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Article

Sacral spina bifida occulta rare occurrence in Byzantine Belentepe population in Muğla, Turkey: A possible case for adequate folic acid intake

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With 7 figures and 5 tables

Abstract: Spina bifida may occur during the first weeks after conception; folic acid deficiency is strongly related to this anomaly. We argue that the low prevalence rate of spina bifida may indicate a relatively good nutrition state of a population, given that folic acid is found in many food products commonly eaten. The aim of this study is to examine the relationship between folic acid intake and spina bifida occulta prevalence in the Belentepe Byzantine population in Anatolian peninsula, and to compare the prevalence rates with various other ancient Anatolian populations by focusing on sacral spina bifida occulta in the Byzantine population. A total of 62 available human sacra were included in the study and compared with other sacra from relevant research using chi-squared test. Four male individuals had sacral spina bifida occulta with a prevalence rate of 6.45%, which is found to be lower in comparison to other ancient populations from western to eastern Anatolia. The present-day ecology of Belentepe indicates that foods rich with folic acid are common in and around the region. While some studies indicate the contrary, a comparison regarding the sacral spina bifida occulta prevalence with other populations in Anatolia shows a correlation between folic acid intake and proximity to a Mediterranean climate.

Keywords: spina bifida occulta; folic acid; nutrition state; Byzantine population; Anatolia

Introduction

Our knowledge of the lifestyles, socioeconomic structures, dietary habits, and/or health conditions of ancient societies depends heavily on their skeletal remains, given that soft anatomical tissues are mostly not preserved. A broad array of bioarchaeological studies helps us catch a glimpse into the past when there is no written evidence available. In such cases, paleopathology, the study of ancient diseases, provides valuable information from almost all bone remains.

The sacrum is one of the lowest parts of the vertebral column. It is formed by the fusion of five sacral vertebrae, structured in an inverted-triangle shape (Steele & Bramblett 1988; Aiello & Dean 1990; Bauman & Dutton 1991; Bass 1995; Mitchell & Mitchell 2001; Cheng & Song 2003; Bogduk 2005; White et al. 2011). As with other vertebral elements, the sacrum can also be subject to anomalies or malformations, (Aufderheide & Rodríguez-Martín 1998; Barnes 2012), such as neural tube defects.

The neural tube is the system in which the brain and spinal cord develops (Lumley et al. 2001; Schoenwolf et al. 2015), including the vertebral column and sacrum. Neural tube defects are described as anomalies that may develop as a result of erroneous closure of neural tube during the third and fourth weeks of intrauterine life (Miner et al. 1997; Fishman 2000; Lumley et al. 2001; Budak 2002; Sadler 2005; Blencowe et al. 2010; Schoenwolf et al. 2015). The sacrum can be heavily affected by these defects.

Spina bifida is one of these congenital neural tube defects that may develop as a consequence of partial fusion of vertebral spinae, or as a complete absence of them (Ferembach 1963; Saluja 1988; Akan 2002; Yuan et al. 2008; Marcovitch 2009; Au et al. 2010; Dorland 2012; Venes 2013; Babbi et al. 2014). While spina bifida is an umbrella term, comprising

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many defective formations on vertebral column (Iqbal 2000; Kumar & Tubbs 2011), researchers often collapse this term into subgroups (e.g. Aufderheide & Rodríguez-Martín 1998; Kumar & Tubbs 2011; Hallock et al. 2012; Singh 2013; Zemirline et al. 2013). However, in an anthropological setting, only spina bifida cystica and spina bifida occulta are used, due to the availability of bones, namely the sacrum, and not soft tissues (Henneberg & Henneberg 1999; Armstrong et al. 2013). The main distinction between these two types is in whether the spinal cord is open, and the lethality of the defect (Fig. 1). While spina bifida cystica is considered severe and mostly fatal (Aufderheide & Rodríguez-Martín 1998; Zemirline et al. 2013), spina bifida occulta may not even be noticed until a medical examination and is considered to be a mild variant of the defect (Aufderheide & Rodríguez-Martín 1998).

The oldest known spina bifida occulta case in the history was found in an Epipalaeolithic cave of Taforalt, Morocco, which is dated between 10,500 and 12,070 BP (Ferembach 1963). Another example was found in the Early Bronze Age site of Bab edh-Dhra, Jordan dated between 3150 and 3000 BCE (Ortner 2003). According to Aufderheide & Rodríguez-Martín (1998), the defect was first described by Recklinghausen in 1882, however Catala (2008) states that it was first described by Nicolas Tulp in 1651.

Even though the definitive etiology of spina bifida occulta is not known (Mann & Hunt 2012), some studies argue that its development is related to genetic and environmental factors (Josan et al. 2008; Armstrong et al. 2013; Molto et al. 2019). Studies show that this defect begins to form during the first weeks of gestation and has a strong correlation with folic acid intake (Botto et al. 1999; Iqbal 2000; Saraç et al. 2007). However, other researchers report that the prevalence of spina bifida occulta is correlated with a microevolutionary trend related to the changing impact of evolutionary forces such as a relaxation of natural selection in human populations (Henneberg & Henneberg 1999, Solomon et al. 2009; Lee et al. 2011).

This study aims to examine the possible relationship between folic acid intake and spina bifida occulta prevalence in the ancient Byzantine Belentepe population by studying the current and ancient dietary habits of the Belentepe region and to compare the prevalence rates with various other ancient Anatolian populations.

Material and methods

Belentepe is an archaeological site located 500 m south of Çakıralan Village in the Milas district of Muğla province in Turkey (Fig. 2). It was built on a limestone hill and is thought to be a small settlement type called a Koinon, which provided resources to the Keramos town of the ancient region of Karia 8 km south (Tırpan 2008; Özbey 2013).

The salvage excavations in Milas, conducted with the support of YKÜTAŞ, first began after the discovery of a

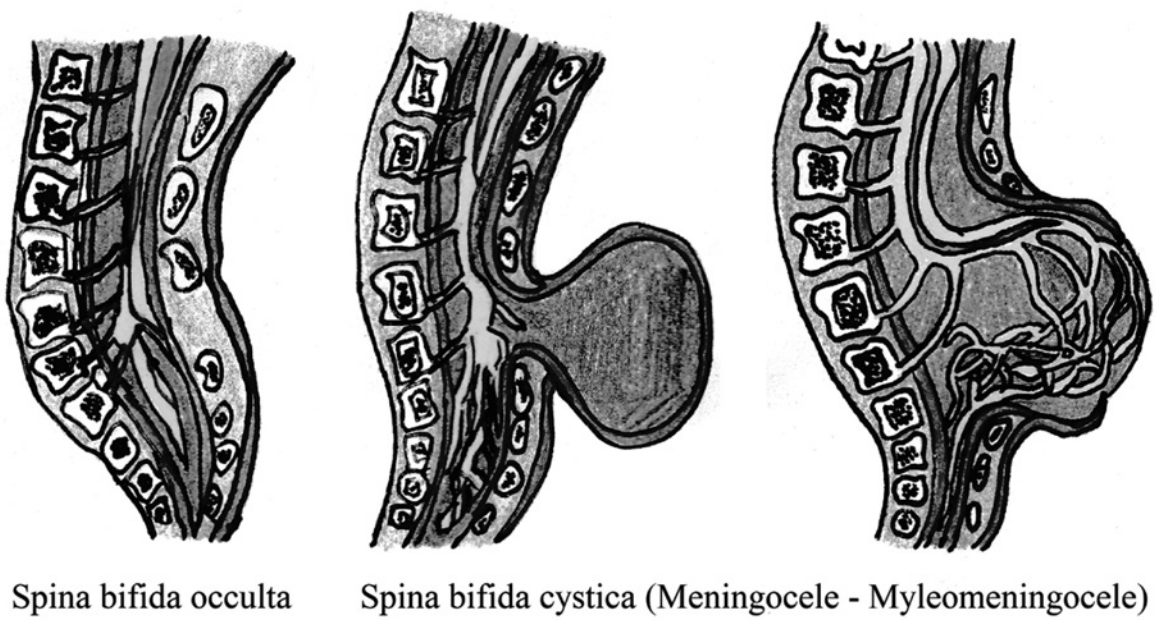


Fig. 1. Different types of spina bifida (lateral view). First image on the left depicts the spina bifida occulta, where the spina of sacral vertebrae is missing. Second image in the middle depicts meningocele, where the meninges are covered with normal skin and a sac filled with cerebrospinal fluid. Third image on the right shows myelomeningocele, where the meninges and cerebrospinal fluid are not covered with skin and left exposed. Meningocele and myelomeningocele are usually named spina bifida cystica. Redrawn after Botto et al. (1999).

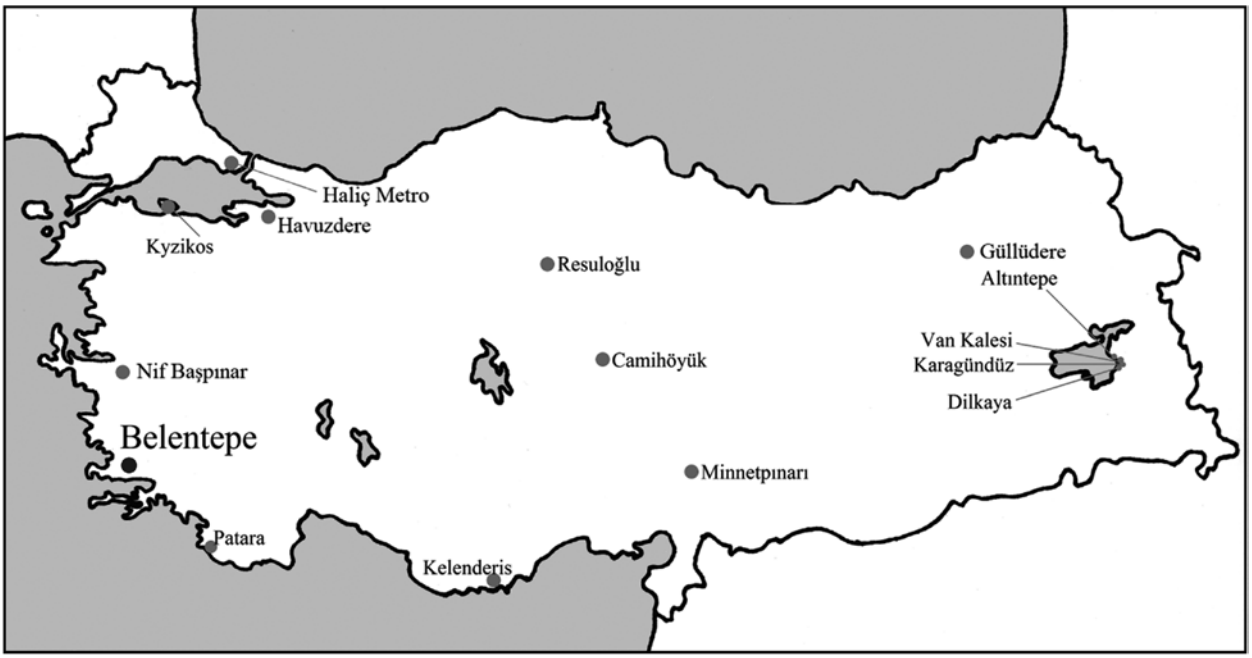


Fig. 2. Location of Belentepe, Muğla and other archaeological sites that are mentioned on the map of Turkey.

grave during drilling operations. These excavations now include the archaeological sites of Belentepe, Mengefe and Hüsamlar (Tırpan 2008; Özbey 2013).

Two drillings in Belentepe revealed an olive workshop along with three Classical Period, three Hellenistic Period and one Byzantine Period settlements (Korkmaz 2011). The fact that many structures from the Byzantine Period are wineries can be considered an indication of wine production and trade in the region (Tırpan et al. 2010; Korkmaz 2011).

A Byzantine necropolis was discovered 100 m south of these structures. The cist graves found in the necropolis show an Eastern Rome/Byzantine burial typology regarding their orientation and construction. The necropolis, however, is now destroyed due to the mining operations in the region. The skeletons in this area were generally buried on their backs with their heads facing West. The arms were laid either parallel to the bodies or held together ventrally (Özbey 2013). Almost all the graves were dug into the limestone given the geology of the area (Korkmaz 2011; Özbey 2013) (Fig. 3).

The skeletons examined in this study belong to 188 individuals from the Eastern Roman/Byzantine Periods recovered from the aforementioned necropolis during the 2011-2013 excavations. Sex determination was done using the morphological features of crania and pelves. The age groups used in the study followed various paleoanthropological Anatolian literature to prevent methodological conflict (e.g. Erdal 2003; Sevim et al. 2007; Yiğit et al. 2008; Başoğlu 2012; Sevim Erol & Yavuz 2015). Accordingly, the sub adult group comprises fetuses, infants (0–2.49 years), children (2.5–14.99 years) and adolescents (15–17.99 years), while the adult group comprises young adults (18–29.99 years), middle adults (30–44.99 years), and older adults (45+ years) (Table 1).

Several criteria were used to determine the sex of the skeletons. On the cranium, various features were examined, such as the robustness of glabella, shape and size of frontal tuberosities, zygomatic bone, orbital sockets, mastoid processes, nuchal crest and occipital protuberance; inclination of frontal bone; robustness of supraorbital arc and mandible; and structure of mental eminence and ramus angle. On the pelvis, several traits were examined: the preauricular sulcus, width of the sciatic notch and pubic angle, shape of foramen obtratorius, and the general size and shape of the pelvis (Workshop of European Anthropologists 1980; Brothwell 1981; Ubelaker 1991; Buikstra & Ubelaker 1994; Bass 1995; White et al. 2011).

The age at death of the individuals was estimated using the most applicable method depending on the preservation state of the bones, such as the developmental phase of symphyseal surface (Todd 1920; Todd 1921; McKern & Stewart 1957; Acsádi & Nemeskéri 1970; Gilbert & McKern 1973; Brooks & Suchey 1990), auricular surface (Lovejoy et al. 1985), cortical and trabecular structure at the midsection of clavicle (Kaur & Jit 1990), eruption stages of deciduous and permanent teeth (Brothwell 1981), and other general skeletal criteria, e.g. epiphyseal fusion of various bones (Workshop of European Anthropologists 1980; Brothwell 1981; Ubelaker 1991; Buikstra & Ubelaker 1994; Bass 1995; White et al. 2011).

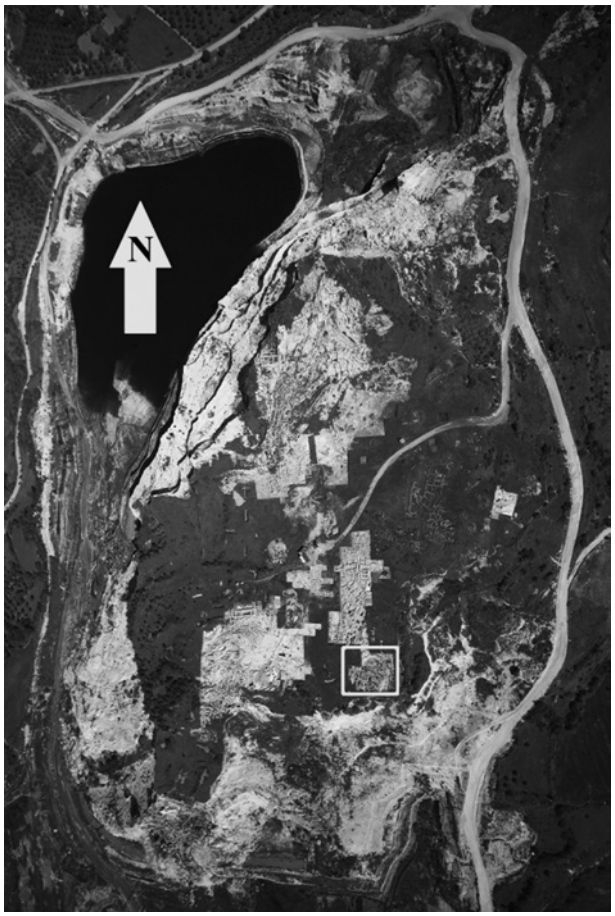


Fig. 3. The area of Belentepe salvage excavations. The white box shows the place of Byzantine Necropolis.

Table 1. Age groups used in the study.

Age groups	Age (yrs)
Sub adults	Fetus
	0–2.49
	2.5–14.99
	15–17.99
Adults	18–29.99
	30–44.99
	45+

Table 2. The demographic information on Byzantine Belentepe sample.

Age groups	Sex	Number of individuals	%
Sub adults		81	43.1
Adults	Females	33	17.6
	Males	58	30.9
	Indet.	16	8.5
Total		188	100

Following these evaluations, only the 62 individuals fitting the criteria (available sacra and fully-closed epiphyses, i.e. individuals who reached adulthood) were included in the study. In order to clarify the topic of this study, a basic anatomical feature of the sacrum, specifically sacral hiatus, should be described briefly:

Sacral hiatus is the openness of the posterior dorsal sacrum, usually observed on S4 and S5 vertebrae, but potentially extending further up than S4 (White et al. 2011). In such cases, a terminological confusion may arise regarding how much openness should be considered spina bifida occulta. While some researchers agree that the hiatus may occur in different shapes and that spina bifida is another distinct problem (e.g. Bennett 1972; Shinde & Bhusaraddi 2014; Sushanth & Shishirkumar 2014), others recognize all open shapes on dorsal sacrum as spina bifida occulta (e.g. Henneberg & Henneberg 1999; Ortner 2003; Albrecht et al. 2007; Senoglu et al. 2008; George et al. 2013; Singh 2013; Ali et al. 2014).

As a result, the present study will consider every openness except for the S4, S5 and S4-S5 hiatus as sacral spina bifida occulta in order to prevent further terminological confusion (Fig. 4).

In order to statistically compare the prevalence rates between Anatolian populations, two groups were formed. The group "West" includes nine archaeological sites: Belentepe is described above; Kyzikos is a Medieval-Roman archaeological site located in Balıkesir; Patara is located in Antalya and the materials studied are from Byzantine-Ottoman; Kelenderis materials are from the Ottoman era and the site is situated in Mersin province; Nif Başpınar is located in İzmir and the materials date to Byzantine Period; Havuzdere is a site in Yalova from the Medieval era; Haliç Metro was discovered in the European side of İstanbul that was dated to the Byzantine period; Resuloğlu is an Early Bronze site in Çorum province and the Camihöyük materials come from the Hellenistic-Roman period in Nevşehir. The group "East" includes six archaeological sites: Minnetpınarı is a Medieval site from Kahramanmaraş; Altıntepe is a Urartian site in Van province, while Van Kalesi, Karagündüz and Dilkaya are from Medieval era, also in Van province and Güllüdere from Erzurum province dates to the Medieval era.

Some of the sacrum data collected from these ancient Anatolian sites are recalculated after the sub-adults in the samples were excluded in order to prevent a methodological inconsistency between comparisons. The number of available sacra in these samples is given in Tables 3, 4. We considered the correlation between the prevalence of sacral spina bifida occulta and the location of corresponding sites with respect to West/East classification by means of Chi-squared independence test with the $\alpha = 0.05$.

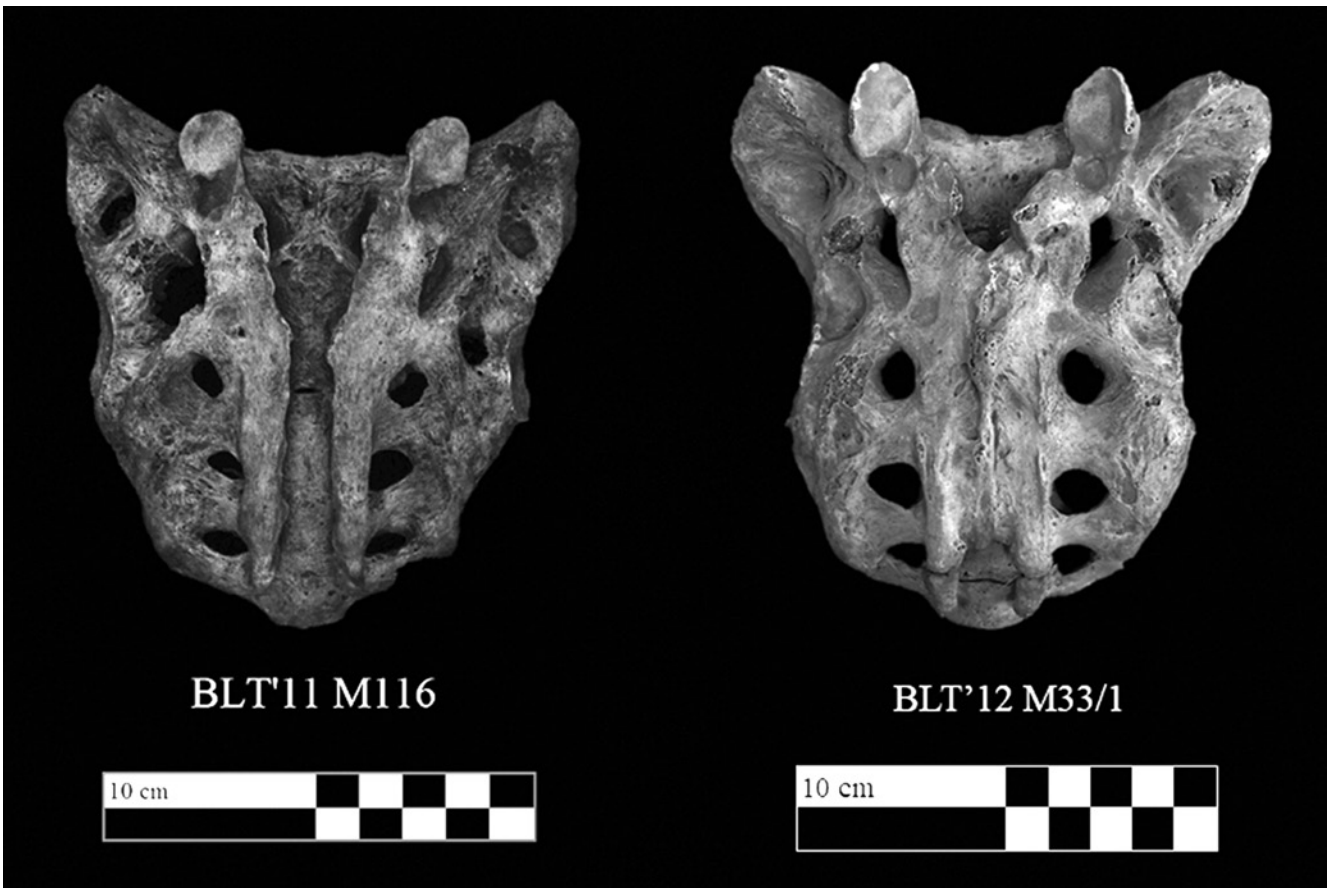


Fig. 4. (Left) Sacral spina bifida occulta example as a completely open sacral canal as found on the individual BLT'11 M116. (Right) Sacral spina bifida occulta example as the S1 opening as found on the individual BLT'12 M33/1.

Table 3. Comparison of sacral spina bifida occulta (SSBO) prevalence rates in some of the ancient Anatolian populations. Note that the prevalence rates were calculated with the number of evaluated adult sacra and not with the total number of individuals in the population.

Ancient population	Period	SSBO / total Sacra (observed / N)	Prevalence	Reference
Belentepe, Muğla	Byzantine	4/62	6.45%	This study
Patara, Antalya	Byzantine – Ottoman	2/16	12.5%	Sevim Erol & Yavuz 2015
Minnetpınarı, Kahramanmaraş	Medieval	3/10	30%	Özdemir & Sevim Erol 2010
Dilkaya, Van	Medieval	15/121	12.4%	Şahin 2019
Haliç Metro, İstanbul	Byzantine	1/5	20%	Çırak 2018
Havuzdere, Yalova	Medieval	13/138	9.42%	Sağır et al. 2018

Results

The 188 individuals studied in the Byzantine Belentepe sample showed 81 sub adult individuals: fetuses, infants, children and adolescents. The remaining 107 individuals are young, middle, and older adults. There are 33 females, 58 males, and 16 indetermined individuals (Table 2).

Four individuals were found to have sacral spina bifida occulta among the 62 evaluated sacra. Accordingly, the prevalence rate of the defect is 6.45%. These four individuals with sacral spina bifida occulta were all males. BLT'11 M10 is a 35-40-year-old middle adult, BLT'11 M116 is a 55-60-year-old older adult, BLT'13 M90 is an adult of indeterminate age and BLT'12 M33/1 is a 25-30-year-old young adult (Fig. 5). The first individual exhibits sacralization as a result of the fusion between the L5 and S1 vertebrae.

Table 3 shows a regional pattern in the sacral spina bifida occulta rates. Belentepe, the westernmost population in this

Table 4. Comparison of sacral spina bifida occulta (SSBO) prevalence rates in various ancient Anatolian populations. Note that the prevalence rates were calculated with the number of adult individuals and not with the number of available sacra or sub adults.

Ancient population	Period	SSBO/total	Prevalence	Reference
Belentepe, Muğla	Byzantine	4/107	3.7%	This study
Patara, Antalya	Byzantine – Ottoman	2/129	1.6%	Sevim Erol & Yavuz 2015
Kyzikos, Balıkesir	Roman – Medieval	1/20	5.0%	Gözlük Kırmızıoğlu et al. 2009
Resuloğlu, Çorum	Early Bronze	3/80	3.75%	Atamtürk & Duyar 2010
Camihöyük, Nevşehir	Hellenistic – Roman	1/24	4.2%	Başoğlu 2012
Kelenderis, Mersin	Ottoman	3/113	2.7%	Çırak 2009
Minnetpınarı, Kahramanmaraş	Medieval	3/71	4.2%	Özdemir & Sevim Erol 2010
Van Kalesi, Van	Medieval	2/79	2.5%	Gözlük et al. 2004
Altıntepe, Van	Urartian	1/133	0.8%	Yiğit et al. 2005
Dilkaya, Van	Medieval	16/119	13.4%	Sarı Özdemir 2004
Karagündüz, Van	Medieval	7/92	7.6%	Sarı Özdemir 2004
Dilkaya, Van	Medieval	15/156	9.6%	Şahin 2019
Haliç Metro, İstanbul	Byzantine	1/9	11.11%	Çırak 2018
Havuzdere, Yalova	Medieval	13/231	5.62%	Sağır et al. 2018
Güllüdere, Erzurum	Medieval	2/18	11.11%	Sevim et al. 2007
Nif – Başpınar, İzmir	Byzantine	1/46	2.17%	Yavuz et al. 2018



Fig. 5. The individuals with sacral spina bifida occulta.

set, shows the lowest sacral spina bifida occulta prevalence with 6.45%, as Patara, Haliç Metro, Havuzdere, Minnetpınarı and Dilkaya follow an increase with 12.5%, 9.42%, 20%, 30% and 12.4% respectively. A general increase in sacral spina bifida occulta prevalence from Belentepe to eastern populations is observable.

In Table 4, a similar pattern is observed with a general increase in sacral spina bifida occulta prevalence going from west to east. Patara, Kelenderis and two Van populations in Eastern Anatolia, namely Altıntepe and Van Kalesi show a deviation from this pattern.

The sacral spina bifida occulta prevalence rate distributions are collected in three categories as the Chi-squared test shows (Table 5). Three categories are formed as less than 5.56, between 5.56 and 7.00, and greater than 7.00. The threshold 5.56 is chosen intentionally due to the average of the whole data in that category. Hence the degree of freedom reads as 2. That makes the critical value 5.99 for p=0.05.

The Chi-squared value was calculated as 10.54, which is greater than the critical value. Accordingly, the null-hypothesis was rejected, and therefore it is possible to deduce that being on the west side of Anatolia is strongly related to a lower prevalence rate of sacral spina bifida occulta.

Discussion

Etiology of sacral spina bifida occulta

During the embryonic phase, the closure of the neural tube occurs in five different areas cranially and caudally in an irregular sequence (Figs 6, 7). The hiatus on the cranial side of the tube closes on the 25–26th day after fertilization, while the caudal side does so on the 27–29th day (Tinkle & Sterling 1997; Fishman 2000; Iqbal 2000; Turan et al. 2000; Özaras 2015). The spine, brain and cranium start to develop after the closure of the neural tube (Botto et al. 1999). In cases in which the closure is defective, serious problems, such as anencephaly, encephalocele, spina bifida cystica (meningocele, myelocele, meningomyelocele) or spina bifida occulta, might occur; these are collectively termed neural tube defects (Budak 2002; Molloy 2005; Somunkıran et al. 2007; Copp et al. 2015). Elements such as genetic factors, high fever in mothers, obesity, medications, environmental pollutants, and diabetes play a role in the incidence of neural tube defects (Tinkle & Sterling 1997; Iqbal 2000; Turan et al. 2000; Akan 2002; Çakmak et al. 2006; Yıldız & Akbayrak 2008; Coşar et al. 2009), yet folic acid deficiency, one of these elements, is argued to be more strongly correlated with these defects.

Etiology of folic acid deficiency

Folic acid, a water-soluble B group vitamin (B9) named after the word *folium*, meaning "leaf" in Latin, is mainly found in green-leafed vegetables, legumes, yeast, liver and other offal (Budak 2002; Dorland 2012; Venes 2013). Folic acid plays an important role in the development of the central nervous system and facilitates the processes in DNA and RNA synthesis as a cofactor (Budak 2002; Yıldız & Akbayrak 2008). When it is deficient, these biological processes cannot operate properly and the adequate amount of DNA for mitosis cannot be synthesized, potentially causing damage or death in cells (Tinkle & Sterling 1997; Yıldız & Akbayrak 2008).

Beside its metabolic effects, a genetic model regarding the preventive effect of folic acid for the neural tube defects was proposed (Van Allen et al. 1993; Tinkle & Sterling 1997). According to this model, the five closure areas on neural tube (Fig. 7) are controlled by different genes. The genes controlling the first area, which includes the sacrum and the spine,

Table 5. Chi-squared independence test.

Observed (R)	**< 5.56**	**5.56 < x < 7**	**> 7**
West	8	0	1
East	2	1	4
Expected (E)	**< 5.56**	**5.56 < x < 7**	**> 7**
West	5.63	0.56	2.81
East	0.44	0.44	2.19
(R – E)	**< 5.56**	**5.56 < x < 7**	**> 7**
	2.38	–0.56	–1.81
	1.56	0.56	1.81
$(R - E)^2/E$	**< 5.56**	**5.56 < x < 7**	**> 7**
West	1.002777	0.5625	1.168055
East	5.580357	0.723214	1.501785
		10.538690 Chi-squared value calculated	
		5.9915 Chi-squared cut-off	

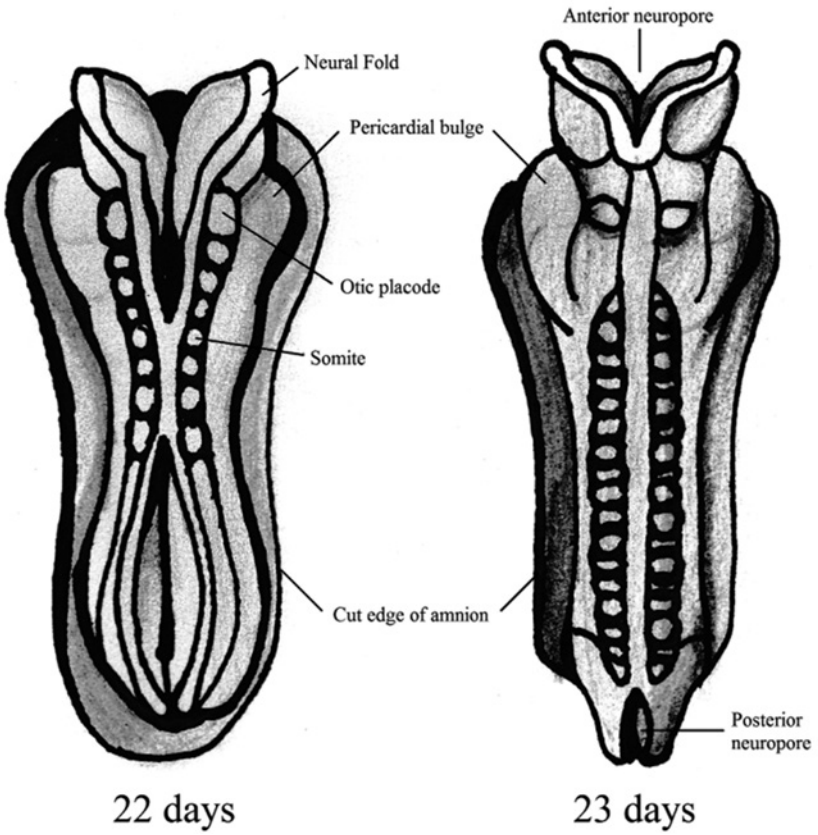


Fig. 6. The normal closure of the neural tube in 22nd and 23rd days of intrauterine life (dorsal view). An error during this procedure may cause a neural tube defect. Redrawn after Sadler (2005).

are sensitive to folic acid deficiency and can be viewed as the cause of neural tube defects (Tinkle & Sterling 1997).

Certain mutations on Methylenetetrahydrofolate reductase (MTHFR) and 5-methyltetrahydrofolate-homocysteine methyltransferase reductase (MTRR) genes are found to be strongly correlated with the occurrence of neural tube defects (Christensen et al. 1999; Blom et al. 2006; Beaudin & Stover 2007; Armstrong et al. 2013). Alterations to these genes, such as single nucleotide polymorphisms (SNPs), affect the allele variations in an individual, constituting a risk factor for neural tube defects, specifically spina bifida (Beaudin & Stover 2007; Armstrong et al. 2013). The alteration in alleles causes the said genes to become MTHFR C677T and MTRR A66G, and may also cause arrested enzyme activity (Tunçbilek 2004). When combined with a low folate environment, these changes can also increase the risk of a neural tube defect.

Accordingly, some recent studies show that there is an important decrease in neural tube defect rates after an intentionally adopted diet with an adequate folic acid intake or during periconceptional usage of folic acid-rich supplements, where the same neural tube defect rates were higher before the said diet was practiced or the supplements were taken (Molloy 2005; Somunkıran et al. 2007; De Wals et al. 2008).

Some recent studies (Solomon et al. 2009; Lee et al. 2011), however, argue that the prevalence of spina bifida occulta is not related to the folic acid intake. They report that the contemporary populations both in Australia and Switzerland show higher prevalence rates compared to the previous generations even though the later generations took more folic acid supplementations. Authors state that the reason for this increase in spina bifida implies a microevoulutionary or secular trend despite the increased usage of folic acid, which is, as stated above, the main factor affecting lower spina bifida rates.

Asserted distribution of folic acid deficiency in Anatolia

In Anatolia, various reports state that folic acid deficiency and neural tube defect prevalence is higher in eastern and northern regions in comparison to western regions (Tunçbilek 2004; Unusan 2004; Saraç et al. 2007). While the general prevalence rate of spina bifida in Turkey is 0.3% (Tunçbilek et al. 1999), İzmir in western Turkey shows a spina bifida prevalence rate of 0.1% (Mandıracıoğlu et al. 2004). This

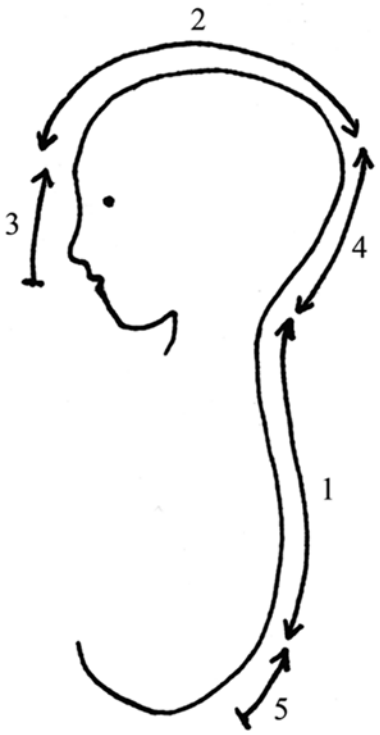


Fig. 7. Five different zones for the neural tube closure. The zone 1 is closely related to folic acid. Redrawn after Van Allen et al. (1993).

rate is 0.3% in Elazığ in eastern Turkey (Saraç et al. 2007). The reason of the increase in the spina bifida prevalence rates from west to east is argued to be the diet of mothers with inadequate folic acid intake in eastern parts of Turkey (Mandıracıoğlu et al. 2004; Tunçbilek 2004; Unusan 2004).

Regional and environmental patterns in sacral spina bifida occulta

The current situation of spina bifida prevalence rates in Turkey may be telltale of its historical state as well. However, there is not enough information from ancient Anatolian populations regarding whether the sacral spina bifida occulta occurrence increases from west to east. After examination of studies from the Anatolian bioarchaeological literature, the prevalence of the individuals with spina bifida in ancient Anatolian populations was calculated and compared with the Byzantine Belentepe population in two different datasets (Tables 3, 4).

There are two different comparisons between ancient Anatolian populations regarding the prevalence rates for the spina bifida given the need for different calculation methods. In Table 3, the "Total" row shows the number of total available sacra in the sample because the studies given in Table 3 explicitly stated that in the whole sample. The studies given in Table 4, however, do not explicitly state the methodology that was used in the research. There is not any clear distinction if the authors have taken the available sacra number into account or if they have solely used the total number of individuals in the samples while calculating the prevalence rate of sacral spina bifida occulta. Since not all the individuals in a skeletal sample may have a sacrum available, differentiating the calculation methods is important when making comparisons between different populations. For instance, if the sacral spina bifida occulta prevalence rate in Byzantine Belentepe population was calculated based on 188 individuals instead of the available 62 sacra, the prevalence rate would change from the current 6.45% to 2.13% accordingly.

Our statistical results show that the sacral spina bifida occulta prevalence increases from western populations to eastern populations. However, when looked at some sites individually, for example Kyzikos, Havuzdere, Haliç Metro, Altıntepe and Van Kalesi, it can be observed that there is an inconsistency in this pattern. There may be several causes for this:

Although Kyzikos sample belongs to the Roman-Medieval period, the definite period to which the sample belongs is not known. Records show that Kyzikos experienced several battles (Koçhan 2011) and the studied individuals may have lived during the aftermath of this warfare. This may have caused a stressful environment and lifestyle, adversely affecting the sacral spina bifida occulta prevalence as an increase in the population. The high dental hypoplasia rates in the population also support this view, indicating relatively bad nutrition (Gözlük Kırmızıoğlu et al. 2009). However, it must be emphasized not exactly knowing which period the sacra belong to is an important missing criterion in analyzing paleodemographic data. This prevents us to asses whether there is a microevolutionary trend in the population with regard to spina bifida prevalence as some studies have indicated (Solomon et al. 2009; Lee et al. 2011).

The authors of Havuzdere study (Sağır et al. 2018) report that the general nutritional and health status of the population is relatively good compared to other ancient Anatolian populations. However, there is no clear information and comparable data regarding the relatively high prevalence of sacral spina bifida occulta. There is also an important scarcity of archaeological data that would normally help making considerations about the lifestyle of the site.

Regarding the Haliç Metro population (Çırak 2018), it is difficult to interpret the spina bifida data, since the author only reported the rates of various pathologies and shared no implications for their prevalence. The only explanation as to why prevalence rate was found to be that high has to do something with the number of available sacra in the study, which is five, or the number of adult skeletons, which is nine. This minimal sample size makes it difficult to make a holistic explanation regarding the sacral spina bifida occulta rates in the West group.

The burial types in Altıntepe sample, specifically rock-cut tombs, are characteristics of a noble and wealthy society (Yiğit et al. 2005). It should be considered that this population had a rich diet, possibly explaining the lowest rates of sacral spina bifida occulta in all the populations, even though Altıntepe has the greatest number of individuals.

There is not enough information concerning the Medieval Van Kalesi population, making it difficult to interpret the relatively low sacral spina bifida occulta prevalence in comparison with the other ancient eastern Anatolian populations. According to Gözlük et al. (2004), the Van Kalesi population has numerous pathologies and trauma, which they relate to a possible case of stressful diet condition in the area. However, it is problematic to reach a certain conclusion from their study regarding the diet of the said population.

That being said, although our statistical results show a meaningful difference between West and East Anatolia regarding the sacral spina bifida occulta prevalence, the discrepancy between methodologies of different studies on the topic made it difficult to interpret the prevalence rates at first. The fact that almost all the methods for identifying sacral spina bifida occulta are different in each study, the total number of sacra and spina bifida varies. This was also partly because the Anatolian studies do not explicitly state the number of individuals along with the number of observed sacra, which, as a result, may have caused the deviating prevalence rates.

Varying sample size in populations is another factor affecting the disparate sacral spina bifida occulta prevalence rates in anthropological samples. For example, although Camihöyük (Başoğlu 2012) and Altıntepe (Yiğit et al. 2005) have the same number of sacral spina bifida occulta, the sample sizes are 24 and 133, and the prevalence rates are 4.2% and 0.8%, respectively.

Nevertheless, when the regional observations on sacral spina bifida occulta prevalence are taken into consideration, the correlation between folic acid intake and cultural cuisines in Anatolia should be noted as well. Since nutrition is directly connected to the environment and climate of a region, it is necessary to elaborate on these for eastern and western Anatolia.

The Mediterranean and Aegean coasts of the Anatolian peninsula have a temperate climate, rich with various green-leafed vegetables such as leek, celery, artichoke, glasswort, sorrel, baby's tears, leaf mustard, milk thistle and numerous fruit types, namely figs, grapes, dates and apples in the present day. The Mediterranean diet also includes olive and olive products, as well as red and white wine. Ovine breeding and fishing also contribute to foodstuffs; offal such as liver and tripe is frequently cooked as casseroles (Gürsoy 2013a; Gürsoy 2013b).

Eastern Anatolia has the highest elevation in Turkey with many hills and mountains, resulting in a regional continental climate. Because of its mountainous landscape, areas suitable for agriculture are sparse and farming is generally difficult due to the harsh climate. The diet is comprised mainly of meat and meat products, various types of cheese, and fruits such as apricots, mulberries, and apples. Pearl mullet is an endemic species to Lake Van and is the only type of fish in the region (Gürsoy 2013b).

The cultural cuisine around the Mediterranean has not changed significantly, as available foodstuffs have generally stayed the same for centuries (Gürsoy 2013a). When the relatively unchanged structure of climate and ecology in Anatolia is taken into consideration, it can be inferred that the local cuisine of present day is formed from cultural accumulation, not only in Mediterranean, but also in Anatolia as a whole. Considering the evidence of continual collection and consumption of endemic plants by the people of the Karia region (Yakar 2007; personal observations), it can also be concluded that the lifestyle of the Byzantine Belentepe population was mainly the same as modern people living in the region. This can imply the correlation between defects and nutrition.

Lastly, a familial relationship between the four individuals with sacral spina bifida occulta in Byzantine Belentepe population may be inferred. Some defects can be considered indications of a biological relationship (Pietrusewsky & Douglas 1992; Molto et al. 2019). However, for this study, it is not possible to validate this hypothesis, as there is currently no genetic or biodistance information on the population.

Conclusions

There are not many detailed publications for the studied populations and almost all information comes from excavation reports or proceedings. A well-planned interdisciplinary research could provide more reliable interpretations, especially isotope analyses, population genetics, and paleoethnobotany. Further research on Belentepe, particularly from a bio- and ethnoarchaeological perspective, will focus on solving these problems. The current state makes it difficult to make a comprehensive description regarding the correlation between regional folic acid intakes.

This study aimed to develop a new perspective into the field of bioarchaeological Anatolian studies by using sacral spina bifida occulta data supported by anthropological findings. In this context, the relation between folic acid intake and spina bifida was examined with the help of recent clinical data. We observed that there is a correlation between the prevalence rates of the said defect, particularly an increase from Western to Eastern Anatolia in connection with a folic acid-rich diet. The sacral spina bifida occulta prevalence rate in Belentepe is 6.45% and it is relatively low when compared with the other ancient Anatolian populations. This shows the geographic interrelation between the folic acid intake from an ecologically rich region Milas and the sacral spina bifida occulta occurrence. However, it should be noted that the methodological differences between studies make defini-

tive interpretations difficult in paleopathology, a topic that is already complex due to limited available data. The limited number of recent medical data and the lack of interdisciplinary studies involving anthropologists, radiologists and pathologists on spina bifida prevalence restrict us in inferring whether a secular trend is visible or microevolutionary effects working on this defect. Although several problems were experienced, we believe that this study is an important attempt in the Turkish bioarchaeological literature trying to explain the etiology of a frequently reported defect.

Conflict of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors agree that there is no conflict of interest of any kind.

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