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UTICAJ NASLEĐA NA POJAVU HIPODONCIJE I HIPERDONCIJE KOD DECE U FEDERACIJI BOSNE I HERCEGOVINE

THE INFLUENCE OF THE INHERITANCE ON THE OCCURRENCE OF HYPODONTIA AND HYPERDONTIA IN CHILDREN IN THE FEDERATION OF BOSNIA AND HERZEGOVINA

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Sažetak

Cilj: Cilj istraživanja bio je da se utvrde i međusobno uporede učestalosti hipodoncije i hiperdoncije u izabranih mestima Bosne i Hercegovine, te procene učešća naslednih faktora u registrovanoj heterogenosti.

Materijal i metode: Kao subjekat istraživanja poslužio je uzorak od 1640 dece školskog uzrasta, oba pola, od 12 do 14 godina. Uzorak je prikupljan iz pet urbanih centara u Federaciji Bosne i Hercegovine: Sarajevo, Mostar, Tuzla, Bihać i Goražd. U cilju procene razlike u broju ispitanika prema polu, kao i u proceni razlike u učestalosti posmatranih anomalija (hiperdontija i hipodoncija) primjenjen je χ^2 test sa granicom statističke značajnosti $p < 0,05$. Fišerov egzaktni test korišten je za procenu povezanosti pojave hiperdoncije i hipodoncije, između dece i roditelja. U statističkim analizama primjenjen je naučnoverifiskovani softver Ver. MedCalc 11.5.0.0.

U cilju procene distinkcije mogućih naslednih i nenaslednih faktora, izvršena je procena heritabilnosti (h), primenom regresione analize (parent-offspring regression).

Rezultati: Identifikovano je ukupno 40 dece sa anomalijama broja zuba – od toga je 16 dečaka i 24 devojčice. Nije primećena statistički značajna razlika u učestalosti hipodoncije i hiperdoncije između dečaka i devojčica, prema geografskom regionu ($\chi^2 = 0,500$; $P = 0,9735$).

Zaključak: Ukupna prevalencija hipodoncije i hiperdoncije iznosi je 2,43. Prevalencija hipodoncije je 1,58, a hiperdoncije 0,85. Relativni rizik za pojavu anomalija broja zuba kod dece iznosi 8,965 i statistički je značajan, ukazujući na to da je verovatnoća pojave navedenog poremećaja kod dece, kod koje jedan od roditelja ima istu anomaliju, veća.

Ključne reči: hipodoncija, hiperdoncija, naslede, deca, Bosna i Hercegovina

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Abstract

Purpose: The purpose of the research was to establish and mutually complement the frequency of hypodontia and hyperdontia in selected locations of Bosnia and Herzegovina, and to assess the participation of hereditary factors in the registered heterogeneity.

Respondents and Procedures: A sample of 1,640 children of school age, both sexes, aged 12–14, served as the subject of research. The sample was collected from five urban centers in the Federation of Bosnia and Herzegovina: Sarajevo, Mostar, Tuzla, Bihać and Goražde. In order to estimate the difference in the number of respondents by sex, as well as in assessing the differences in the frequency of observed anomalies (hyperdontia and hypodontia), a χ^2 test with a statistical significance limit $p < 0,05$ was applied. The Fisher Exact Test was used to assess the correlation between the occurrence of hyperdontia and hypodontia between children and parents. Scientifically verified ver. Ver. MedCalc 11.5.0.0. In order to evaluate the distinction between possible hereditary and non-positive factors, an assessment of heritability was performed (h) by applying regression analysis (parent-offspring regression).

Results: A total of 40 children with anomalies of the number of teeth were identified, of which 16 boys and 24 girls. There was no statistically significant difference in the frequency of hypodontia and hyperdontia between boys and girls with respect to geographic regions ($\chi^2 = 0,500$; $P = 0,9735$).

Conclusion: The total prevalence of hypodontia and hyperdontia was 2,43. The prevalence of hypodontia is 1,58, and the hyperdontia is 0,85. The relative risk of anomalies in the number of teeth in children is 8,965 and is statistically significant, indicating that the likelihood of the occurrence of this disorder in children whose at least one parent has the same anomaly is greater.

Key words: hypodontia, hyperdontia, heritage, children, Bosnia and Herzegovina

Uvod

Ukupna promenjivost ljudskih individua, kao i svih ostalih živih bića, određena je genetičkim i negenetičkim faktorima, odnosno genotipom i fenotipom. S obzirom na to da se u genetičkoj analizi posmatra ograničeni obim individualne promenjivosti, smatra se da se pojam genotipa odnosi i na genetičke faktore pojedinih svojstava i njihovih kombinacija^{1,2,3}.

Organizam nije prost zbir pojedinačnih osobina i elemenata, pa posedovanje jednog gena ne mora značiti da njegovi nosioci nužno imaju odgovarajuće obeležje. Razvojne faze u formiranju bilo kog organa, uključujući i zube, obuhvataju niz zbijanja, koja se uopšteno mogu nazvati indukcija skupine ćelija, migracija ćelija, interakcija ćelija sa novom sredinom i diferencijacija u nova tkiva^{4,5}. U svakoj od razvojnih faza mogu nastati poremećaji, a posledice su različite pojave abnormalnosti zuba^{9,10,11}. Većina odontogenskih studija, koje su koristile denticiju miševa kao model razvoja, pokazale su to da poziciju, broj, dimenziju i oblik nekoliko zuba kontroliše kompleksni sistem gena, čija modifikacija može uzrokovati zubne anomalije. Različite anomalije mogu se dogoditi i u zavisnosti od razvojnog stadijuma, u kojem se promena dešava: anomalije broja zuba (hiperdoncija i hipodoncija), strukturalne abnormalnosti i slično (14, 15, 16).

Glavne polazne intencije preduzetih istraživanja bile su:

- procena učestalosti hipodoncije i hiperdoncije kod dece školskog uzrasta u Federaciji Bosni i Hercegovini;

- diferencijacija relativnog udela naslednih i nenaslednih faktora u fenotipskoj ekspresiji hipodoncije i hiperdoncije;

- procena moguće anticipacije hipodoncije i hiperdoncije između generacija roditelja i potomaka.

Introduction

The total variability of human individuals as well as all other living beings is determined by genetic and non-genetic factors, that is, genotype and phenotype. Given that a limited extent of individual variability is observed in the genetic analysis, it is considered that the term genotype also refers to the genetic factors of certain properties and their combinations^{1,2,3}.

The organism is not a simple set of unique properties and elements, so the possession of a single gene does not have to mean that its carriers necessarily have an appropriate character. Developmental phases in the formation of any organ, including the teeth, include a series of events, which can generally be termed cell group induction, cell migration, cellular interaction with a new medium, and differentiation into new tissues^{4,5}. Disturbances may occur in each of the developmental phases, and the consequences are different in the abnormalities of the teeth⁶. Most of the odontogenic studies using dentition in mice as a model of development have shown that the position, number, dimension and shape of several teeth control the complex system of the genes whose modification can cause dental anomalies. Different anomalies may occur depending on the developmental stages in which the change occurs: anomalies in the number of teeth hyperdontia and hypodontia, structural abnormalities, and the like^{7,8}.

The main starting points of the research undertaken were:

- Estimation of the frequency of hypodontia and hyperdontia in children of school age in the Federation of Bosnia and Herzegovina

- Differentiation of the relative share of hereditary and non-persistent factors in the phenotypic expression of hypodontia and hyperdontia.

- Estimation of the possible anticipation of hypodontia and hyperdontia between generations of parents and offspring

Ispitanici i metode

Za istraživanje bila su odabrana deca školskog uzrasta, starosti od 12 do 14 godina, sa stalnom denticijom. Za svakog ispitanika uzeti su detaljni anamnistički podaci i evidentirani su u individualne kartone. Polazeći od činjenice da nasledni faktori igraju veliku ulogu u nastanku dentalnih anomalija, urađena je i porodična anamneza, sa ciljem utvrđivanja postojanja eventualne anticipacije posmatranih pojedinih anomalija, između generacija srodnika i potomaka.

Ovim radom obuhvaćeno je 1640 dece u kantonalnim centrima Sarajeva, Tuzle, Goražda, Mostara i Bihaća. (Slika 1). Ukupan broj dece i broj dece po polu školskog uzrasta pregledanih u Federaciji Bosne i Hercegovine prikazan je u tabeli 1.

U cilju procene razlike u broju ispitanika prema polu (dečaci i devojčice), kao i u proceni razlika u učestalosti posmatranih anomalija (hiperdoncija i hipodoncija) primenjen je χ^2 test sa granicom statističke značajnosti $p < 0,05$. Isti test korišćen je za procenu razlika učestalosti prema lokaciji hiperdoncije i hiperdoncija, kao i u proceni razlika u prevalenciji ovih poremećaja između ispitanika iz FBiH i ostalih evropskih i svetskih populacija prikazanih u prethodnim studijama.

Fisherov egzaktni test korišćen je za procenu povezanosti pojave hiperdoncije i hipodoncije kod dece i roditelja. Signifikantni nivo statističke značajnosti iznosio je $p < 0,05$.

U statističkim analizama primenjen je naučnoverifikovani softver Ver. MedCalc 11.5.0.0 (*MedCalc Software, Maria*). U cilju procene distinkcije mogućih naslednih i nenaslednih faktora izvršena je procena heritabilnosti (h), primenom regresione analize (*parent-offspring regression*).

Respondents and methods

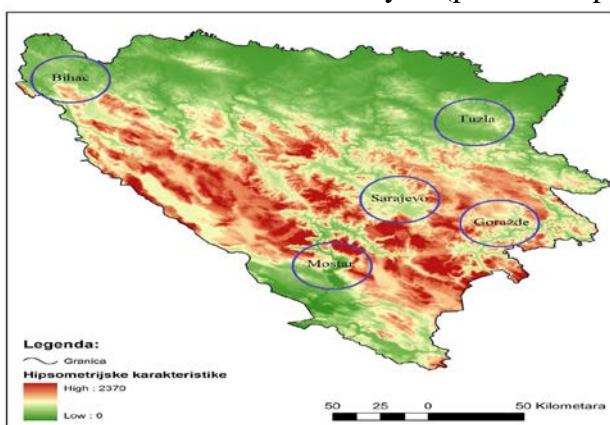
For the research, children of school age aged 12–14 years with permanent dentition were selected. For each respondent, detailed anamnestic data was taken and recorded in individual cartons. Starting from the fact that hereditary factors play a major role in the onset of dental anomalies, a family history was also made to determine the possible anticipation of the observed individual anomalies between the generations of relatives and offspring.

This work covers 1,640 children in cantonal centers: Sarajevo, Tuzla, Gorazde, Mostar and Bihać (Figure 1). The total number and number of children by sex of school age examined in the Federation of Bosnia and Herzegovina is shown in Table 1.

In order to estimate the difference in the number of respondents by sex (boys boys), as well as in assessing the differences in the frequency of the observed anomalies (hyperdontia and hypodontia), χ^2 test with a statistical significance limit $p < 0,05$ was applied. The same test was used to estimate the frequency differences according to the location of hyperdontia and hypodontia, as well as in estimating the differences in the prevalence between FBiH and other European and world populations described in the previous studies.

Fischer's exact test was used to assess the correlation between the occurrence of hyperdontia and hypodontia between children and parents. Significant level of statistical significance was $p < 0,05$.

Scientifically verified ver. Ver. MedCalc 11.5.0.0 (*MedCalc Software, Maria*). In order to evaluate the distinction between possible hereditary and non-positive factors, an assessment of heritability was performed (h) by applying regression analysis (*parent-offspring regression*).



Slika 1. Geografski položaj obuhvaćenih kantonalnih centara
Figure 1. Geographical location of the cantonal centers covered

Tabela 1. Ukupan broj i broj dece po spolu školskog uzrasta pregledanih u Federaciji Bosne I Hercegovine

Table 1. Total number and number of children by sex of school age examined in the Federation of Bosnia and Herzegovina

Grad City	Ukupan broj pregledane dece Total number of children examined	Broj dečaka Number of boys	%	Broj devojčica Number of girls	%
Sarajevo	335	210	63	125	37
Tuzla	328	134	41	194	59
Goražde	320	115	36	205	64
Mostar	325	175	54	150	46
Bihać	332	208	63	124	37
Ukupno Total	1640	843	51	802	49

Rezultati

Pregledom su obuhvaćeni učenici i učenice, čiji odnos nije bio podjednak, zbog razlika u polnoj strukturi pojedinih mesta. Broj dečaka varira od 115 ili 36%, koliko je obuhvaćeno pregledom u Goraždu, do 210 ili 63%, od ukupnog broja učenika u Sarajevu.

Drugacija je slika kada je reč o ženskoj populaciji; najmanje ih je pregledano u Bihaću i Sarajevu 124, odnosno 125, što je 37%, a najviše u Goraždu, 205 ili 64%, od ukupne školske populacije (Slika 2, Slika 3).

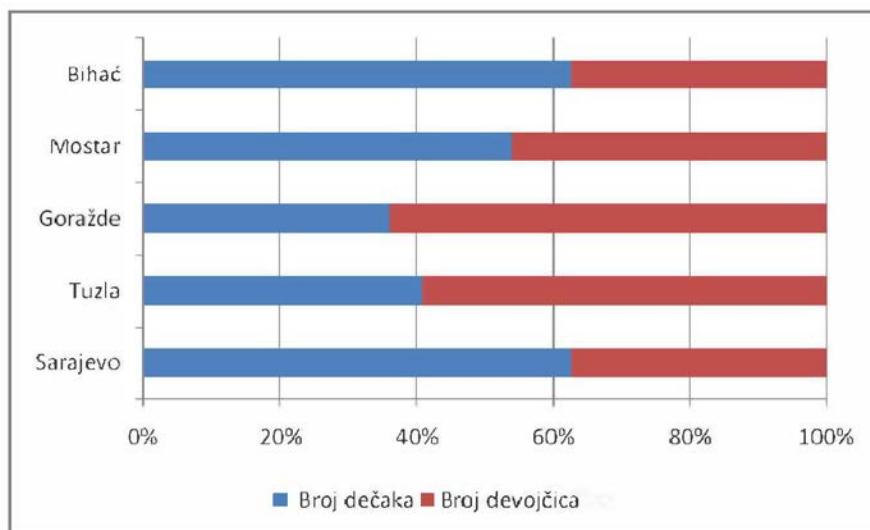
Ukupno je identifikovano 40 dece sa anomalijama broja zuba, od čega 16 dečaka i 24 devojčice. Nije primećena statistički značajna razlika u ukupnoj učestalosti navedenih poremećaja između dečaka i devojčica (Tabela 2 i Slika 4). Takođe, nije primećena statistički značajna razlika u učestalosti navedenih anomalija, shodno geografskim regionima ($\chi^2 = 0,500$; $P = 0,9735$).

Results

The survey covered students and pupils, both sexes, whose relationship was not the same, because of differences in the sexual structure of particular places. The number of boys varied from 115 or 36%, which was included in the examination in Gorazde to 210 or 63% of the total number of students in Sarajevo.

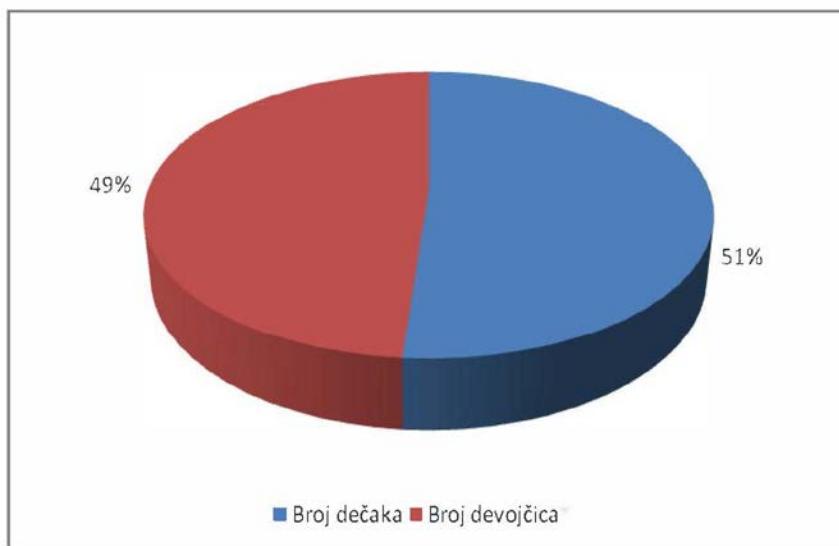
A different picture is with the female population; at least 124 were surveyed in Bihać and Sarajevo 124, or 125, which is 37%, and most in Gorazde 205 or 64% of the total school population. This relationship of geographical distribution in the Federation of Bosnia and Herzegovina can best be seen in the annexes of Figure 2 and Figure 3.

In total, 40 children with teeth anomalies were identified, of which 16 boys and 24 girls (Table 7 and Figures 33 and 34). There was no statistically significant difference in the overall incidence of these disorders between boys and girls (Table 4 and Figure 33). Also, a statistically significant difference in the frequency of the mentioned anomalies with respect to the geographic region ($\chi^2 = 0.500$; $P = 0.9735$) was not observed.



Slika 2. Procentualna spolna distribucija dece školskog uzrasta prema navedenim centrima u Federaciji Bosne i Hercegovine

Figure 2. Percentage sexual distribution of children of school age according to the mentioned centers in the Federation of Bosnia and Herzegovina

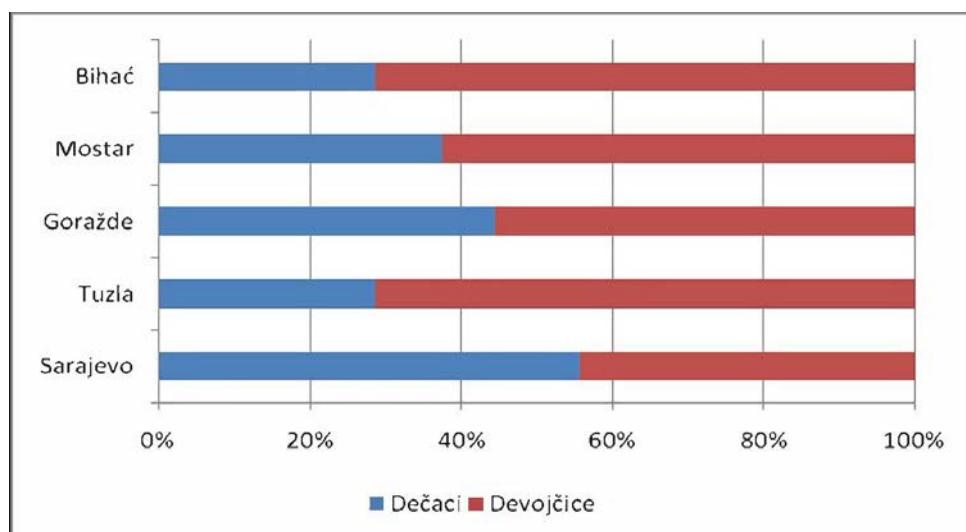


Slika 3. Procentualna spolna distribucija pregledanih učenika prema istraživanim mestima u Federaciji Bosne i Hercegovine

Figure 3. Percentual sexual distribution of examined pupils by research sites in the Federation of Bosnia and Herzegovina

Tabela 2. Ukupan broj dece sa anomalijama broja zuba u gradovima Federacije Bosne i Hercegovine**Table 2.** Total number of children with teeth anomalies in the cities of the Federation of Bosnia and Herzegovina

Grad City	Ukupan broj dece sa hipodoncijom i hiperdoncijom Total number of children with hypodontia and hyperdonia Boys	Dečaci Boys	Devojčice Girls	Razlika između dečaka i devojčica The difference between boys and girls
Sarajevo	9	5	4	$\chi^2=0.0000$ P=0.9996
Tuzla	7	2	5	$\chi^2=1.138$; P=0.2860
Goražde	9	4	5	$\chi^2=0.0000$; P=0.9996
Mostar	8	3	5	$\chi^2=0.250$; P=0.6171
Bihać	7	2	5	$\chi^2=1.138$; P=0.2860
Ukupno Total	40	16	24	$\chi^2=2.450$; P=0.1175

**Slika 4.** Procentualna spolna distribucija dece sa anomalijama broja zuba**Figure 4.** Percentage sexual distribution of children with teeth anomalies

Hipodoncija je primećena kod 26 dece – kod 11 dečaka i 15 devojčica. Nije primećena statistički značajna razlika u ukupnoj učestalosti hipodoncije između dečaka i devojčica. Takođe, nije primećena statistički značajna razlika u učestalosti hipodoncije, shodno geografskim regionima ($\chi^2 = 0,2462$; $P = 0,6515$). (Tabela 3, Slika 5).

Ukupno, detektovano je 14 dece sa hiperdoncijom, 6 dečaka i 8 devojčica. Nije primećena statistički značajna razlika u ukupnoj učestalosti hiperdoncije između dečaka i devojčica (Tabela 4 i Slika 6), kao ni razlika u učestalosti navedenih anomalija, shodno geografskim regionima ($\chi^2 = 1,000$; $P = 0,258$).

Primena Fišerovog egzaktnog testa, takođe, ukazuje na statistički značajnu povezanost pojave anomalija broja zuba i prisutnosti istih poremećaja kod roditelja ($P = 0,000432$). Primenom pomenutog testa, utvrđeno je da 42% dece, kod kojih je primećena anomalija broja zuba (hipodoncija ili hiperdoncija), ima barem jednog roditelja sa istim poremećajem, dok u slučaju dece bez navedenih poremećaja samo 5% dece ima jednog od roditelja sa anomalijom broja zuba (Slika 7). Kada se posmatra samo hipodoncija, zabeležena je statistički značajna povezanost pojave hipodoncije i prisutnosti iste anomalije kod roditelja ($P = 0,016002$). Od ukupnog broja dece, kod kojih je zabeležena hipodoncija, 50% ima bar jednog roditelja sa istim poremećajem, dok u slučaju dece kod kojih nije detektovana hipodoncija samo 6,67% roditelja ima ovu anomaliju. (Slika 8).

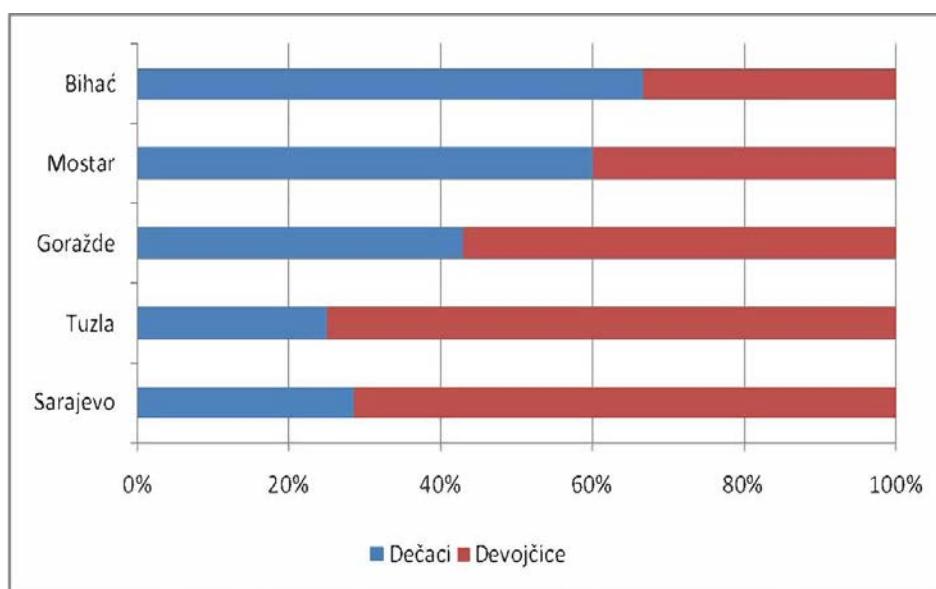
Kod hiperdoncije, nije uočena statistički značajna povezanost pojave ove anomalije i prisutnosti iste kod roditelja ($P = 0,061246$). Od ukupnog broja dece kod koje je zabeležena hiperdoncija, 27% ima bar jednog roditelja sa istom anomalijom, dok u slučaju dece kod koje nije detektovana hiperdoncija, 3% ima jednog roditelja sa hiperdoncijom (Slika 9).

Hypodontia was observed in 26 children, of which 11 boys and 15 girls (Table 3 and Figure 5).

A total of 14 children with hyperdontia were detected, of which 6 boys and 8 girls. No statistically significant difference was observed in the overall incidence of hyperdependence between boys and girls (Table 4 and Figure 6), nor the difference in the frequency of the abnormalities mentioned with respect to the geographic region ($\chi^2 = 1,000$; $P = 0,258$).

The use of Fischer's exact test also indicated a statistically significant relationship between the occurrence of anomalies in the number of teeth and the presence of the same parental disorders ($P = 0,000432$). Using this test, it was found that 42% of children with an anomaly of the number of teeth (hypodontia or hyperdontia) had at least one parent with the same disorder, while in the case of children without these disorders, only 5% of children had one of the parents with an anomaly of the number of teeth (Figure 7). When only hypodontia is observed, a statistically significant relationship between the occurrence of hypodontia and the presence of the same anomaly in the parent was observed. ($P = 0,016002$). Of the total number of children with hypodontia, 50% had at least one parent with the same disorder, while in the case of children with no hypodontia detected, only 6,67% of parents had the same anomaly (Figure 8).

A statistically significant relationship between the occurrence of this anomaly and the presence of the same in the parent was not observed in hyperdontia ($P = 0,061246$). Of the total number, 27% of children with a hyperdependence had at least one parent with the same anomaly, while 3% of children with no hyperdontia detected had one parent with hyperdontia (Figure 9).



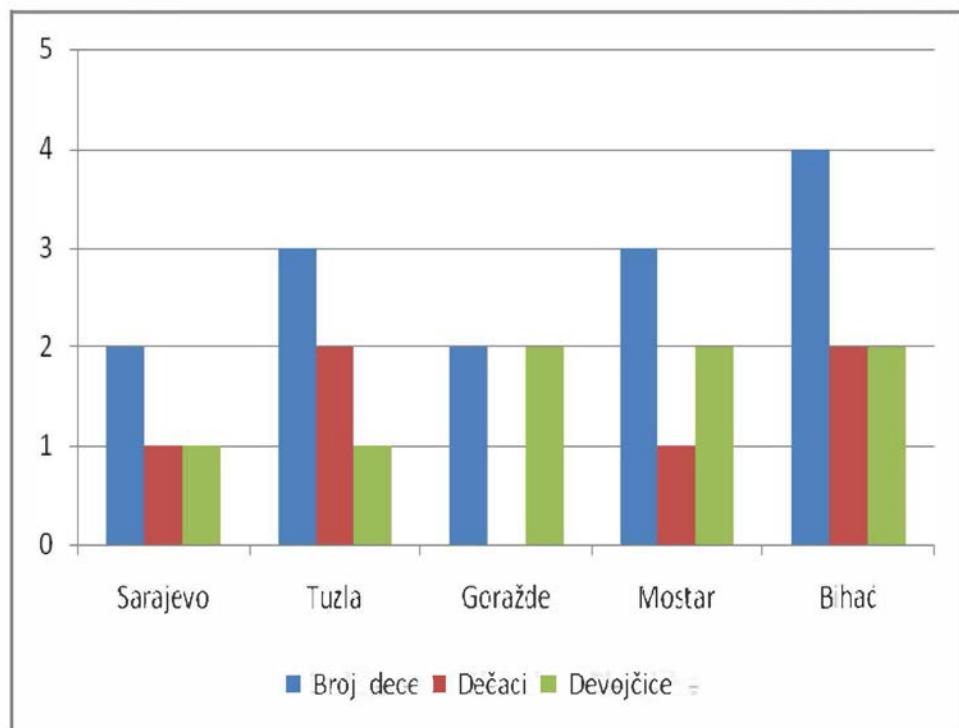
Slika 5. Procentualna spolna distribucija dece sa hipodoncijom

Figure 5. Percentage sexual distribution of children with hypodontia

Tabela 3. Tabelarni prikaz učestalosti hipodoncije u gradovima u Federaciji Bosne i Hercegovine

Table 3. Tabular presentation of the frequency of hypodontia in cities in the Federation of Bosnia and Herzegovina

HIPODONCIJA HYPODONTIA	Broj dece Number of children	Dečaci Boys	Devojčice Girls	Razlika između dečaka i devojčica The difference between boys and girls
Sarajevo	7	2	5	$\chi^2=1.138; P=0.2860$
Tuzla	4	1	3	$\chi^2=0.500; P=0.4795$
Goražde	7	3	4	$\chi^2=0.000; P=0.9974$
Mostar	5	3	2	$\chi^2=0.000; P=1.0000$
Bihać	3	2	1	$\chi^2=0.000; P=0.9999$
Ukupno Total	26	11	15	$\chi^2=0.692; P=0.4054$



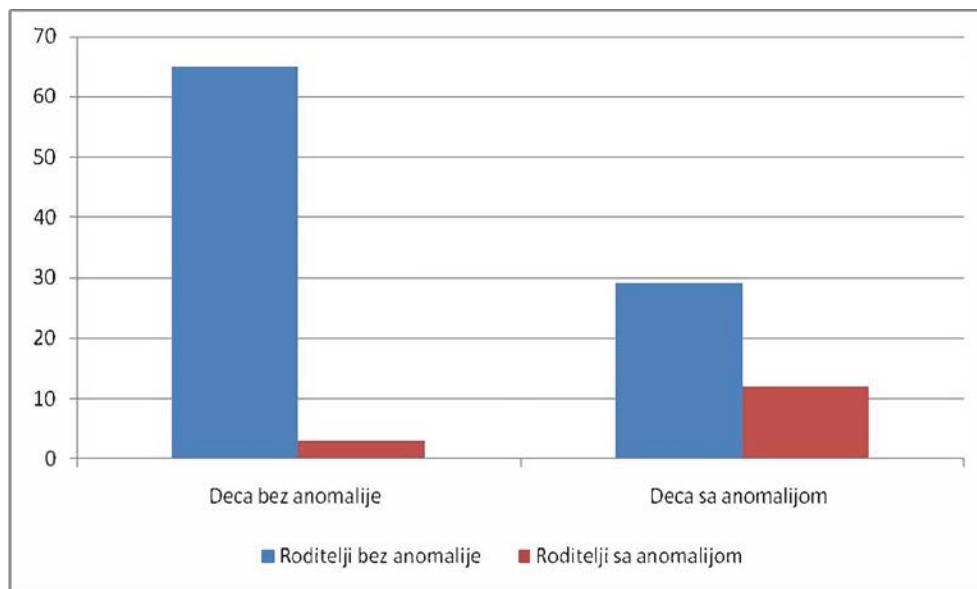
Slika 6. Grafički pregled geografske distribucije učestalosti hiperdoncije kod pregledane dece i dece prema spolu

Figure 6. Graphical overview of the geographical distribution of the frequency of hyperdontia in the surveyed children and children by sex

Tabela 4. Tabelarni prikaz učestalosti hiperdoncije po gradovima u FBIH

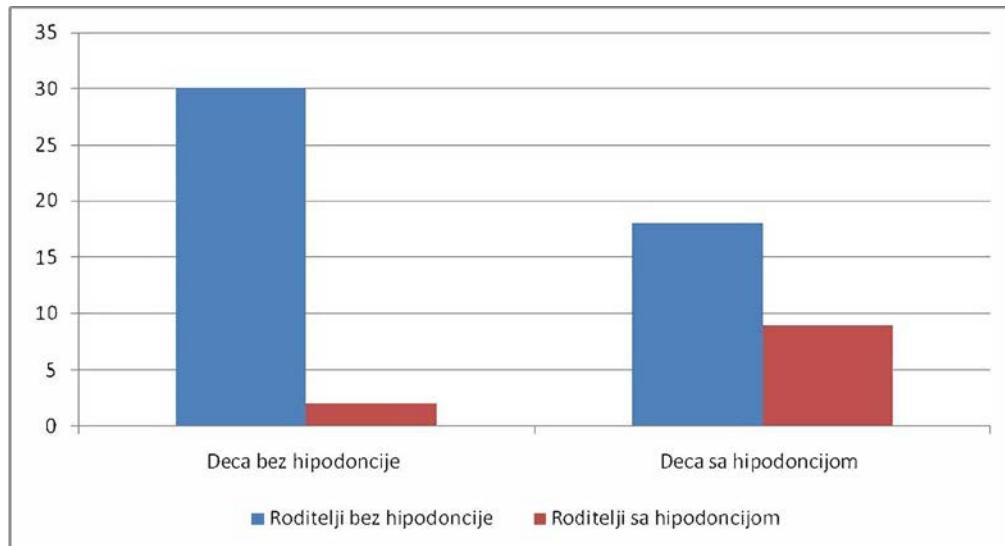
Table 4. Tabular overview of frequency of hyperdontia by city in FBIH

HIPERDONCIJA HYPERDONTIA	Broj dece Number of children	Dečaci Boys	Devojčice girls	Razlika između dečaka i devojčica The difference between boys and girls
Sarajevo	2	1	1	$\chi^2=1.000; P = 0.3173$
Tuzla	3	2	1	$\chi^2=0.000; P=0.9999$
Goražde	2	0	2	$\chi^2=1.000; P = 0.3173$
Mostar	3	1	2	$\chi^2=0.000; P=0.9999$
Bihać	4	2	2	$\chi^2=0.500; P = 0.4795$
Ukupno Total	14	6	8	$\chi^2=0.143; P = 0.7049$



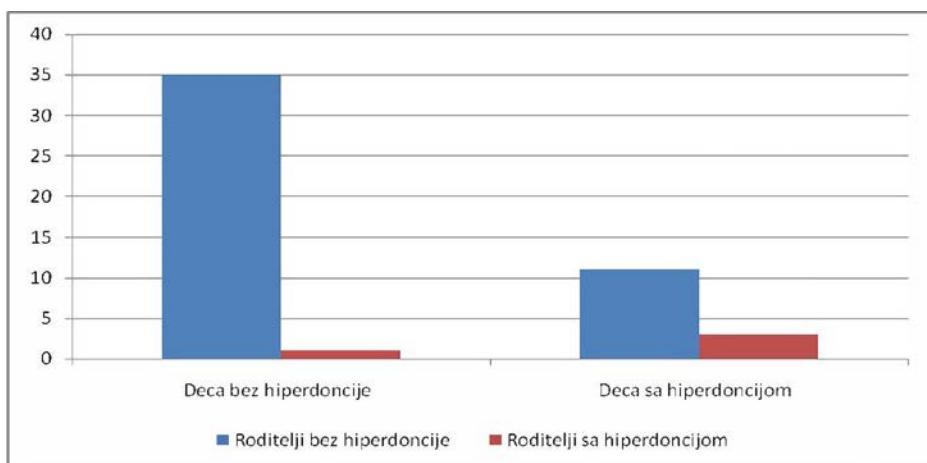
Slika 7. Učestalost pojave anomalija broja zuba kod dece s obzirom na prisutnost kod roditelja

Figure 7. Frequency of anomalies in the number of teeth in children due to the presence of parents



Slika 8. Učestalost pojave hipodoncije kod dece s obzirom na prisutnost kod roditelja

Figure 8. Frequency of hypodontia in children with regard to presence in parents



Slika 9. . Učestalost pojave hiperdoncije kod dece s obzirom na prisutnost kod roditelja

Figure 9. The frequency of hyperdontia in children with regard to the presence of parents

Diskusija

Odontogeneza zuba razvija se putem dobro organizovane serije induktivnih događaja, uključujući gene i signalne molekule, koji predstavljaju glavne signalne puteve, pomoću kojih se regulišu epitelno-mezenhimne interakcije. Napredak u genetici i molekularnoj biologiji upućuje na to da više od 300 gena učestvuje u raznim fazama razvoja zuba.

Mutacije pojedinih gena, hromozoma i njihovih delova, odgovornih za ranu fazu morfogeneze zuba, mogu nastati kao posledica materijalnih promena u hemijskoj strukturi i kvantitetu genetičke informacije (DNK) i, kao takvi, delovati na molekule i mreže za signalizaciju, koje regulišu njegov razvoj. Efekti tih mutacija su manje ili više fenotipski vidljivi, zavisno od količine zahvaćenog genetičkog materijala.

U pomenutom istraživanju, identifikovano je 40 dece sa hipodoncijom i hiperdoncijom – 16 dečaka i 24 devojčice. Procentualna polna distribucija dece sa anomalijama broja zuba, u istraživanim mestima, u Federaciji Bosne i Hercegovine iznosi 60% devojčica i 40% dečaka.

Ukupna razlika između učestalosti hipodoncije kod dečaka i devojčica, prema gradovima u FBiH iznosi $\chi^2 = 0,692$; $P = 0,4054$.

Prema ovim podacima, može se konstatovati da nema statistički značajne razlike u ukupnoj učestalosti hipodoncije između dečaka i devojčica, prema gradovima u Federaciji Bosne i Hercegovine. Takođe, nije primećena značajna razlika ni u učestalosti hipodoncije, shodno posmatranim geografskim regionima, u kojima su prikupljeni podaci ($\chi^2 = 0,2462$; $P = 0,6515$).

Discussion

Teeth odontogenesis develops through a well-organized series of inductive events involving genes and signaling molecules that represent the main signaling pathways that regulate epithelial-mesenchymal interactions. Progress in genetics and molecular biology suggests that more than 300 genes participate in various stages of tooth development.

Mutations of certain genes, chromosomes, and their parts responsible for the early phase of morphogenesis of the tooth may be the result of material changes in the chemical structure and quantity of genetic information (DNA), and as such affect the molecules and signaling networks that regulate its development. The effects of these mutations are more or less phenotypically visible, depending on the amount of genetic material affected.

In this research, 40 children with hypodontia and hyperdontia were identified, of which 16 boys and 24 girls. The gender distribution percentage of children with teeth anomalies in the investigated places in the Federation of Bosnia and Herzegovina is 60% of girls and 40% of boys.

The total difference in the frequency of hypodontia between boys and girls in the FBiH cities is $\chi^2 = 0.692$; $P = 0.4054$

According to these data, it can be concluded that there is no statistically significant difference in the overall frequency of hypodontia between boys and girls in the cities of the Federation of Bosnia and Herzegovina. In addition, there was no significant difference in the frequency of hypodontia with respect to the geographical regions in which the data were collected ($\chi^2 = 0.2462$; $P = 0.6515$).

Ukupna razlika između učestalosti hiperdoncije kod dečaka i devojčica, prema gradovima u FBiH iznosi: $\chi^2 = 0,14$; $P = 0,7049$.

Iz prezentovanih podataka može se konstatovati da nema statistički značajne razlike u ukupnoj učestalosti hiperdoncije između dečaka i devojčica, prema obrađenim mestima u Federaciji Bosne i Hercegovine.

Takođe, nije primećena značajna razlika u učestalosti hiperdoncije, shodno geografskim regionima, kojima pripadaju obrađena mesta u Federaciji Bosne i Hercegovine ($\chi^2 = 1,000$; $P = 0,258$).

Imajući u vidu da su genetički faktori krucijalni u nastanku hiperdoncije i hipodoncije, očekivano je da nema ni razlike između navedenih populacija, u pogledu učestalosti anomalija broja zuba. S obzirom na to da različiti gradovi imaju relativno diferencirane geografske karakteristike, kao i nivo polutanata, kao mogućih mutagena, možemo indirektno zaključiti da ti faktori nisu imali presudni uticaj na učestalost pojave hiperdoncije i hipodoncije.

Ukupna prevalencija (%) dece sa anomalijama broja zuba iznosi 2,43. Kod hipodoncije, prevalencija (%) iznosi 1,58, a kod hiperdoncije 0,85. Poredjenje procenjene prevalecnije hipodoncije, u ovoj studiji sa vrednostima prevalencije preuzetih iz relevantnih svetskih studija, ukazuje na statistički značajnu razliku u odnosu na sve posmatrane populacije. Iste takve komparacije vezane za hiperdonciju ukazuju na to da prevalencija ovog poremećaja u bosanskohercegovačkoj populaciji, u principu, ne odstupa statistički značajno od zabeleženih prevalencija u evropskoj populaciji i populaciji SAD („belačka populacija”), dok je u komparaciji sa azijskim populacijama i populacijama SAD („afroamerička populacija”) primećena značajna razlika. U slučaju komparacije sa španskom populacijom, treba naglasiti da, iako je zabeležena statistički značajna razlika u prevalenciji, ona se može pripisati veoma velikoj razlici u uzorku, budući da je u studiji španske populacije ispitano 36057 individua. Ukoliko se broj ispitanih sa navedenom prevalencijom „svede” na približan broj tretiranih u ovome radu (1640), nije zabeležena statistički značajna razlika u prevalencijama hiperdoncije (Tabele 5 i 6).

Statistička obrada podataka primenom Fišerovog egzaktnog testa ukazuje na sledeće:

The total difference in the frequency of hyperdontia between boys and girls in the FBiH cities is: $\chi^2 = 0.14$; $P = 0.7049$.

From the presented data, it can be concluded that there is no statistically significant difference in the overall frequency of hyperdontia between boys and girls in the treated areas in the Federation of Bosnia and Herzegovina.

Further, there was no significant difference in the frequency of hyperdontia with regard to the geographical regions to which the treated sites in the Federation of Bosnia and Herzegovina belong ($\chi^2 = 1.000$; $P = 0.258$).

Bearing in mind that the genetic factors are crucial in the emergence of hyperdontia and hypodontia, it is to be expected that there is no difference between these populations in the frequency of anomalies in the number of teeth. Given that different cities have relatively differentiated geographical characteristics, as well as levels of pollutants as potential mutagens, we can indirectly conclude that these factors did not have a decisive influence on the frequency of the occurrence of hyperdontia and hypodontia.

The total prevalence (%) of children with anomalies of the number of teeth is 2.43. In hypodontia, the prevalence (%) is 1.58 and in hyperdontia is 0.85. By comparing the estimated prevalence of hypodontia in this study with the prevalence values from the relevant studies published worldwide, there is a statistically significant difference in relation to all observed populations. The same comparisons for hyperdontia indicate the prevalence of this disorder in the Bosnian population in principle does not deviate statistically significantly from those recorded in the European and US population ("white population"), while in comparison with the Asian and US population ("African American population"), there is a significant difference. In the case of comparison with the Spanish population, it should be emphasized that, although a statistically significant difference in prevalence was noted, it can be attributed to a very large difference in the sample, where 36.057 individuals were examined in the study of the Spanish population. If the number of subjects with the stated prevalence is "reduced" to the approximate number of the treated in this paper (1.640), no statistically significant difference in the prevalence of hyperdontia was recorded (Table 5, 6).

Statistical data processing using Fisher Exact Test indicates the following:

- 42% dece, kod kojih je primećena anomalija broja zuba, ima barem jednog roditelja sa istom anomalijom;
 - u slučaju dece bez navedenih poremećaja, samo 5% dece ima nekog od roditelja sa anomalijom broja zuba.
- Iz navedenih rezultata može se zaključiti da postoji statistički značajna povezanost pojave anomalija broja zuba kod dece i prisutnosti istih kod roditelja ($P = 0,000432$).

- 42% of children with anomalies in the number of teeth have at least one parent with the same disorder

- In the case of children without these disorders, only 5% of children have one of the parents with anomalies in the number of teeth.

From the above results, it can be concluded that there is a statistically significant association between the occurrence of anomalies in the number of teeth in children and the presence of the same anomalies in the parents ($P = 0.000432$).

Tabela 5. Prikaz prevalence hipodontije iz prethodnih studija i usporedba sa Bosanskohercegovačkom školskom populacijom

Table 5. An overview of the prevalence of hypodontia from previous studies and a comparison with the Bosnian-Herzegovinian school population

Populacija i lokacija Population and location	Reference References	Broj pregledane dece Number of children examined	Prevalenca Prevalence (%)	X2 test (usporedba sa našim podacima) (comparison with our data)	P vrednost P value
Hong Kong Hong kong	Davis (1983)	1093	6.9	Razlika Difference % = 5.320 $\chi^2 = 50.607$	$P < 0.0001$
Japan Japan	Endo et al. (2006)	3358	8.5	Razlika Difference % = 6.920 $\chi^2 = 89.347$	$P < 0.0001$
Danska Denmark	Rølling (1980)	3325	7.8	Razlika Difference % = 6.220 $\chi^2 = 77.490$	$P < 0.0001$
Saudijska Arabija Saudi Arabia	Al-Emran (1990)	500	4.0	Razlika Difference % = 2.420 $\chi^2 = 9.578$	$P = 0.0020$
Irska Ireland	O'Dowling et McNamara (1990)	3056	11.3	Razlika Difference % = 9.720 $\chi^2 = 137.471$	$P < 0.0001$
Švedska Sweden	Blackman and Wahlin (2001)	739	7.4	Razlika Difference % = 5.820 $\chi^2 = 51.041$	$P < 0.0001$
Jordan Jordan	Albashaireh et Khader (2006)	1045	5.5	Razlika Difference % = 3.920 $\chi^2 = 31.399$	$P < 0.0001$
Turska Turkey	Altug-Atac et Erdem (2007)	3403	2.6	Razlika Difference % = 1.020 $\chi^2 = 4.753$	$P = 0.0292$
Kenija Kenya	Ng'ang'a et Ng'ang'a (2001)	618	6.3	Razlika Difference % = 4.720 $\chi^2 = 34.228$	$P < 0.0001$

Tabela 6. Prikaz prevalence hiperdoncije iz prethodnih studija i usporedba sa Bosanskohercegovačkom školskom populacijom

Table 6. Prevalence of hyperdontia prevalence from previous studies and comparison with Bosnian-Herzegovinian school population

Populacija i lokacija Population and location	Reference References	Broj pregledane dece Number of children examined	Prevalenca Prevalence (%)	X2 test (usporedba sa našim podacima) (comparison with our data)	P vrednost P value
Hong Kong Hong Kong	Davis (1987)	1093	2.7	Razlika Difference % = 1.850 $\chi^2 = 13.212$	P = 0.0003
USA ¹	Buenaviaje et Rapp (1984) *	2439	0.5	Razlika Difference % = 0.350 $\chi^2 = 1.379$	P = 0.2402
Švedska Sweden	Bäckman et Wahlin (1984)	739	1.9	Razlika Difference % = 1.050 $\chi^2 = 3.976$	P = 0.05
Španija Spain	Fernández Montenegro et al. (2006)	36057	0.4	Razlika Difference % = 0.450 $\chi^2 = 6.581$	P = 0.0103
Turska Turkey	Altug-Atac et Erdem (2007)	3403	0.4	Razlika Difference % = 0.450 $\chi^2 = 3.343$	P = 0.0675
USA ²	Harris et Clark (2008) *	1100	0.6	Razlika Difference % = 0.250 $\chi^2 = 0.269$	P = 0.6043
USA ³	Harris et Clark (2008)**	600	6.0	Razlika Difference % = 5.150 $\chi^2 = 51.204$	P < 0.0001
Mađarska	Gábris et al. (2006)	2219	1.5	Razlika Difference % = 0.650% $\chi^2 = 2.786$	P = 0.0951

Zaključak

Prethodni nalazi jasno sugeriju na zaključak, u kome se ističe to da hipodoncija i hiperdoncija, genetički uzrokovane, imaju visok stepen heritabilnosti i relativno heterogene modele nasleđivanja. Na njihovo fenotipsko ispoljavanje nedvosmisleno utiču i opšti, geografski i ostali faktori, kao i faktori okruženja. Može se konstatovati da je poznavanje prirode i složenosti modela genetičke kontrole nasledne komponente hipodoncije i hiperdoncije još uvek nepotpuno i da je u narednim istraživanjima neophodno prikupljanje bogatijih, relevantnih genealoških podataka.

Conclusion

Previous findings clearly suggest that hypodontia and hyperdontia as well as periodontal disease genetically caused have a high degree of heritability and relatively heterogeneous inheritance patterns. Their phenotypic expression is undoubtedly influenced by general geographic and other environmental factors. It can also be noted that the knowledge of the nature and complexity of the genetic control model of the hereditary component of the observed dental anomalies is still incomplete and that in the subsequent research it is necessary to collect richer funds of relevant genealogical data.

LITERATURA / REFERENCES

1. Matalova E, Fleischmannova J, Sharpe PT, Tucker AS., Tooth agenesis: from molecular genetics to molecular dentistry. *J Dent Res* 2008;87(7):617-23.
2. Mattheeuws N, Dermaut L, Martens G., Has hypodontia increased in Caucasians during the 20th century A metaanalysis. *Eur J Orthod* 2004;26:99-103.
3. Arte S., Phenotypic and Genotypic Features of Familial Hypodontia. Academic Dissertation, University of Helsinki, 2001.
4. Hadžiselimović R., N. Pojskić., Uvod u humanu imunogenetiku. Ingeb, 2005 Sarajevo;
5. Harris EF Dental development and anomalies craniosynostosis and facial clefting. New York. Wiley-Liss, Inc., 425-467, 2002.
6. Pemberton T. J., Gee J., Pragna I., Patel P. I., Gene discovery for dental anomalies. *J. Am. Dental Assoc.*, 137: 743-752, 2006.
7. Khalaf K, Robinson DL, Elcock C, Smith RN, Brook AH, Determination and comparison of size variables of upper central incisors in patients with supernumerary teeth. In: Brook A, editor. *Dental morphology*. UK: Sheffield Academic Press Ltd.; 2001. p. 343—50.
8. Hewson A, McCue J, Kavanagh P, McNamara T. Supernumerary central incisor: orthodontic management. *J Ir Dent Assoc* 1995; 41:34-5.
9. Jumlongrangs D, Lin JY, Chapra A, Seidman CE, Seidman RL, Maas RL, et al., A novel missense mutation in the paired domain causes nonsyndromic oligodontia. *Hum Genet* 2004; 114:242.
10. Kim J-W, Simmer JP, Lin BP-J, Hu JC-C., Novel Msx1 frameshift causes autosomal-dominant oligodontia. *J Dent Res* 2006; 85:267-71.
11. Klein ML, Nieminen P, Lammi L, Niebuhr E, Kreiborg S. Novel Mutation of the Initiation Codon of PAX9 Causes Oligodontia. *J Dent Res* 2005; 84: 43-7.
12. Koch G., Sven Poulsen S., *Pediatric Dentistry – A Clinical Approach*. Blackwell Science Ltd, Oxford, 2003.
13. Konjhodžić-Raščić H., Vuković A., Zukić S., Bajsman A., Prcić A., Dental anomalies among Students of Faculty of Dentistry, University of Sarajevo. *Clinical Science*, 2006.
14. Mostowska A, Kobiela A, Trzeciak WH., Molecular basis of non-syndromic tooth agenesis: mutations of MSX1 and PAX9 reflect their role in patterning human dentition. *Eur J Oral Sci* 2003;11:365-70.
15. Muhammad A, Fazal R, Masoom Y., A novel missense mutation in the ectodysplasin-A (EDA) gene underlies X-linked recessive nonsyndromic hypodontia. *Int J Dermatol* 2010;49:1399-402.
16. Morphogenetic fields within the human dentition: a new, clinically relevant synthesis of an old concept. *Arch Oral Biol* 2009;54:s34–44.
17. Rajab LD, Hamdan MAM., Supernumerary teeth: review of the literature and a survey of 152 cases. *Int J Paediatr Dent* 2002;12:54.
18. Slavkin HC., The human genome, implication for oral health and diseases, and dental education. *J Dent Educ* 2001;65:463-79. 122. Mossey PA, Orth
19. Suda N, Hattori M, Kosaki K, Banshodani A, Kozai K, Tanimoto K, et al., Correlation between genotype and supernumerary tooth formation in cleidocranial dysplasia. *Orthod Craniofac Res* 2010; 13:197–202.
20. Tallon-Wolton V, Manzanares-Cespedes MC, Arte S, Carvalho-Lobato P, Valdivia-Gandur I, Garcia-Susperregui A, et al., Identification of a novel mutation in PAX9 gene in a family affected by oligodontia and other dental anomalies. *Eur J Oral Sci* 2007;115:427–32.
21. Thesleff I, Sharpe P., Signalling networks regulating dental development. *Mech Dev* 2007;67:111–23.
22. Thesleff I., Genetic basis of tooth development and dental defect. *acta Odontol Scand* 58: 191-194, 2000.
23. Wang H, Zhao S, Zhao W, Feng G, Jiang S, Liu W, et al., Congenital absence of permanent teeth in a six-generation Chinese kindred. *Am J Genet* 2000; 90:193–8.
24. Welbury R. R., Duggal M. S., Hosey M-T., *Paediatric Dentistry*. Oxford Medical Publications, Oxford University Press, New York, 2005.
25. Vastardis H, Karimbux N, Guthua SW, Seidman JG, Seidman CE., A human MSX1 homeodomain missense mutation causes selective tooth agenesis. *Nat Genet* 1996;
26. Vastardis H., The genetics of human tooth agenesis: new discoveries for understanding dental anomalies. *Am J Orthod Dentofacial Orthop* 2000; 117: 650-6.
27. Venter JC. The Sequence of the Human Genome. *Science* 2001; 291: 1304-51.
28. Vieira AR, Meira R, Modesto A, Murray JC., MSX1, PAX9, and TGFα Contribute to Tooth Agenesis in Humans. *J Dent Res* 2004; 83: 723-7.
29. Zergollern Lj. Et al., *Humana genetika*. Medicinska naklada, Zagreb, 1994.
30. Welbury R. R., Duggal M. S., Hosey M., *Paediatric Dentistry*. Oxford Medical Publications, Oxford University Press, New York, 2005.
31. Sardilović D., Raghavendra M.S., Complete Rehabilitation of Mouth Cavity After Early Childhood Caries Treatment: A Case Report, University of Niš, Faculty of Medicine and Clinic of Dentistry, *Acta Stomatologica NAISI* Vol 33. No 76, 2017.
32. Ranta R. Numeric anomalies of teeth in concomitant hypodontia and hyperdontia. *J Craniofac Genet Dev Biol* 1988;8:245-51.
33. Savarrio L, McIntyre GT. To open or to close space--that is the missing lateral incisor question. *Dent Update*. 2005;32(1):16-25.
34. Sletten DW, Smith BM, Southard KA, Casko JS, Southard TE. Retained deciduous mandibular molars in adults: a radiographic study of long-term changes. *Am J Orthod Dentofacial Orthop*. 2003;124(6):625-30.
35. Behr M, Proff P, Leitzmann M, Pretzel M, Handel G, Schmalz G, et al. Survey of congenitally missing teeth in orthodontic patients in Eastern Bavaria. *Eur J Orthod*. 2011;33:32–6. [PubMed] [Google Scholar]
36. Sheikhi M, Sadeghi MA, Ghorbanizadeh S. Prevalence of congenitally missing permanent teeth in Iran. *Dent Res J (Isfahan)* 2012;9 (Suppl 1):105–11. [PMC free article] [PubMed] [Google Scholar]
37. Cantekin K, Dane A, Miloglu O, Kazancı F, Bayrakdar S, Celikoglu M. Prevalence and intra-

- oral distribution of agenesis of permanent teeth among Eastern Turkish children. Eur J Paediatr Dent. 2012;13:53–6. [PubMed] [Google Scholar]
38. Kirzioğlu Z, Köseler Sentut T, Ozay Ertürk MS, Karayilmaz H. Clinical features of hypodontia and associated dental anomalies: A retrospective study. Oral Dis. 2005;11:399–404. [PubMed] [Google Scholar]
39. Gábris K, Fábián G, Kaán M, Rózsa N, Tarján I. Prevalence of hypodontia and hyperdontia in paedodontic and orthodontic patients in Budapest. Community Dent Health. 2006;23:80–2. [PubMed] [Google Scholar]