phase, the examiners were given also explanations about radiographic and CBCT imaging.

The age and gender were recorded for all patients and, for the cases of PAT, gender, age, localization and radiographic appearance were recorded. Diagnosis of PAT on the radiographs was made only if unequivocal pneumatization of the articular eminence could be seen or if the defect was located in the articular eminence posterior to the zygomaticotemporal suture as a well-defined unilocular or multilocular radiolucency. PAT was classified as unilocular or multilocular as in the study by Tyndall and Matteson (5).

Unilocular PAT was identified as single radiolucent oval defect with well-defined bony borders. Multilocular PAT was identified as numerous radiolucent small cavities.

**Data Analysis**

The data were analysed with IBM Statistical Package for Social Sciences (SPSS) for Windows 15.0 (SPSS Inc, Chicago, IL). Descriptive statistical methods (mean, SD, and frequency) were used for evaluation of the data. Chi-square test was used to compare qualitative data. Values of  $p < 0.05$  were interpreted as significant.

**Results**

A total of 300 patients met the inclusion criteria aged between 18 and 85 with 134 (44,7%) male and 166 (55,3%) female. The mean age is  $47.13 \pm 14.75$  years. Of the 300 patients, 21 of the patients (7%) were between 18-24 years, 46 (15,3%) between the ages of 25-34, 68 (22,7%) between the ages of 35-44, 62 (20,7%) are between the ages of 45-54 and 103 (34,3%) are above the age of 55 (Table 1).

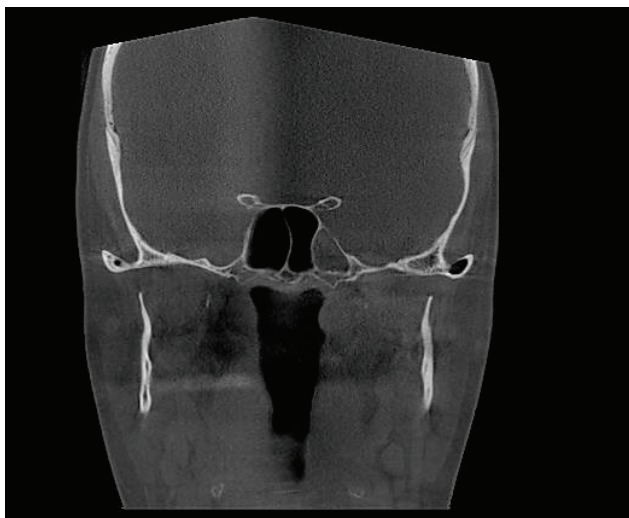
**Table 1:** Distribution of age and gender

|        |          | n   | %    |
|--------|----------|-----|------|
| Age    | 18-24    | 21  | 7,0  |
|        | 25-34    | 46  | 15,3 |
|        | 35-44    | 68  | 22,7 |
|        | 45-54    | 62  | 20,7 |
|        | Above 55 | 103 | 34,3 |
| Gender | Male     | 134 | 44,7 |
|        | Female   | 166 | 55,3 |

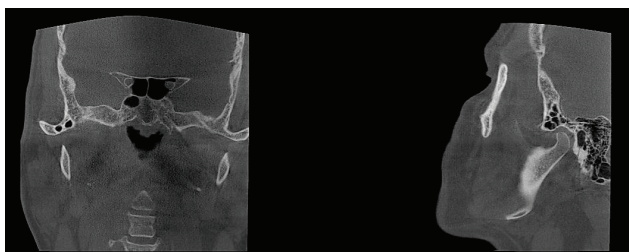
While pneumatization was not seen in 67.3% of cases, it was seen 14% on bilateral sides (Figure 1), 10% on the right side (Figure 2) and 8.7% on the left side. 51% of those which had pneumatization were unilocular (Figure 3) and 49% were multilocular (Figure 4) (Table 2).

**Table 2:** Prevalence of PAT and PAT type

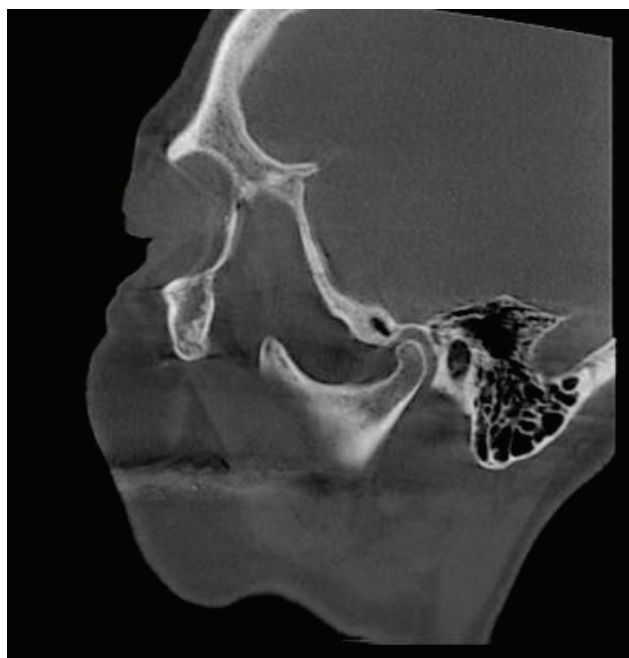
|                 |              | n   | %    |
|-----------------|--------------|-----|------|
| PAT             | Absent       | 202 | 67,3 |
|                 | Bilateral    | 42  | 14,0 |
|                 | Right        | 30  | 10,0 |
|                 | Left         | 26  | 8,7  |
| PAT type (n=98) | Unilocular   | 50  | 51,0 |
|                 | Multilocular | 48  | 49,0 |



**Figure 1:** Coronal cone beam computed tomography images of bilateral pneumatized articular eminence



**Figure 2:** Sagittal and coronal cone beam computed tomography images of unilateral pneumatized articular eminence



**Figure 3:** Sagittal cone beam computed tomography images of unilocular pneumatized articular eminence





**Figure 4:** Sagittal cone beam computed tomography images of multilocular pneumatized articular eminence

There was no statistically significant difference between the rates of PAT and PAT type according to age groups ( $p > 0.05$ ) (Table 3).

There was no statistically significant difference between the rates of PAT and PAT type according to gender ( $p > 0.05$ ) (Table 4).

### Discussion

Digital or conventional a number of imaging modalities have been used to evaluate bone quality, quantity, and location of anatomic structures. Although, panoramic radiographies are the most commonly used and relied imaging modality by clinicians and their relatively low cost and widespread availability, there are inherent fundamental limitations due to its modality such as superimpositions, magnifications, distortions and low image quality (11,12). Furthermore, because of the difficulty of interpretation anatomical structures on two-dimensional plane, development of three-dimensional imaging techniques has accelerated.

In order to overcome of those above mentioned disadvantages and to obtain more accurate images of anatomical structures, CT is used for evaluating anatomic variations also with preoperative anatomical evaluations, pathologies and bone integrity as it supplies adequate spatial resolution (13,14). On the other hand, it is generally known that CT is liable for the majority of the medical radiation doses in the populations of modern societies. CBCT may definitely take on the same role in anatomical evaluations, pathologies and bone integrity, making it possible to obtain high-resolution axial, coronal, and sagittal sections (15). CBCT technology allows clinicians precious information

**Table 3:** Assessment of PAT and PAT types according to age groups

|                    |              | Yaş        |            |            |            |            | p     |
|--------------------|--------------|------------|------------|------------|------------|------------|-------|
|                    |              | 18-24      | 25-34      | 35-44      | 45-54      | 55+        |       |
|                    |              | n (%)      | n (%)      | n (%)      | n (%)      | n (%)      |       |
| PAT                | Absent       | 11 (52,4%) | 33 (71,7%) | 40 (58,8%) | 47 (75,8%) | 71 (68,9%) | 0,127 |
|                    | Bilateral    | 5 (23,8%)  | 7 (15,2%)  | 16 (23,5%) | 6 (9,7%)   | 8 (7,8%)   |       |
|                    | Right        | 2 (9,5%)   | 4 (8,7%)   | 6 (8,8%)   | 3 (4,8%)   | 15 (14,6%) |       |
|                    | Left         | 3 (14,3%)  | 2 (4,3%)   | 6 (8,8%)   | 6 (9,7%)   | 9 (8,7%)   |       |
| PAT type<br>(n=98) | Unilocular   | 4 (40%)    | 6 (46,2%)  | 15 (53,6%) | 4 (26,7%)  | 21 (65,6%) | 0,137 |
|                    | Multilocular | 6 (60%)    | 7 (53,8%)  | 13 (46,4%) | 11 (73,3%) | 11 (34,4%) |       |

Chi-square test

**Table 4:** Assessment of PAT and PAT types according to gender

|                |              | Gender     |             | p     |
|----------------|--------------|------------|-------------|-------|
|                |              | Male       | Female      |       |
|                |              | n (%)      | n (%)       |       |
| PAT            | Absent       | 91 (67,9%) | 111 (66,9%) | 0,511 |
|                | Bilateral    | 15 (11,2%) | 27 (16,3%)  |       |
|                | Right        | 16 (11,9%) | 14 (8,4%)   |       |
|                | Left         | 12 (9%)    | 14 (8,4%)   |       |
| PAT type(n=98) | Unilocular   | 22 (51,2%) | 28 (50,9%)  | 0,980 |
|                | Multilocular | 21 (48,8%) | 27 (49,1%)  |       |

Chi-square test

not only about anatomical structures, but also about the pathologies or findings outside the primary area of interest. Owing to wide spread use of CBCT, it became difficult to misdiagnose anatomic variants, developmental anomalies or artifacts as pathological entities(16). Considering above mentioned arguments, we evaluated CBCT images for analyzing PAT.

There are various studies evaluating incidence of PAT with different imaging techniques. In 1986, Kaugars et al (17) evaluated panoramic radiographs of 784 patients retrospectively for the presence of PAT. The radiographs of eight patients showed signs of PAT. These eight patients ranged in age from 32 to 69 years, and four patients had bilateral involvement of the temporal bone. They did not give a mean age for their total population but they provided a mean age for each of the three subpopulations (children, adolescents, and adults). The mean age of their adult group, which comprised 61% of the total patients, was 41.2 years.

Orhan et al (8), in 2005, found PAT in 19 (1.88%) patients with a mean age of 36.6 (SD 21.06) years in 1,006 panoramic radiographs.. Seven cases were males and 12 cases were females. Twelve cases of PAT were unilateral. Bilateral PAT was found in seven (36.9%) patients.

Yavuz et al (18) evaluated PAT in 8107 panoramic radiographs of patients and found PAT in 83(1.03%) of individuals with 41 females and 42 males. In their study, PATs were located on the right side in 60 individuals and on the left side in 50 individuals. Also, PATs were unilateral in 56 cases and bilateral in 27 (total of 110 PATs).

Khojastepour et al (19) evaluated 3,098 panoramic radiographs belonging to 1,735 females and 1,363 males retrospectively for the presence of PAT. PAT was found in 2.1 % of cases including 41 females and 23 males (with a mean age of 33.23±12.43 and 35.64±13.24 years, respectively, range 19-69 years). There were 40 unilateral and 24 bilateral cases in their study.

Shokri et al (20) evaluated digital panoramic radiographs of 1563 patient with a mean age of 32.6±7.63 years. PAT was found in 98 cases in their study, representing a prevalence of 6.2% with a mean age of 22.8±7.9 and a range of 8 to 60 years . Sixty-four (65.3%) pneumatized articular tubercles were unilateral, with 30 lesions on the right and 34 on the left side. Bilateral PAT were found in 34 patients.

There are also studies in which the prevalence of PAT have assessed on CBCT images. Miloglu et al (4) in 2011 reported a study of 514 cases o; 41 cases (mean age of

30.6±11.4years) had PAT with a rate of 8% ; 19 patients were males and 22 were females. In their study, PAT was found to be unilateral in 23 cases and bilateral in 16 cases.

Another study with CBCT by Ladeira et al (10) also stated a higher rate (21.3%) of PAT. They found 204 PATs in 140 patients and male and female individuals were about 63% and 37%, respectively; PAT was unilateral in 76 cases and bilateral in 64. The mean age of the individuals was 43.02 years

İlgüy et al (21) evaluated PAT of 111 patients on CBCT images with a mean age of 48.86±18.31 years. Among all the patients, 73 (65.8%) had PAT. 42 (37.8%) of the patients had PAT bilaterally; The percentage of PAT was higher for females (73.6%) than males (51.3%) in their study .

In our study, prevalence of PAT was 32.7% in 300 patients aged between 18 and 85 with 134 (44.7%) male and 166 (55.3%) female and a mean age of 47.13 ± 14.75 years. Pat was observed 32.1% of males and 33.1% of females. PAT was unilateral in 56 cases and bilateral in 42 in our study. Our results show higher prevalence than the PAT in studies using panoramic radiography as in agreement with the results of the studies using CBCT.

In our study, the type of pneumatization was classified as unilocular and multilocular, as the studies mentioned above. Unilocular pneumatization with a well-limited oval single radiolucent defect is defined as multilocular pneumatization if multiple radiolucent cavities are present. 41.5% of the cases with PAT were recorded as unilocular and 58.5% as multilocular in the research done by Miloğlu et al (4). Khojastepour et al found (19) 49(55.6%) unilocular and 39 (44.3%) multilocular cases. 44 of the PATs were unilocular type, and 66 of the PATs were multilocular type in the study done by Yavuz et al (18). Shokri et al (20) found 53.1% of unilocular and 46.9% of multilocular PAT in their study. 38.5% PAT of unilocular and 61.5% PAT of multilocular type were observed in Orhan and his colleagues' study (8). In our study, 50(51%) of the PAT cases were of unilocular type and 48(49%) of multilocular type. Our study is in agreement with all the studies whether done by panoramic radiography or CBCT.

There is no need to treat PAT. If a specialist investigates pneumatization with no symptoms, it should be kept under observation. The differential diagnosis of PAT is done with giant cell tumour, hemangioma, aneurysmal bone cyst, eosinophilic granuloma, metastatic tumor and fibrous dysplasia. All these entities are qualified by painful

enlargement of the cheek and seen radiographically as expansive and destructive lesions.

## Conclusion

The findings of this study point out that CBCT is a true and confident tool for the detection of the definite size and type of pneumatization and the relationship of pneumatization to the adjacent tissue. In case of surgical treatment is planned or for the differential diagnosis of suspected cases, panoramic radiographs should be supported with CBCT.

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# Evaluation of Diagnostic Efficiency of Ultrasonography in Temporomandibular Joint Disorders: A Pilot Study

## Temporomandibular Eklem Bozukluklarında Ultrasonografinin Diagnostik Etkinliğinin Değerlendirilmesi: Bir Pilot Çalışma

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### Abstract

**Objective:** Temporomandibular Joint diseases (TMD) and disorders refer to a complex of conditions, manifested by pain in jaw area and associated muscles and limitations in the ability to make the normal movements of speech, facial expression, eating, chewing, and swallowing. Ultrasonography (US) is a non-invasive, cost-effective, easy-to-use imaging method using sound waves, without ionizing radiation and as a diagnostic procedure it has been shown to be accurate for the diagnosis of TMD. The purpose of this pilot study is to evaluate the diagnostic efficacy of ultrasonography imaging in temporomandibular joint disorders.

**Material and Method:** The retrospective ultrasonography images of 20 patients (female, male) who had been referred to Marmara University, Faculty of Dentistry, Oral Diagnosis and Radiology Clinic with a complaint related to Temporomandibular joint (TMJ) were evaluated in terms of condylar surface irregularities, joint space reduction and joint effusion.

**Results:** A total of 20 patients (% 70 female, %30 male, mean age: 33,75) and 40 TMJ were evaluated and in % 15 erosive – degenerative changes, in % 82,5 condylar surface flattening and in % 27,5 increased joint capsule width was observed.

**Conclusion:** Ultrasonography is a non-invasive technique suitable for visualization of TMJ and evaluation of TMD in routine clinical practice.

**Keywords:** Temporomandibular Joint Disorders, Ultrasound, Radiology

### Öz

**Amaç:** Temporomandibular eklem hastalıkları (TMD) ve rahatsızlıkları, çene bölgesinde ve ilgili kaslarda ağrı ile ortaya çıkan ve normal konuşma, yüz ifadesi, yeme, çiğneme ve yutma hareketlerini kısıtlayabilen durumları ifade eder. Ultrasonografi (US), invazif olmayan, düşük maliyetli, kullanımı kolay ve iyonlaştırıcı radyasyon olmaksızın ses dalgalarının kullanıldığı, bununla birlikte; diagnostik prosedür olarak TMD teşhisi için doğruluğu kanıtlanmış bir görüntüleme yöntemidir. Bu pilot çalışmanın amacı, temporomandibular eklem hastalıklarında ultrasonografik görüntülemenin tanısal etkinliğinin değerlendirmektir.

**Gereç ve Yöntem:** Temporomandibular eklem (TME) ile ilgili şikayetleri bulunan, Marmara Üniversitesi Diş Hekimliği Fakültesi Oral Diağnoz ve Radyoloji Kliniğine başvuran 20 hastanın (kadın, erkek) retrospektif ultrasonografi görüntüleri kondiler yüzey düzensizlikleri, eklem boşluğunda daralma ve efüzyon açısından değerlendirilmiştir.

**Bulgular:** Toplam 20 hasta (% 70 kadın, % 30 erkek, yaş ortalaması :33,75) ve 40 TME değerlendirilmiş ve % 15 eroziv – dejeneratif değişiklik, % 82,5 kondiler yüzeyde düzleşme ve % 27 oranlarında artan eklem kapsülü genişliği gözlenmiştir.

**Sonuç:** Ultrasonografi, TME' nin görüntülenmesi ve rutin klinik uygulamada TMD'nin değerlendirilebilmesi için uygun ve invaziv olmayan bir tekniktir.

**Anahtar Kelimeler:** Temporomandibular Eklem Bozuklukları, Ultrason, Radyoloji

### Introduction

The chewing system in individuals is the unit responsible for the speech, chewing and swallowing of the body. This system consists of joints, ligaments, bones, teeth and supporting tissues and muscles. Furthermore, the coordination of these structural components is provided by neurological control systems (1).

Temporomandibular joint (TMJ) is composed of mandibular condyle, temporal bone, articular disc, ligaments

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and various muscles. It is a ginglymodiartrodial joint with a sliding axis, which is located below the temporal bone between the mandibular fossa and the mandibular condyle, in front of the external auditory canal (1-4). In this system, a biconcave-shaped dense fibrous connective tissue arises in the articulating disc (1, 4,5) in order to ensure the conformity of the articular surfaces between the mandibular mandible of the condyle head and the mandibular fossa at the temporal bone. Metabolic needs of the tissues are provided through synovial fluid containing mucopolysaccharide which makes the joint surfaces lubricious in the joint system. Since articular surfaces and discs do not contain blood vessels, the metabolic needs of the tissues are provided by synovial fluid that surrounds the joint surface and at the same time lubricates the joint surfaces (3,4,6,7).

Temporomandibular joint dysfunctions (TMD) are manifested by limitations of normal jaw movements, speech, facial expressions, eating, drinking and swallowing functions and pain in the jaws which affect chewing muscles (8-12). According to the World Health Organization (WHO) report, temporomandibular dysfunction is one of the most common diseases in the mouth and jaw region (13). According to the Diagnostic Criteria for Temporomandibular Joint Disorders (CDC / TMD) scale, the most important symptoms of Temporomandibular dysfunction (TMD) are noise (click, creep) and reduction (14-16).

Among the TMJ dysfunctions, the deviations are the most frequently seen (17-19). Patients with TMJ disorders often complain of tenderness, pain, difficulty in opening the mouth, and tenderness in the TMJ region and these complaints are the reasons for referral to patients' clinics. In the diagnosis of TMD, history and clinical examination results should be correlated with radiological findings (4).

Different imaging modalities are used in examining the anatomical structures of TMJ complex. Prevention of exposing the patient to unnecessary radiation dose is important in selecting the imaging method (4,11,20-22). Computerized tomography (CT), magnetic resonance imaging (MRI) and arthrography are the most commonly used methods of imaging TMJ, and MRI is accepted as the gold standard in the literature (23-26). However, despite its advantage in imaging, features such as an expensive imaging technique, the inability to use in cardiopulmonary patients and heart pacemakers limit the use of MRI (27).

Ultrasonography (US) is a noninvasive, low cost, easy to use imaging method which transmits high-frequency sound waves to the tissue through a probe (transducer). In this

technique, sound waves reflected from textures of varying intensities are subsequently displayed on a screen (11, 28-31). In US, a much higher (2-10 MHz) frequency of sound waves are used (11,28,32,33). Ultrasonography can be used to diagnose disc displacements, effusion, intra-articular defects in TMJ (32,33). In ultrasonographic images of the TMJ, the hyperechoic areas are the white areas representing the margins of the bone and joint capsule, the hypoechoic areas are the black areas representing the bone tissue, empty space, and water, and the isoechoic or grey areas represent the connective tissue and muscular tissue (34,35). When TMJ is displayed, information about joint space, joint disc position, joint fluid and ligament adhesions can be obtained using a linear probe with a frequency of 7.5-12 MHz (28).

Imaging of TMJ and articular disc was first performed by Nebeith and Speculand (36) in 1991 using a 3.5 MHz probe. Stefanoff et al. (37) have shown successful results in asymptomatic patients using a 5 MHz probe. Based on the TMD studies in literature between 1991 and 2006, Melis et al. (20) reported that US has a sensitivity of 13-100% in disc displacement, 70.6-83.9% in effusion, and 70-94% in condylar erosion. These studies portrayed the diagnostic reliability of ultrasonography in the diagnosis of TMJ disorders. Therefore, the aim of this study is to evaluate the diagnostic efficacy of ultrasonography imaging in temporomandibular joint dysfunctions.

## Materials and Method

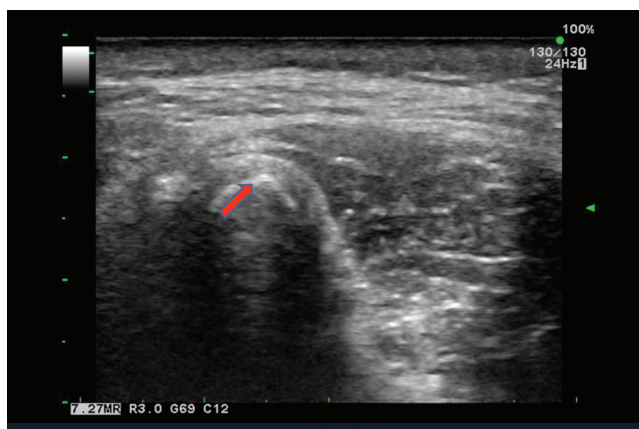
The study evaluated 20 patients and 40 joints with a mean age of 33.7 years who are over 15 years of age, with complaints of TMD and records of USG images. 20 patients over 15 years old from the archive in Oral and Maxillofacial Radiology Department, who had complaints of TME, who did not use any medication for bone diseases and who don't have any developmental anomalies were included in the study. Confirmation for the study was acquired from the Department of Non-invasive Clinical Research Ethics Committee, Marmara University Faculty of Medicine (Protocol No: 092016501). The written informed consent was acquired from each subject to inform about the study's object and procedure. This study was carried out to the recommendations of the Helsinki declaration.

Examinations were performed by using an Aloka Prosound  $\alpha 6$  equipped with a 8 MHz-wide bandwidth linear active matrix transducer ranging from 1 to 15 MHz. Transcutaneous B mode images of the right and left TMJs

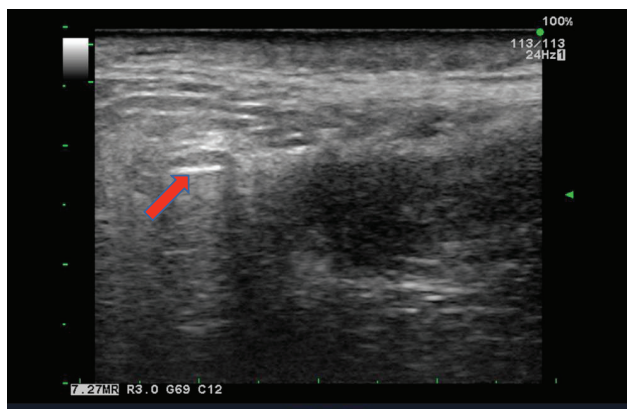
were obtained with the patient in the supine position. The patient was asked to open and close their mouth and, on palpation of the pre-auricular region, an arbitrary position of the head of the condyle and TMJ was obtained (Figure 1). Once this position was achieved, a linear transducer was placed in a transverse direction in close contact with the skin. The transducer was then tilted obliquely until an optimal visualization of the head of the condyle was visible on the screen. The TMJ was assessed for the following parameters: destructive changes including condylar erosions, synovial width alterations and effusions (Figure 2-4).



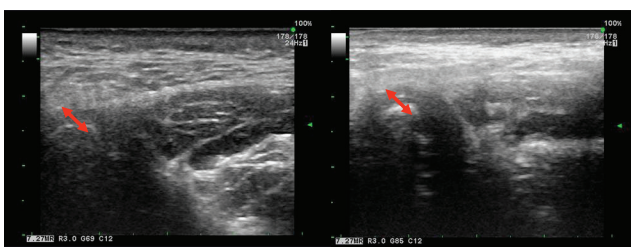
**Figure 1.** After obtaining position of the joint by palpation of the pre-auricular region, the transducer is placed in close contact with the skin with the mouth closed.



**Figure 2.** Joint surface irregularity. The surface of the condylar head appears hyperechoic and an irregularity can be appreciated on the margin.



**Figure 3.** Flattening of the condylar surface



**Figure 4.** Increase in width of the approximating surfaces. This could be an indication of synovial width alterations.

## Results

Ultrasonography was performed on all 40 TMJs. The examinations revealed that in % 15 erosive – degenerative changes, in % 82,5 condylar surface flattening and in % 27,5 increased joint capsule width was observed. The results of the ultrasonography examinations of the TMJs are summarized in Table 1.

**Table 1.** Distribution of Temporomandibular Joint Disorders

|                                 |                                       | Right    | Left     |
|---------------------------------|---------------------------------------|----------|----------|
|                                 |                                       | n (%)    | n (%)    |
| condylar surface irregularities | <i>erosive – degenerative changes</i> | 4 (20%)  | 2 (10%)  |
|                                 | <i>condylar surface flattening</i>    | 14 (70%) | 19 (95%) |
| increase in joint space width   |                                       | 4 (20%)  | 13 (65%) |

## Discussion

Temporomandibular joint (TMJ); consists of the mandibular condyle which is separated from the mandibular fossa by an articular disc, ligaments, and muscles (3). TMJ disorders are

recognized as one of the most common causes of orofacial pain and TMDs affect around 8–12 % of the population (27,34, 38). In clinical practice, CT and MRI can help in the confirmatory diagnosis of hard-tissue and soft-tissue alterations in the TMJ, respectively, an effective screening modality is still lacking. Pathologies affecting the head and neck region, which includes the salivary glands, lymphatics, thyroid, nerves, and vascular structures, are accessible to ultrasound imaging and have been routinely imaged using ultrasonography (27, 39). However, reports on its use in the detection of TMDs in routine clinical practice are limited (5,14,16,25,27). Magnetic resonance imaging (MRI) has been reported as the most precise method for visualizing the disc-condyle relationship (16). The accuracy of MRI is about 95% when sagittal and coronal scans are evaluated (14). With the advantages of being noninvasive and less expensive than other methods, US has been used as a new method for diagnosing TMJ disc displacement (14, 27,31).

The aim of this study was to evaluate the diagnostic efficacy of ultrasonography imaging in temporomandibular joint disorders. Emshoff et al.(40), conducted a study on 29 patients who were aged between 19 to 62 years. Accuracy was found to be 91% in closed mouth position and it was 93% in open mouth position. Another study was conducted by Emshoff et al. (41), on 208 patients who were aged 13 to 78 years. The sensitivity, specificity and diagnostic accuracy were 80-68% both in closed mouth-open mouth, 87-93% (closed mouth-open mouth) and 82-82% (closed mouth – open mouth), which were lesser than those which were reported in a previous study. In the present study a total of 20 patients (% 70 female, %30 male, mean age: 33,75) and 40 TMJ were evaluated in closed mouth position and in % 15 erosive – degenerative changes, in % 82,5 condylar surface flattening and in % 27,5 increased joint capsule width was observed.

Byhatti et al. (42), conducted a study on 100 patients with a 12 MHz transducer using dynamic ultrasonography. Sensitivity in closed mouth position was found to be 80%, while in the open mouth position, it was found to be 76%. Except for study of Byhatti et al. (42), in all the other studies, US diagnosis was compared to MRI diagnosis, as it has been so far described as the gold standard and the most reliable method in diagnosis of TMJ disorders (11, 14,20,40,41).

Bonafe et al. (43) found the estimated sensitivity to be 22.5% in closed mouth position, which was lower than that was seen in previous studies. The specificity in closed mouth

position was 96.6%. In 2001, Jank et al. (44) introduced the use of a high resolution transducer of 12 MHz to visualize the TMJ structures more accurate. The authors reported the disc as a hypoechoic structure in the glenoid fossa surrounded by a hyperechoic rim. Their results, comparing ultrasonography with diagnoses based on MRI, achieved a sensitivity, specificity and accuracy at closed-mouth position of 78%, and a sensitivity, specificity and accuracy of 61%, 88% and 77%, respectively, at maximum-mouth opening position.

When MRI was taken as the gold standard, TMJ disorders in a majority of studies ranged from 41%-90% in disc displacement (11,14,20,27,40,41). In case of TMJ effusion and condylar effusion, sensitivities ranged from 20-80% and 83% respectively (11,27,40-42). In the available literature, it was found that ultrasonography was an acceptable diagnostic tool for detection of disc displacement, condylar erosion and articular effusion.

## Conclusion

The present study has several limitations because of the small sample size and lack of High Resonance Ultrasonography (HR-US) usage and MRI correlations with the ultrasonographic findings. Since our study sample is small we could not evaluate the sensitivity and specificity in our study. Moreover, it can be concluded that, US with the added benefit of reduced cost, remains another effective, noninvasive technique, to define the disk, its position, and the presence of TMJ internal derangements. Future studies with larger sample sizes and MRI correlations need to be conducted.

## Acknowledgement

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# The Clinical Rehabilitation and Cathepsin K Gene Analysis of a Turkish Family With Pycnodysostosis

## Piknodizostosis Sendromlu Bir Türk Ailenin Klinik Rehabilitasyonu ve Katepsin K Geni Analizi

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### Abstract

Pycnodysostosis (PKND) is a rare, autosomal recessive disease characterized by short stature, severe bone fragility exophthalmos and oral manifestations such as micrognathia. It usually demonstrates typical craniofacial deformities, such as hypoplastic midface, anterior cross-bite, grooved palate and dental crowding. The aim of this case report is to report the rehabilitation and analyze the *cathepsin K* for pycnodysostosis under reported cases of three siblings with PKND. A family with 5 siblings, 3 effected and 2 non – effected, were examined clinically and radiologically, and restorative treatments and protective applications were carried out in the effected members. To clarify the underlying reason, *cathepsin K* was amplified and sequenced directly by using specific primers. All the affected members carried L7P variation as homozygous state, whereas unaffected had the heterozygous state of the same condition. Early diagnosis and treatment is important with PKND patients, since bone fractures easily occur during dental treatment and limited mouth opening makes it difficult to access the treated area. Frequent recalls should be planned for PKND patients. Regular oral care and early preventive treatments ensure the patients a better life quality. Also, we suggest that L7P variation of *cathepsin K* may be a diagnostic criterion for PKND.

**Keywords:** Pycnodysostosis, cathepsin K, clinic, genetic

### Öz

Psikozitozis (PKND), kısa boy, şiddetli kemik kırılabilirliği, ekzoftalmi ve mikrognati gibi oral belirtilerle karakterize, nadir görülen, otozomal resesif bir hastalıktır. Genellikle hipoplastik orta yüz, ön çapraz kapanış, derin damak ve dental çapraşıklık gibi tipik kraniofasiyal deformiteler ile görülür. Bu olgu sunumunun amacı, PKND'li üç kardeşin dental tedavilerini sunmak ve bildirilen vakalar altında pycnodysostosis için Katepsin K'yı analiz etmektir. Kliniğimize başvuran ailenin 5 çocuğundan üçünde piknodizostosis görülürken, diğer iki kardeş sağlıklıydı. Çocukların detaylı klinik ve radyolojik muayeneleri yapıldıktan sonra etkilenen bireylerin gerekli restoratif ve koruyucu tedavileri tamamlandı. Altta yatan nedeni açığa çıkarmak amacıyla, Katepsin K amplifiye edildi ve spesifik primerler kullanılarak doğrudan sekanslandı. Etkilenen tüm kardeşler homozigot bir durum olarak L7P varyasyonu taşıırken, sağlıklı kardeşlerde ise aynı durumun heterozigot hali gözlemlendi. Piknodizostosis sendromlu hastalarda kemik kırıklarının kolay oluşması ve tedaviler için erişimi zorlaştıran sınırlı ağız açıklıkları nedeniyle erken tanı ve müdahale oldukça önemlidir. PKND hastaları için sık kontroller planlanmalıdır. Düzenli ağız bakımı ve koruyucu tedavilerin erken dönemde yapılması hastalara daha iyi bir yaşam kalitesi sağlamaktadır. Katepsin K'nın L7P varyasyonunun PKND için bir tanı kriteri olabileceğini düşünmekteyiz.

**Anahtar Kelimeler:** Piknodizostosis, katepsin K, klinik, genetik

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### Introduction

Pycnodysostosis (PKND) (OMIM 265800) is a rare, autosomal recessive disease characterized by short stature, total/partial dysplasia of the terminal phalanges, severe bone fragility, exophthalmos, beaked nose and oral manifestations such as micrognathia. It was first described by Maroteaux and Lamy in 1962. It belongs to the group of craniofacial bone dysplasias, as a form of dwarfism with craniofacial malformation similar to cleidocranial dysplasia

(1,2). PKND has an estimated incidence of 1.7 per 1 million births, without predilection for gender. It can be associated to consanguinity between the parents in 30% of cases (3,4).

The gene responsible for the PKND, *cathepsin K (CTSK)* (MIM# 601105), lies on 1q21, has 8 exons and 7 introns (5). Protein product of the gene, Cathepsin K, is a lysosomal cysteine protease and has major roles in osteoclast-driven bone resorption, degradation of type I and type II collagens, osteopontin, and osteonectin (6). Many mutations affect the mature active domain of CTSK protein and caused CTSK deficiency because of the abnormal degradation of bone matrix proteins (7). As a result, high bone density and decreased bone turnover occurs. Because of sclerotic and fragile bones, most individuals affected by PKND have a history of recurrent fractures of the long bones. Pycnodysostosis is usually diagnosed at an early age due to the typical phenotype with proportionate dwarfism and peculiar facies (1,3).

Pycnodysostosis usually demonstrates typical craniofacial deformities, such as hypoplastic midface, obtused mandibular gonial angle, anterior cross-bite and grooved palate. Intraoral features include delayed exfoliation of deciduous teeth, tooth misalignment and dental crowding. Dental crowding, hinders good oral hygiene leading to a high rate of caries and periodontal disease in these patients. In addition, enamel hypoplasia, and obliterated pulp chambers have been observed. Because of several morphological changes of maxillofacial structures PKND patients requiring specialized dental care (8-10).

Clinical manifestations of this syndrome are the main source of diagnosis. Comprehensive dental treatment comprising full oral rehabilitation. Orthodontic and orthognathic treatment becomes a challenge because of the reduced bone turnover of PKND (11).

The aim of this case report is to examine the *CTSK* for the onset of pycnodysostosis under reported cases, and discuss the presented management issues of PKND patients.

## Case Reports

Three of five siblings (FE 16(♀), ME 10(♀), HE 4(♀)) with PKND applied to Marmara University, Faculty of Dentistry, Department of Pediatric Dentistry, Istanbul, Turkey. The other two siblings (AE 14 (♂), ME 10(♀)) were PKND-unaffected. Parents are healthy and they have consanguineous marriage. Patients did not show disturbances of behavior or

sociability. All the siblings' detailed clinical and radiological examination was performed.

### – Case 1 –

A 16 year old female patient, short stature, diagnosed with PKND at the age of 4, based on clinical features, including beaked nose and micrognathia. Extra-oral examination presents dystrophic fingernails, a slightly retrognathic, convex profile and mid-facial hypoplasia with proptosed eyes. According to the panoramic radiograph the maxillary right first premolar, mandibular left and right second premolars and all third molars were congenitally absent. Both the maxilla and mandible were hypoplastic. and the mandibular angle was obtuse with prognathism. Intraoral examination revealed occlusal alterations, narrow and grooved palate, dental crowding, posterior cross bite and caries (Figure 1A and 1B). The periodontal examination of the patient composed of poor oral hygiene, visible plaque accumulation and gingival bleeding. Taking into consideration the fragility in these patients, appropriate restorative treatments and protective applications like fluoride or fissure sealant application were preferred. Patient was given oral hygiene education and recall visits occurred in every 3 months during the 18-month follow-up period (Figure 1C and 1D).

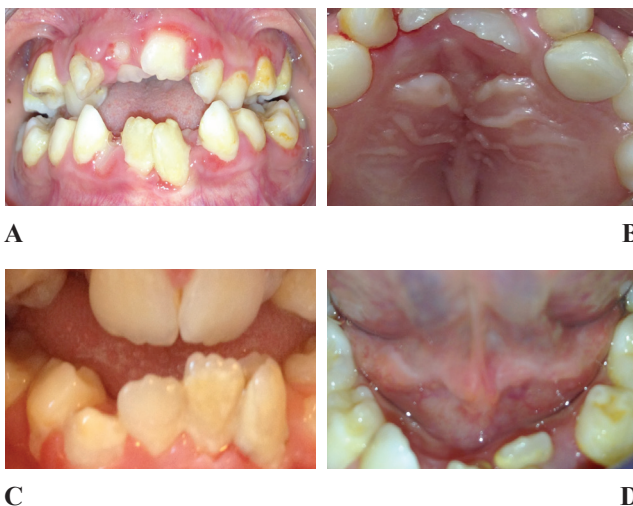


**Figure 1:** Frontal (A) and palatal (B) view of Case 1 at first appointment, frontal (C) and occlusal (D) view after 18 – month follow-up.

### – Case 2 –

A 10 year old female patient diagnosed with PKND, while her twin (ME) was not affected. She has short

stature and presents facial asymmetry. The patient's main complaints were her facial appearance and tooth caries. Clinical examination of the patient presents short stature and retrognathic convex profile. Panoramic radiography showed maxillary left lateral incisor, all permanent second premolars and all third molars are congenitally absent. In intraoral examination, anterior cross-bite, grooved palate, delayed exfoliation of deciduous teeth, dental crowding, and caries observed (Figure 2A and 2B). Changes in gingival color and contour, edema, and very poor oral hygiene were present. These findings diagnosed as plaque-induced marginal gingivitis. The child brushed her own teeth once a day, without supervision from any adult. For a better oral hygiene the patient was given oral hygiene education. Restorative treatments of caries and treatment of marginal gingivitis are been completed. To provide the better oral hygiene protective treatments were made and recall visits occurred in every 3 months (Figure 2C and 2D).

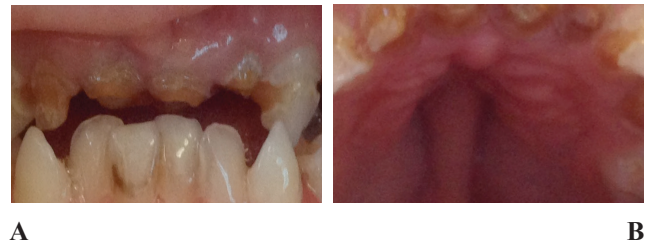


**Figure 2:** Frontal (A) and palatal (B) view of Case 2 at first appointment, frontal (C) and occlusal (D) view after 18 – month follow-up.

**-Case 3 –**

A 4 year old female have been diagnosed with PKND at around 3 years of age, based on clinical manifestations, being the youngest of 3 affected siblings. The mother reported the similar aspects between the affected siblings after the second year, including that the child was small for her age and all the affected siblings presented similar facial features. Intraoral examination revealed grooved palate and dental caries. No features of enamel hypoplasia are seen in intraoral examination (Figure 3A and 3B). Panoramic radiography has not been taken because of her age. The

patient is non-cooperative because of her age. Protective treatments and minimal invasive restorative treatments were preferred and recall visits revealed in every 3 months.



**Figure 3:** Frontal (A) and palatal (B) view of Case 3 at first appointment.

**Genotyping**

To analyze *CTSK* in family members, genomic DNA was isolated from buccal cells by using “Buccal Amp™ DNA Extraction Kit”, by following manufacturer’s instructions. Study protocol is in accordance with the principles of the Declaration of Helsinki II. Parents signed the informed consents prior to enrollment to the study. Primers and polymerase chain reaction conditions were carried out as previously described (5). Amplicons were sequenced by using ABI Prism Kit and on an Sanger autosequencer. Three of the siblings carried CC genotype, whereas 2 of the unaffected siblings and patients had CT genotype. T>C transition at exon 2 leads the change of the amino acid leucine (L) to amino acid proline (P).

**Discussion**

Pycnodysostosis has a number of characteristic clinical and radiographic signs that differentiate it from other osteosclerotic conditions. General features include short stature, generalized diffuse osteosclerosis with a tendency for fracture after minimal trauma, and hypoplastic clavicles. Cranial and maxillofacial features include prominent eyes with blue sclerae, relative proptosis, beaked nose, frontoparietal bossing, open fontanelles and cranial sutures, hypoplastic paranasal sinuses, an obtuse mandibular gonial angle, often with relative prognathism, a hypoplastic maxilla and mandible and a highly retrognathic profile. Intraoral findings include a grooved palate, dental crowding, overly retained deciduous teeth and delayed eruption of permanent dentition, tooth misalignment, enamel hypoplasia. The development of severe dental caries, obliterated pulp chambers and periodontal diseases have also been described.



All these findings, especially the intraoral findings, were consistent with the present case reports (1-3,8).

The diagnosis of pycnodysostosis is primarily based on clinical features and radiographs, but the confirmatory test is a cathepsin K gene mutation analysis. During the 1990s, the genetic defect was located on chromosome 1q21, which led to specific genetic testing and accurate diagnosis. A mutation in the gene that codes for the enzyme cathepsin K inhibits the normal function of the osteoclasts. Other uncommon clinical disorders of reduced bone resorption include osteopetrosis, osteogenesis imperfecta, cleidocranial dysplasia and idiopathic acroosteolysis. In fact, in pycnodysostosis, the number of osteoclasts is normal but the region of demineralized bone surrounding them is larger than normal. Recognition of these signs is important in order to make the diagnosis and prevent possible complications (2-4,8).

PKND patients usually have a normal life span. Bone fragility and a history of frequent fractures may suggest a diagnosis of abnormalities in the material composition and structure of bone. Early diagnosis can ensure a better life quality, which require proper attention to risk factors during treatment planning. Unfortunately, PKND patients need dental care later in life, having missed early childhood prevention of oral disease. Early intervention to qualify dental crowding has been recommended to the pediatric patient to allow better dental alignment and oral hygiene of the primary and erupting permanent dentition reducing chances of dental impaction, periodontal disease, and dental caries (1,3,6). In the present study, almost all intraoral features of PKND such as dental crowding, dental caries, periodontal diseases, persistence of deciduous teeth observed, the congenital absence of many permanent teeth were observed.

Enamel hypoplasia was mentioned in the literature as one of the alterations commonly found in patients with pycnodysostosis. However, the patients of this report did not present signs of alterations in the enamel or in the shape of teeth. Furthermore, alteration was noted in the tooth eruption, similar to the report of Hunt *et al.*, who observed a delay in eruption (12). According to the literature both Class II and Class III malocclusions are in association with PKND. Norholt *et al.* stated that these patients often present a Class III dentition owing to the maxillary hypoplasia (13). Presented patients have dental Class III malocclusion.

There is no specific treatment for this anomaly and the current treatment options for dental caries is only restorative

or protective treatments. Recommendations or information about the effective and reliable orthodontic treatment of children or young adults with pycnodysostosis are not available in the literature. Orthodontic and orthopaedic movements are dependent on osteoclastic activity, bone resorption and remodeling capacities. Because of high risk of fracture and low remodeling capacity orthognathic surgery and orthodontic treatment have not been previously described for PKND affected patients. Only in one recent case report distraction osteogenesis technique was used (2,10,13). Taking into consideration the fragility in our patients, appropriate restorative treatments and protective applications were preferred, but orthodontic treatment could not be carried out. Patients were given oral hygiene education and recall visits is occurred in 3-months period.

Tooth extraction in patients with pycnodysostosis is carried out during surgery as atraumatically as possible to reduce the risk of fracture, especially in the mandible. However, post-extraction osteomyelitis may develop because of the increased bone density (1,14). It is important with such patients to bear in mind the increased risk of pathological fractures during dental operations and tooth extraction because of bone fragility. However, in spite of the fragility, bone healing is normal (4).

In this study, three of the siblings carry L7P variation of the gene, whereas healthy siblings had the same variation as heterogeneous. T>C transition at exon 2 leads the change of the amino acid leucine (L) to amino acid proline (P). This amino acid change is considered to affect the signal peptide sequence of protein, as indicated in other studies (15).

Many have reported on clinical and radiological findings associated with this syndrome; however, only a few have added their restorative treatments and genetic investigation to their reports. In this case report we did appropriate restorative treatments and protective applications to the patients. Because of serious limitations imposed by dentofacial discrepancies, it would be advisable for PKND patients to be treated as high-risk patients with frequent recall visits in order to prevent dental caries and periodontal disease, providing early intervention if restorative procedures become needed (9).

## Conclusion

The dentists should recognize the radiographic and clinical maxillofacial features of pycnodysostosis, which allows correct treatment planning avoiding risks and ensuring better

treatment plan for PKND patients. The ideal approach to the management of gingival, dental and craniofacial problems associated with PKND should be multidisciplinary, involving the pediatric dentist, orthodontist and oral and maxillofacial surgeon. Early diagnosis and treatment is important with PKND patients, since bone fractures easily occur during dental treatment and limited mouth opening makes it difficult to access the treated area. Child patients with pycnodysostosis should receive special dental care, particularly preventive treatment, because of the group of mouth alterations described, in addition to periodical follow-up of their growth and craniofacial development. Frequent recalls should be planned for all PKND patients. Regular oral care and early preventive treatments ensure the patients a better life quality. Conclusively, we suggest that L7P mutation may be a diagnostic criteria for this anomaly, but extended number of studies is needed to fulfill the role of this gene on the onset of the anomaly.

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# Clinical Findings of Children With Epidermolysis Bullosa: Case Reports of Three Siblings

## Büllozalı Çocukların Klinik Bulguları: Üç Kardeş Vaka Çalışması

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### Abstract

Epidermolysis bullosa (EB) is a group of inherited bullous disorders characterized by blistering of the skin and mucosa in response to trauma. EB patients require special precautions during dental treatment because of the high risk of lesioning the soft tissue when handling cutting instruments close to the skin and oral mucosa. In this case report, clinical and oral findings of three siblings with epidermolysis bullosa, whose parents were relatives, are presented. The first case was a 5-year-old girl with skin lesions, microstomia, ankyloglossia and poor oral health. The second case was a 4-year-old girl having only deformity on her foot fingernail without any oral tissue involvement. The third case was a 2-year-old boy with numerous dermal blisters, ankyloglossia and poor dental status. Oral health of these children was maintained by improving oral hygiene, preventive measures and regular visits.

**Keywords:** Epidermolysis bullosa, oral health, oral manifestations

### Öz

Epidermolizis bülloza, (EB) deri ve mukozada travmaya karşı cevap olarak meydana gelen bül oluşumuyla karakterize ailesel geçişli bir vezikülobüllöz hastalıktır. EB hastalarının dental tedavilerinde kullanılan aletlerin yumuşak doku lezyonu oluşturması riski yüksektir ve özel önlem gerektirmektedir. Bu vaka raporunda, ebeveynleri akraba olan, EB'li üç kardeşin klinik ve oral bulguları sunuldu. Birinci vaka deri lezyonları, mikrostomi, ankiloglossi ve kötü ağız hijyenine sahip 5 yaşındaki bir kız çocuğu idi. İkinci vaka olan 4 yaşındaki kız çocuğunda sadece ayak tırnağında deformite mevcuttu. Üçüncü vaka, deride çok sayıda kabarcığı bulunan ankiloglossi ve kötü ağız sağlığına sahip 2 yaşındaki bir erkek çocuk idi. Bu çocukların ağız sağlığı, oral hijyenin sağlanması, koruyucu uygulamalar ve düzenli kontroller ile idame edildi.

**Anahtar Kelimeler:** Epidermolizis bülloza, Ağız sağlığı, Oral bulgular

### Introduction

The term epidermolysis bullosa (EB) describes a heterogeneous group of inherited blistering mucocutaneous disorders which have a specific defect in the attachment mechanisms of the epithelial cells, either to each other or to the underlying connective tissue (1, 2). This dermatological condition is a severe autoimmune disease (3, 4).

The incidence of EB was reported varying between 1:50 000 to 1:500 000 live births (1). The most reliable figures on prevalence of EB are derived from the National Epidermolysis Bullosa Registry, which collected cross-sectional and longitudinal data on about 3300 patients in the United States from 1986 to 2002 (5, 6, 7,8). Over a 5-year period (1986 to 1990), the prevalence of EB was estimated to be approximately 8 per million live births (5). Data from the Australasian Epidermolysis Bullosa Registry provided a prevalence estimate of 1 case per 100 000 live

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births. Prevalence rates ranging from 15 to 32 cases per 100 000 have been estimated in the United Kingdom (6, 7) EB can be seen in all racial and ethnic groups and genders are affected equally (1, 9, 10).

EB can be inherited in either autosomal dominant or recessive fashion. Four major forms of EB have been described, depending on the level of skin involvement: EB simplex (EBS) involving the intra-epidermal layer; junctional EB (JEB) involving the lamina lucida; dystrophic EB (DEB) involving the sublamina densa; and Kindler syndrome involving multiple layers of the epidermis (11, 12, 13). However, more than 20 subtypes of EB have been recognized in the literature (1).

The etiopathogenesis of all forms of EB resides in mutations in more than 10 different genes coding for mutated proteins located at different levels in the epidermis/dermis (14). Indeed, mutations in transglutaminase 5, plakoglobin, plakophilin 1 and desmoplakin are responsible for the suprabasal form of EBS; mutations in keratins 5/14, plectin, BP230, kindlin-1, exophilin 5 for the basal form of EBS; mutations in integrins  $\alpha 6\beta 4$ , integrin  $\alpha 3$ , collagen type XVII, and laminin-322 for the JEB and, mutations in collagen type VII for both dominant and recessive forms of DEB (12, 15).

EB is diagnosed by examining the basal membrane with transmission electron microscopy, immunohistochemical analysis, and other supplementary examinations such as immunofluorescence, optical microscopy, and enzymatic analysis. In some cases, fetoscopy for prenatal diagnosis of EB may be suggested (1, 2).

All major types of EB patients show skin and mucosa fragility in different levels clinically. Repeated episodes of cutaneous breakdown heal with scarring on hands and feet resulting in the fusion of the fingers into a mittenlike deformity in DEB patients (7). In addition, patients with EB have some oral alterations such as dental anomalies of shape, position, and structure (hypoplasia and hypomineralization); tongue denudation and limited mobility, ankyloglossia, and microstomia (11, 16, 17, 18, 19, 20, 21).

Dental treatment is aimed at avoiding the formation of new bullae during treatment procedures under local anesthesia. Therefore, dental management of DEB patients requires lubrication of mucosal tissues and dental instruments in order to avoid adherence (22). The suction tip is advised to lean on hard dental tissues to avoid further epithelial sloughing (22). Special dental management involve the use of soft toothbrush and non-irritant irrigation techniques. Soft

diets are also recommended because of the lesions involving the oral mucosa and gastrointestinal tract (23).

The aim of this case report was to present clinical and oral findings of three siblings with EB, whose parents had consanguineous marriage.

## Case Reports

Our first case was a 5-year-old girl with DEB, who was born with the skin lesions on the legs and hospitalized immediately (Figure 1). She had skin lesions on the ears, scalp, knees, elbows and fingers, and lesions on oral mucosa with poor oral hygiene. Intraoral examination was conducted with difficulty due to microstomia and limited opening. The patient had ankyloglossia and a smooth tongue with obliteration of the oral and lingual vestibules. Her dental status was poor with multiple advanced dental caries in most of her teeth.



Figure 1. Case 1 showing skin and oral manifestations.



The second case was a 4-year-old girl with EBS (Figure 2). When she was born, she had blisters on her feet that healed within 20 days and thereafter she had not presented any lesions related with EB except deformity on her right foot fingernail. No involvement of oral mucosa was seen along with normal structured teeth.



**Figure 2.** Case 2 with normal intraoral structures presenting only a minor deformity on her right foot fingernail.

Our last case was a 2-year-old boy with DEB, who had oral mucosa lesions when he was born (Figure 3). His skin lesions appeared after he refused breastfeeding when he

was 2 months old. He had numerous blistering on his face, ears, trunk, hand and feet with mittenlike deformity. Similar to the first case, the patient was ankyloglossia. His dental status was poor with caries in most of his teeth.



**Figure 3.** Case 3 showing lesions on skin and oral mucosa.

Cases were managed by bathing daily and drying with gentle movements to prevent trauma. An antibacterial ointment was used on the lesions and gauze wrapped around the affected areas. Oral hygiene instructions were given,

soft toothbrush was recommended, and dental therapy was performed under local anesthesia. The pedigree of the family is presented in Figure 4.

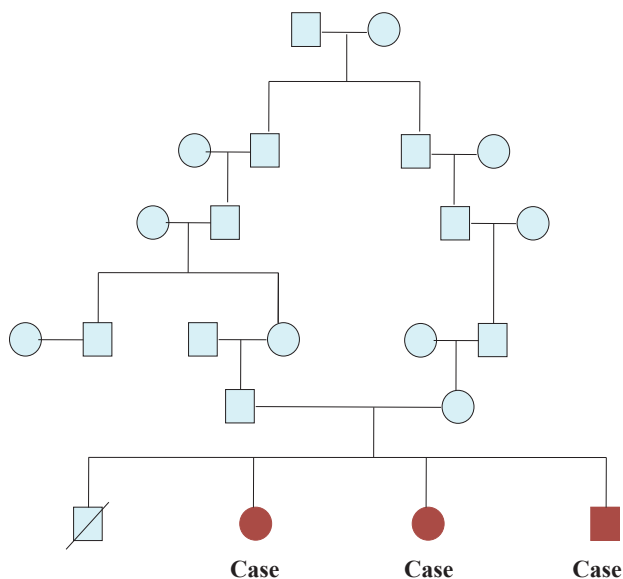


Figure 4. Pedigree of the family

## Discussion

EB is a heterogeneous group of rare genetic disorders characterized by marked fragility of the skin and mucous membranes in which vesiculobullous lesions occur in response to trauma and other physical, thermal and chemical causes (23). Due to the consanguineous marriage of parents, fetoscopy for prenatal diagnosis of EB could have been suggested to prevent the birth of other children with this disorder.

EB is a challenge to health professionals because there is no definitive cure (13, 17, 24). Although all major types of EB have skin and mucosal lesions, DEB is the most aggressive form of EB (11, 25). The first and third cases were diagnosed DEB and they had oral manifestations such as mucosal erosions, reduced vestibular sulcus depth, ankyloglossia, microstomia and caries. But the second case, which was diagnosed as EBS, had only skin lesions on her feet and no involvement of oral mucosa. These dermal and oral findings of our cases are consistent with reported literatures (12,13,15,16).

EB patients require special precautions during dental treatment because of the high risk of lesioning the soft tissue when handling cutting instruments close to the skin and oral mucosa (16, 18). Cariogenic food, limited mouth opening as a result of persistent wounds and poor oral hygiene caused

by pain are the predisposing factors to dental caries (19, 20). In these cases, minimal intervention has so far preserved the oral cavity and monthly topical fluoride application helped to control dental caries (26).

The patient maintains continuous contact with the health team to avoid complex treatments. Numerous alternative therapies have been used for the treatment of blisters. The application of aloe vera gel diminishes the subdermal temperature by providing a refreshed sensation, reducing the healing period and promoting the antimicrobial activity (27, 28). This product possesses buffering capacity, immunological effect, and a self-cleaning effect (28). EB treatment is generally focused on support rather than perforating the blisters since this procedure contributes to acceleration of the healing process and lateral spreading of the blisters. Currently, researchers are focusing their attention on gene and cell therapy, recombinant protein infusions, intradermal injections of allogenic fibroblasts and stem cell transplantation (29). Other developing therapies are directed toward the enhancement of wound healing and better quality of life for EB patients (2, 9, 22, 26, 29).

A multidisciplinary approach involving the nutritionist, pediatrician, dermatologist, plastic surgeon, hematologist, gastroenterologist, ophthalmologist, cardiologist, pediatric dentist, nurse and occupational therapist is essential (9, 10, 12, 29).

## Conclusion

This case report emphasizes that patients with EBS need special precautions during dental treatment because of probable blister formation. Moreover, these patients require an early multidisciplinary approach to improve their quality of life, with the dentist playing an important role in oral health management.

## Acknowledgement

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## Hızlandırılmış Diş Hareketinde Düşük Doz Lazer Kullanımı

### Low Level Laser Therapy For Accelerated Orthodontic Tooth Movement

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#### Öz

Günümüzde, giderek daha fazla sayıda yetişkin birey ortodontik tedavi talep etmektedir. Kısa sürede iyi bir tedavi sonucuna ulaşmak isteyen yetişkin hastaların artması ve uzun süreli ortodontik tedavilerin (çürük, beyaz lezyon, periodontal problemler ve kök rezorpsiyonu gibi) olası yan etkileri nedeniyle araştırmacılar diş hareketini hızlandırmayı amaçlayan çalışmalara yönelmiştir. Diş hareketini hızlandırmak amacıyla yapılan güncel uygulamalar arasında düşük doz lazer terapisi, titreşimli elektromanyetik alanlar, elektriksel akım, kortikotomi, distraksiyon osteogenezi ve mekanik titreşim sayılabilmektedir. Bu derlemede diş hareketini hızlandırmak amacıyla uygulanan güncel fizyolojik yaklaşımlardan biri olan düşük doz lazer terapısından bahsedilecektir. Bu konudaki birçok çalışmada bulgular genel olarak DDLT'nin diş hareketi hızını artırdığına yöneliktir. Ancak DDLT'nin diş hareketi üzerinde etkili olmadığını belirten çalışmalar da mevcuttur. Literatürdeki çalışmaların bütününe bakıldığında; insanlarda klinik uygulama rutinlerini ve etkilerini belirginleştirmek açısından bu konuda daha fazla çalışma yapılması gerektiği sonucuna varılabilir. Bununla birlikte, periodontal dokular açısından güvenli bir yöntem olan DDLT'nin ortodontik tedavi kaynaklı diş ağrılarını azaltması, invazif olmaması, uygulama kolaylığı, hastaya rahatsızlık vermemesi ve fizyolojik bir yaklaşım olması gibi özellikleri göz önüne alındığında ortodonti alanında önemli faydaları ve kullanım alanları olacağı öngörülebilir.

**Anahtar Kelimeler:** Düşük doz lazer terapisi, Hızlandırılmış diş hareketi, İş hareketi teknikleri

#### Abstract

Contemporarily, more adult patients seek orthodontic treatment. This increasing number of adult patients who usually demand good results in a short treatment period and the possible side effects of a prolonged orthodontic treatment (such as caries, white spot lesions, periodontal problems and root resorption) lead researches to search for methods that accelerate orthodontic tooth movement. Low-level laser therapy, electrical current, pulsed electromagnetic fields, corticotomy, distraction osteogenesis and mechanical vibration can be listed among the methods that intend to increase the orthodontic tooth movement rate. This paper aims to review the current literature about low-level laser therapy (LLLT), which is one of the physiological approaches for accelerated orthodontic tooth movement. There are many studies on animal and human subjects, which report positive effects of LLLT on orthodontic tooth movement rate. However there are also studies that found no acceleratory effects of LLLT. In an overview of the literature, it can be concluded that more studies are necessary to clarify the clinical application methods and effects on humans. Still, considering the advantages of LLLT such as easy application, no patient discomfort, reducing orthodontically induced pain, being a non-invasive, periodontally safe and physiological approach, it can be foreseen that LLLT can have clinical use and benefits.

**Keywords:** Low level laser therapy, Accelerated tooth movement, Tooth movement techniques

Uzun süreli ortodontik tedavinin hasta konforu ve uyumunu azaltması, eksternal kök rezorpsiyonu ve çürük riskini artırması ve giderek daha fazla sayıda yetişkin hastanın ortodontik tedavi talep etmesi gibi faktörler araştırmacıları diş hareketini hızlandırmaya yönelik çalışmalara yönlendirmiştir. Günümüzde diş hareketini hızlandırmak amacıyla yapılan uygulamalar arasında düşük doz lazer terapisi, titreşimli elektromanyetik alanlar, elektriksel akım, kortikotomi, distraksiyon osteogenezi ve mekanik titreşim sayılabilmektedir. Bu alandaki çalışmalar 5 ana başlık altında incelenebilir:

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- 1) Biyomekanik yaklaşım: Kapaklı braketler
- 2) Fizyolojik yaklaşım: Doğrudan elektrik akımı ya da düşük doz lazer terapisi
- 3) Farmakolojik yaklaşım: Lokal olarak sitokin ya da hormon enjeksiyonu
- 4) Cerrahi destekli yaklaşım: Periodontal ligament (PDL) distraksiyon osteogenezi, dentoalveoler distraksiyon osteogenezi, selektif dekortikasyon, piezo-insizyon
- 5) “Cerrahi-benzeri” yaklaşım: Submukozal PRP enjeksiyonu

Bu derlemede diş hareketini hızlandırmak amacıyla uygulanan güncel fizyolojik yaklaşımlardan biri olan düşük doz lazer terapısından bahsedilecektir.

1917 yılında Einstein uygun boyutlu bir fotonun, uyarılmış durumda bulunan bir moleküle çarpması halinde, bu molekülün daha düşük enerji seviyesine geçerken, kendisine çarpan fotonla aynı doğrultuda hareket eden ve aynı büyüklükte bir foton salacağını ortaya koymuştur.<sup>1</sup> Einstein’ın ileri sürdüğü foton salımının bir gaz odacığının mikrodalga ışınları ile uyarılması sonucunda gerçekleştirilmesi ile “*Microwave Amplification by Stimulated Emission of Radiation*” prensibi ortaya çıkmıştır.<sup>2</sup> Bu tanımın baş harflerinin birleşimi ile kısaca MASER olarak adlandırılan bu prensibin, ışık dahil herhangi bir dalga boyundaki tüm elektromanyetik dalgalara uygulanması ile de “*Light Amplification by Stimulated Emission of Radiation*” (LASER) kavramı doğmuştur.<sup>3</sup>

Lazer ortamı olarak bilinen katı, sıvı veya gazla dolu bir odacığın, dışsal bir etken (enerji kaynağı) ile uyarılması sonucu meydana gelen spontan foton salınımı, hareketli fotonlar oluşmasına neden olur. Bu hareketli fotonlar, lazer odacığının optik resonatör olarak adlandırılan aynalarla kaplı iki ucu arasında yansıyarak ortamı terk etmeden önce, lazer ortamı içindeki diğer atomların da uyarılmasına yol açarak yeni bir emisyon meydana getirirler. Bu sırada oluşan lazer ışığı yeterli genliğe ulaştığında, bir tanesi kısmi geçirgen olan aynadan dışarı çıkarak konsantre bir ışık demeti oluşturmaktadır. Bu olay bir lazer atışını açıklamaktadır.

Lazer ışığı normal ışıktan farklı fiziksel özelliklere sahiptir: Sadece tek renk ve dalga boyuna sahiptir (monokromatik’tir); ışık hüzmesi konsantre, güçlü ve doğrusaldır; ışık dalgası, tüm fotonlar aynı fazda bulunduğundan organize biçimde hareket etmektedir (koherent’tir). Bu özellikler sayesinde lazer ışını yüksek

seviyede enerjinin ufak noktalara odaklanmasını sağlar. Lazer ışığı dokuya girdikten sonra yansıtılabilir, absorbe edilebilir, direkt geçebilir ya da saçılabilir. Doku ile lazer probu arasındaki mesafe ve hedef dokunun özellikleri, lazerin dokuda oluşturması istenen etki açısından değerlendirilmelidir.

Diş hekimliğinde güncel olarak kullanılan lazer tiplerine kısaca değinmek gerekirse;<sup>4</sup>

### Argon Lazer

Görünür spektrumda yer alır. Diş hekimliğinde 488 nm ve 514 nm olmak üzere 2 dalga boyu uygulanmaktadır. Dalga boyları dişin sert dokusunda absorbe edilmediğinden yumuşak doku uygulamalarında, hemostaz ve beyazlatma işlemlerinde etkin ve güvenli bir şekilde kullanılabilir.

### Diyot Lazer

Diş hekimliğinde 800-980 nm arasında dalga boyları uygulanabilmektedir. Aliminyum-galyum-arsenik (AlGaAs) içeren diyot lazerler 810 nm; İndiyum-galyum-arsenik (InGaAs) içerenler 980 nm dalga boyunda emisyon yapar. Bu dalga boyları, pigmente dokularda yüksek oranda emilim gösterirler, dokudaki penetrasyon derinliği 2-3 mm’dir ve dokuda ısı artışına neden olmazlar. Düşük doz lazer tedavilerinde biyostimülasyon amacı ile sıklıkla kullanılmaktadırlar.

### Neodymium:YAG (Nd:YAG) Lazer

Elektromanyetik spektrumda infrared bölgede yer alır ve 1064 nm dalga boyuna sahiptir. Melanin içeren dokularda hemoglobin içeren dokulara kıyasla daha yüksek emilimi bulunmaktadır. Diş sert dokularında çok az emilmesi sebebiyle dişe komşu yumuşak dokularda uygulanan yumuşak doku işlemlerinde iyi bir hemostaz ile birlikte çalışılmasını sağlar.

### Erbiyum:YAG (Er:YAG) Lazer

Günümüzde diş hekimliğinde yaygın olarak kullanılan lazerlerden biridir. Er:YAG lazer 2936 nm; Erbiyum chromium: YSGG lazer ise 2780 nm dalga boyunda lazer emisyonu gerçekleştirmektedir. Bu lazerler, su ve hidroksiapatite yüksek absorpsiyon gösterirler. Bu özellikleri

sayesinde dokuyu hassasiyetle kesebilmektedir ve kemiği ilgilendiren cerrahilerde başarıyla kullanılabilir. Yumuşak dokuda hemostaz sağlaması ve yumuşak dokuya termal olarak çok az hasar vermesi sebebiyle de cerrahi yaraların iyileşmesi daha hızlı olmaktadır.

### Karbondioksit Lazer

10.600 nm ile ışık spektrumunda kızıl ötesi alandadır. İyi hemostaz sağlar, dokuda yüzeysel bir penetrasyonu vardır ve hidroksiapatite afinitesi yüksektir. Birçok cerrahi uygulamada kullanılabilir.

Ortodonti alanında lazerler, sert ve yumuşak doku uygulamaları, mine ve porselen yüzeylerinin pürüzlendirilmesi, braketlerin sökümü, biyostimulasyon ile hızlandırılmış diş hareketi sağlanması, diş hareketine bağlı ağrının azaltılması gibi farklı amaçlarla kullanılabilir. Uzun süreli ortodontik tedavinin hasta konforu ve uyumunu azaltması, eksternal kök rezorpsiyonu<sup>5,6</sup> ve çürük riskini<sup>7-9</sup> artırması ve giderek daha fazla sayıda yetişkin hastanın ortodontik tedavi talep etmesi gibi faktörler araştırmacıları özellikle diş hareketini hızlandırmaya yönelik çalışmalara yönlendirmiştir. Günümüzde diş hareketini hızlandırmak amacıyla yapılan çeşitli uygulamalar arasında düşük doz lazer terapisi fizyolojik bir yaklaşım olarak sınıflandırılmaktadır.<sup>10</sup>

Lazer ışınlarının dokuda en fazla 1°C'lik ısı artışı yaratarak oluşturduğu etkilere 'biyostimulan etkiler' denmektedir. Lazer ışınlarının biyostimulan etkilerinden faydalanılarak yapılan tedaviler 'Düşük Doz Lazer Terapisi', 'fotobiyostimulasyon', 'fotobiyomodülasyon' veya 'lazer biyoaktivasyonu' gibi farklı isimlerle anılmaktadır. Soğuk lazer olarak da bilinen düşük doz lazer terapisi, (DDLTL) dokularda ısı artışına sebep olmayan bir ışınlama sağlar<sup>11</sup>. Etki mekanizması, hücre altı foto-reseptörlerin görünür kırmızı ve yakın-kızılötesi dalga boylarına yanıt verme kapasitesi ile çalışır. Bu reseptörlerin uyarılması ile dokuların enzimsel ve fotokimyasal aktivitelerinde değişiklikler meydana gelir.<sup>12,13</sup> Elektron taşınma zinciri, solunum döngüsü ve oksidasyon mekanizmaları etkilenerek hücre metabolik süreçlerde artış oluşur.<sup>6</sup> Aynı zamanda fibroblastik aktivitelerde (fibroblast proliferasyonu, kollajen salgılanması, kollajen matris deposisyonu) artış; osteoblastik ve osteoklastik farklılaşmada/aktivitelerde ve kemik rezorpsiyonunda artış ve alveoler kemik döngüsünün hızlanması gibi etkileri gösterilmiştir.<sup>11,12</sup> Lazer uygulamasının nöronal etkisi ise membran potansiyelinin stabilizasyonu ile ağrı sinyalinin engellenmesi şeklinde

gerçekleşir. Lazer uygulamasını takiben ağrılı uyarana karşı C-fibrillerinde pulpal cevabın baskılandığı gösterilmiştir.<sup>13</sup> Bununla birlikte prostaglandin E2 gibi ağrılı duyuların oluşmasında rol oynayan enflamatuar ajanların azalmasına da etkili olduğu bildirilmiştir.<sup>14</sup> Özetle DDLTL'nin; kemik hücresel aktivitesi, kemik yapısı, kemik iyileşmesi, fibroblast aktivitesi ve enflamatuar süreç üzerinde etkileri mevcuttur.

DDLTL'nin ortodontik tedavi sırasında doğal olarak oluşan enflamatuar reaksiyonlar üzerinde vazodilatasyon, mast hücrelerinde degranülasyon ve bununla birlikte doku iyileşmesini ivmelendiren enflamatuar ajanların salınması gibi çeşitli etki mekanizmalarının olduğu düşünülmektedir.<sup>11</sup> DDLTL'nin dokular üzerindeki bu etkilerinden yola çıkılarak, ortodontik tedavi sırasında diş hareketini hızlandırarak tedavi süresini kısaltabileceği, diş hareketine bağlı ağrıyı azaltabileceği ve tedavi sonrasında nüksü azaltabileceği öngörülmekte ve bu yönde çalışmalar yapılmaktadır.

Diş hareketini hızlandırmak amacıyla en sık kullanılan lazer türü gallium-aluminyum-arsenid (GaAlAs) diode lazerdir. DDLTL, ilgili dişlerin genellikle bukkal, palatal, mesial/distal yada servikal, orta ve apikal mukozaları üzerinden uygulanabilir. Uygulanan dalga boyları 630–860 nm ve enerji dozu 4.5-6.0 J/cm<sup>2</sup> arasında değişkenlik göstermektedir.<sup>16-24</sup> Doz hesaplamalarındaki birimleri kısaca açıklamak gerekirse; Joule (J) verilen enerjiyi ifade eder ve miliwatt (mW)\* saniye(sn) = miliJoule olarak hesaplanır. Uygulanan enerji dozu ise enerji (J) /ışınlanan alan (cm<sup>2</sup>) = J/cm<sup>2</sup> olarak hesaplanır.

Literatüre baktığımızda bu konudaki bulgular genel olarak DDLTL'nin diş hareketi hızını artırdığına yöneliktir. Kawasaki ve Shimizu ile Yoshida ve ark. ratlarda yaptıkları çalışmalarda 12 ve 21 günlük sürelerde diş hareketinin 1.3 oranında arttığını bildirmişlerdir.<sup>15,16</sup> Yamaguchi ve ark. 50 Wistar ratı üzerinde yürüttükleri deneysel çalışmalarında GaAlAs (810 nm) lazer cihazı ile 54 J/cm<sup>2</sup> lazer uygulamış; ortodontik diş hareketinin hızlandığını gözlemlemişlerdir.<sup>17</sup> Fujita ve ark.nın yine ratlar üzerinde yaptıkları bir çalışmada ise 54 J/cm<sup>2</sup> lazer uygulanan gruptaki deneklerde diş hareketi miktarının ve RANKL immuno-reaktivitesinin kontrol grubuna kıyasla arttığı bulunmuştur.<sup>18</sup> Kim ve ark. köpeklerde yaptıkları bir çalışmada 2 aylık süreçte diş hareketinde 2,08 kat artış bulmuşlardır.<sup>19</sup> Goulart ve ark. yine köpeklerde yaptıkları bir çalışmada birinci grupta 3 sn. boyunca 5.25 J/cm<sup>2</sup>; ikinci grupta 25 sn. boyunca 35 J/cm<sup>2</sup> enerji yoğunluğunda lazer uygulamışlardır.<sup>20</sup> Buna göre 21 günlük sürede birinci grupta diş hareketi hızı kontrol

grubuna göre %50 oranında artarken ikinci grupta %90 azalma göstermiştir. Buna göre Goulart ve ark. köpeklerde yapılan bu çalışmada 5 J/cm<sup>2</sup> ve toplamda 1.89 J enerji yoğunluğu ile uygulanan DDLT'nin ivmelendirici etkisi olurken 35 J/cm<sup>2</sup> ve toplamda 12.6 J enerji yoğunluğu ile uygulanan DDLT'nin doku cevabını baskılayan bir biyolojik etkisi olduğunu bildirmişlerdir. Abi-Ramia ve ark. 2010 yılında yaptıkları bir çalışmada ortodontik diş hareketi ve DDLT'nin dental pulpa üzerindeki etkilerini incelemişlerdir. Fareler üzerinde yaptıkları bu çalışmada vaskülerizasyonda anlamlı bir artış bulmuşlar ve bunun pulpal doku tamirini artırabileceği çıkarımında bulunmuşlardır.<sup>21</sup>

DDLT'nin diş hareketi üzerindeki etkilerini insanlar üzerinde inceleyen çalışmalardan ilki 2004 yılında Cruz ve ark tarafından yapılmıştır.<sup>22</sup> On bir hasta ile yapılan bu çalışmada çift taraflı premolar dişi çekimini takiben kanin distalizasyonu sırasında bir taraf kontrol grubu olarak kullanılırken diğer tarafta 780 nm dalga boyu 20 mW ve 5 J/cm<sup>2</sup> yoğunluğunda 10'ar defa 10 sn. süresince ve her ay 4 kez GaAlAs diyot lazer uygulanmıştır. Lazer uygulanan kanin dişleri, kontrol grubu kanin dişlerine göre 60 günlük süreç içerisinde %34 daha hızlı retrakte olmuşlardır. Youssef ve ark. 2008 yılında 15 yetişkin birey ile benzer bir klinik çalışma yapmışlardır. Bu çalışmada lazer tarafına 809 nm, 100 mW ve 8J (bukkal ve lingualden 40'ar sn.) dozunda DDLT uygulanmış ve 6 aylık sürede lazer uygulanan taraftaki diş hareketinin kontrol tarafına göre yaklaşık 2 kat daha hızlı olduğunu bulmuşlardır.<sup>23</sup> Doshi-Mehta ve Bhad-Patil ise 2012 yılında 20 hasta ile yaptıkları bir çalışmada sürekli modda, 800 nm dalga boyu ve 0,25 mW güçte 10 sn. ışınlama süresi ile uyguladıkları DDLT'nin deneysel tarafta kanin dişinin distalizasyon hızını ilk 3 ayda kontrol tarafına göre 1,3 kat (%56 oranında) artırdığını belirtmişlerdir. Toplamda 4,5 ay süren distalizasyon süresi boyunca ise genel artışın %30 olduğunu bildirmişlerdir.<sup>24</sup> Genç ve ark. 2013 yılında 20 hasta ile yaptıkları çalışmada keser retraksiyonunun 0, 3, 7, 14, 21 ve 28. günlerinde bukkal ve palatal yüzeylerden 5'er noktadan dişlere DDLT uygulamışlardır. Bunun sonucunda DDLT'nin diş hareketini belirgin bir şekilde hızlandırdığını bulmuşlardır. Bununla birlikte dişeti oluşu sıvısında nitrik oksit seviyelerinde belirgin bir değişiklik saptamamışlardır.<sup>25</sup>

DDLT'nin diş hareketi üzerinde etkili olmadığını belirten çalışmalar da mevcuttur. Limpanichkul ve ark. 12 genç yetişkin birey ile yaptıkları çalışmada; 860 nm, 100 mW, 1.11 W/cm<sup>2</sup>, 25 J/cm<sup>2</sup> değerlerinde uyguladıkları DDLT'nin kanin distalizasyon hızında kontrol ve lazer grupları arasında herhangi bir farklılık oluşturmadığını

belirtmişler ve yüzeye uyguladıkları 25 J/cm<sup>2</sup>lik dozun hızlandırıcı ya da baskılayıcı herhangi bir etki oluşturmak için yeterli olmayabileceği sonucuna varmışlardır.<sup>26</sup> Seifi ve Shafeei, 18 Yeni Zelanda tavşanı kullanarak farklı dalga boylarında DDLT'nin diş hareketi üzerindeki etkilerini incelemişlerdir.<sup>27</sup> Birinci grupta 9 gün 850 nm lazer 100 nsn. lik atışlar halinde toplam 3 dk. uygulanmıştır. İkinci grupta ise 630 nm lazer 5 dk. boyunca aralıksız uygulanmıştır. Sonuç olarak her iki lazer grubunda da kontrol grubuna göre diş hareketinin yavaşladığı; lazer uygulanan gruplar arasında hız açısından anlamlı bir fark olmadığını belirtmişlerdir. Buna rağmen araştırmacılar, bu çalışmanın sonuçlarına dayanarak düşük doz lazerin diş hareketi hızını yavaşlattığı kanısına varılamayacağını; teorik olarak uygulanan enerji miktarının çok etkili olduğunu, dolayısıyla insanlar için önerilen dozların tavşanlar için uygun olmayabileceğini bildirmişlerdir. Long ve ark. da hızlandırılmış ortodontik diş hareketi ile ilgili yapılan çalışmaları değerlendiren sistematik derlemelerinde, DDLT'nin periodontal sağlık ve diş kökleri açısından güvenli olduğu, ve ancak diş hareketini hızlandırmadığı şeklinde bir sonuca varmışlardır.<sup>28</sup>

Literatürdeki çalışmaların bütününe bakıldığında; insanlardaki uygulama rutinlerini ve etkilerini belirginleştirmek açısından bu konuda daha fazla çalışma yapılması gerektiği sonucuna varılabilir. Bununla birlikte, periodontal dokular açısından güvenli bir yöntem olan DDLT'nin ortodontik tedavi kaynaklı diş ağrılarını azaltması, invazif olmaması, uygulama kolaylığı ve fizyolojik bir yaklaşım olması gibi özellikleri de düşünüldüğünde ortodonti alanında önemli faydaları ve kullanım alanları olacağı öngörülebilir.

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