International Journal of Paleopathology 49 (2025) 119–127

Contents lists available at ScienceDirect

International Journal of Paleopathology

journal homepage: www.elsevier.com/locate/ijpp

Case study

Insights into the anatomical expressions of anencephaly in three infants from 17th to 19th- century Lisbon, Portugal

Marina Lourenço [a,b,c,*,1], Francisco Curate [b], Eugénia Cunha [a,d]

[a] University of Coimbra, Centre for Functional Ecology, Laboratory of Forensic Anthropology, Department of Life Sciences, Calçada Martim de Freitas, Coimbra 3000-456, Portugal
[b] University of Coimbra, Research Centre for Anthropology and Health, Department of Life Sciences, Calçada Martim de Freitas, Coimbra 3000-456, Portugal
[c] Era Arqueologia S.A., Calçada de Santa Catarina, 9C, Cruz Quebrada 1495-705, Portugal
[d] National Institute of Legal Medicine and Forensic Sciences, Rua Manuel Bento de Sousa, 3, Lisboa 1169-201, Portugal

ARTICLE INFO

Keywords:
Neural tube defects
Congenital anomalies
Non-adults
Rare diseases

ABSTRACT

Objective: This study aims to analyse and compare the cranial morphological variations in three individuals, each exhibiting different severity levels of malformations.
Materials: Three nearly complete and well-preserved skeletons of infants from the São Domingos children's necropolis in Lisbon, Portugal, dating from the 17th to early 19th centuries.
Methods: Macroscopic and metric assessments were performed aimed at creating a detailed description of the skeletons.
Results: The three infants exhibit an absence of the upper cranial vault, accompanied by several cranial bone alterations such as abnormal development and morphology of the occipital, sphenoid, temporal, and frontal bones. Additionally, two of the infants present maxillary and dental anomalies.
Conclusions: The three infants from the São Domingos necropolis provide crucial insights into the presence of anencephaly in an historical population, representing an exceptionally rare archaeological find. The distinct cranial abnormalities strongly support the diagnosis and highlight varying severity levels of the condition.
Significance: These examples enhance the recognition of anencephaly in archaeological contexts and deepen the understanding of its varied bone expressions. Examining skeletal variations within the same condition also complements the broader palaeopathological discussion of rare diseases.
Limitations: The lack of soft tissue preservation reduces a comprehensive assessment of anencephaly in skeletal remains. The archaeological context presents challenges such as fragmentation. Additionally, determining postnatal survival is difficult due to the subtle or absent skeletal indicators that might suggest survival beyond birth.
Suggestions for further research: Biomolecular genetics analysis could be a valuable approach for future research.

1. Introduction

Neural tube defects (NTDs) are among the most common congenital anomalies affecting the central nervous system (CNS), occurring when the neural tube fails to close during the first 28 days of embryonic development (Padmanabhan, 2006; Van Gool et al., 2018). Anencephaly is recognized by the European Surveillance of Congenital Anomalies as a severe form of NTD (Bergman et al., 2024), being characterised by brain underdevelopment, absence of nervous system tissue, and the lack of a cranial vault (Bergman et al., 2024; Fields et al., 1978; Obeidi et al., 2010). It can be categorized into two primary types: holo-anencephaly, which involves the complete absence of the forebrain and cranium, and mero-anencephaly, where a rudimentary brain is present with preserved vegetative functions (Santana et al., 2016; Shewmon, 1988; Van Allen et al., 1993).

The major defects manifest in the cranial vault, where bones derived from the neurocranium are severely affected, while those derived from the chondrocranium are comparatively less affected (Garol et al., 1978; Siebert et al., 1987). Parietal bones are absent in most severe cases (Garol et al., 1978). In addition to central nervous system abnormalities,

* Correspondence to: CC Martim de Freitas, 3000-456 Coimbra, Portugal.
E-mail addresses: mar.lourenco22@gmail.com (M. Lourenço), fcurate@uc.pt (F. Curate), cunhae@antrop.uc.pt (E. Cunha).
[1] https://orcid.org/0000-0002-5056-6016

https://doi.org/10.1016/j.ijpp.2025.04.001
Received 29 October 2024; Received in revised form 28 March 2025; Accepted 11 April 2025
Available online 21 April 2025

Fig. 1. Infants in situ (top row) and in anatomical position (bottom row). a) and b) Infant 1; c) and d) Infant 2; e) and f) Infant 3.

anencephaly is associated with cervical rachischisis (incomplete fusion of neural arches), cleft palate, heart and lung defects, clubfoot, overlapping fingers, rocker-bottom feet, extra digits, underdeveloped adrenal glands, microphthalmia, enlarged pinnae, absence of kidneys, and omphalocele (Munteanu et al., 2020).

The aetiology of anencephaly remains uncertain but most cases are of multifactorial origin, and environmental and genetic risk factors include maternal folic acid deficiency, exposure to nitrates, pesticides, organic solvents, excess vitamin A intake, and low socioeconomic status (Barron, 2016; Munteanu et al., 2020; Padmanabhan, 2006; Salari et al., 2022; Van Gool et al., 2018). Maternal conditions, such as obesity or gestational diabetes, paternal exposure to toxins, and foetal factors, are also associated with increased risk (Aguilar-Garduno et al., 2010; Barron, 2016; Munteanu et al., 2020; Padmanabhan, 2006). The prevalence varies across regions and periods, ranging from 0.29 per 10,000 births to 6.7 per 10,000 (Shewmon, 1988). Current estimates suggest a worldwide prevalence of 5.1 per 10,000 births (Salari et al., 2022).

Stillbirths are frequently associated with this condition, possibly due to the inability of the foetus to withstand mechanical distortion during vaginal delivery (Padmanabhan, 2006; Shewmon, 1988). These infants are often born prematurely (33 –36 gestational weeks) with low birth weight and growth delays (Padmanabhan, 2006; Shewmon, 1988). The lifespan depends on the severity of the condition and the medical care provided. While most die shortly after birth, there are rare cases of individuals surviving up to 2.5 years under intensive life support, or more in less severe mero-anencephaly cases (Byrne et al., 2005; Funayama et al., 2011; Santana et al., 2016; Shewmon, 1988).

Anencephaly can be detected early through first-trimester ultrasonography (Munteanu et al., 2020; Salari et al., 2022; Van Gool et al., 2018). Advances in prenatal care and the widespread use of folic acid supplementation have reduced its incidence, yet anencephaly remains a present-day concern rather than a condition of the distant past (Barron, 2016; Padmanabhan, 2006; Van Gool et al., 2018).

Archaeological cases are rare, with most data coming from clinical studies. However, examples of mummified foetuses and a few skeletonized cases have been documented (Dudar, 2010; Dupras et al., 2003; Saint-Hilaire, 1826). This study presents a systematic analysis of the skeletons of three archaeological individuals, with a particular focus on

Table 1
Measurements of the skeletal elements of Infants 1, 2, and 3.

Bone	Measurement (mm)	Infant 1	Infant 2	Infant 3
Pars basilaris	Length	12.88	13.92	15.21
	Width	13.67	15.19	14.01
Right *Pars lateralis*	Length	-	20.14	16.72
	Width	-	15.88	14.37
Left *Pars lateralis*	Length	-	18.22	17.55
	Width	-	15.76	14.27
Right *Pars petrosa*	Length	31.39	29.62	28.55
	Width	13.71	11.88	12.12
Left *Pars petrosa*	Length	28.96	28.48	27.43
	Width	14.20	11.37	12.36
Right Mandible	Full Length	-	49.24	50.23
Left Mandible	Full Length	55.76	50.62	50.65
Right Clavicle	Length	-	-	45.91
Left Clavicle	Length	50.06	48.62	43.37
Right Ilium	Length	-	38.09	34.69
	Width	-	32.49	30.54
Left Ilium	Length	39.72	38.69	34.30
	Width	32.81	33.20	30.24
Right Ischium	Length	20.67	19.67	18.98
Left Ischium	Length	20.04	-	19.18
Right Pubis	Length	-	18.01	-
Left Pubis	Length	18.18	17.43	16.95

examining and comparing their cranial morphological differences associated with anencephaly. The identification of these examples within the same necropolis represents an unprecedented discovery. Given the rarity of published cases of anencephaly in paleopathology, this finding holds particular relevance, as it may aid in the identification of such cases in archaeological contexts.

2. Materials and methods

This study focuses on three infants exhibiting severe cranial bone alterations. These individuals were exhumed in the large São Domingos Children Necropolis (SDCN), a Dominican all-male monastery in Lisbon, Portugal, comprising 2798 individuals. The ages at death ranged from 20 gestational weeks to 16 years, with a predominant presence of perinates and infants (n = 2662; 95.1 %), while adolescents were notably scarce, accounting for only three cases (0.1 %). Most of the graves were individual (83.7 %, n = 1977), while only 16.3 % (n = 385) were multiple (n = 58), predominantly double burials, often containing individuals of different ages at death. Additionally, no specific geographic orientation was followed in the ritual placement of the graves. Radiocarbon analysis (Vilnius Radiocarbon Laboratory) dates this necropolis to the second half of the 17th century and the early 19th century, with results ranging from 1655 ± 26 years to 1811 ± 28 years. The Convent of São Domingos was part of a complex that included the Royal Hospital of All Saints - "Hospital Real de Todos os Santos" -, which housed a baby hatch, historically known as foundling wheels, a mechanism designed for the anonymous and safe abandonment of infants (Reis, 2001). Some of the interred children likely came from this context. Adornment objects like gold and silver earrings suggest that some were of higher socioeconomic status, while others were possibly deem "illegitimate" or were unbaptized. The precise socio-historical context of this necropolis remains uncertain, as historical records mentioning these particular children's burial site has not yet been identified.

A detailed macroscopic and metric analysis of the skeletons focusing on the morphology of the cranial base and facial bones was conducted. Age at death was estimated using dental calcification and eruption patterns (AlQahtani et al., 2010), and the maximum length of long bones (Cardoso et al., 2014).

3. Results

The three infant skeletons are nearly complete and well-preserved according to Bello et al. (2006). Their Anatomical Preservation Index (API) values are 72.2 %, 79.0 %, and 84.7 % for Infants 1, 2, and 3, respectively. The Bone Representation Index (BRI) values are 52.4 %, 78.1 %, and 81.7 %, while the Qualitative Bone Index (QBI) values are 75.2 %, 85.4 %, and 89.4 %, respectively. Individual 1 was buried in a double grave alongside another infant, positioned supine with a west-east orientation. Infants 2 and 3 were buried in single graves. Infant 2 was positioned in a semi-foetal posture with a southeast-northwest orientation, face down, while Infant 3 was placed in a right lateral

Table 3
Key morphological features of the cranial bones present in the three infants.

Cranial bone	Morphological features
Pars basilaris	Elongated and narrow
	Verticalized position
Pars lateralis	Shortened and narrow
	Short condylar and jugular limbs
Pars squama	Composed only by the *pars supra-occipitalis*
	Non-developed *pars interparietalis*
	Inward folding on the superior border of the *pars supra-occipitalis*
Sphenoid	Thickened with lesser and greater wings shortened
	Narrow body
Parietal	Extremely underdeveloped
	Pronounced narrowing and elongation
Temporal	Shortened *pars petrosa*
	Reduced zygomatic processes
	Diminished squamous part
Frontal	Absence of frontal *squama*
	Diminished frontal bone
	Horizontal orientation
	Posteroinferior and lateral deviation
Zygomatic	Rhomboid shape
	Shortened frontal and temporal processes
	Significantly thickened

Table 2
Measurements of the long bones of Infants 1, 2, and 3, along with age-at-death estimations based on Cardoso et al. (2014).

Bone		Infant 1		Infant 2		Infant 3	
		Max length (mm)	Bone age (months)	Max length (mm)	Bone age (months)	Max length (mm)	Bone age (months)
Humeri	Right	69.43	1.9	-	-	68.48	1.6
	Left	68.50	1.6	70.36	2.3	68.59	1.6
Ulnae	Right	62.09	2.3	65.53	3.9	61.57	2.0
	Left	61.93	2.2	64.84	3.6	61.61	2.1
Radii	Right	53.19	1.4	55.97	2.8	53.34	1.5
	Left	51.56	0.6	55.44	2.5	54.02	1.8
Femora	Right	84.47	2.5	82.25	2.0	81.00	1.7
	Left	83.01	2.1	81.79	1.8	81.65	1.8
Tibiae	Right	70.68	2.0	69.25	1.5	69.48	1.6
	Left	70.58	2.0	69.98	1.8	69.63	1.6
Fibulae	Right	-	-	64.71	2.3	-	-
	Left	-	-	65.10	2.4	66.32	2.8

Fig. 2. Occipital bone. a) Pars supra-occipitalis fused with pars lateralis, outside view (top), inside view (middle) and pars basilaris (bottom) of Infant 1; b) Pars supra-occipitalis with a semi-circular shape, and a narrower inward-folded margin, outside view (top), inside view (middle) and pars lateralis and pars basilaris (bottom) of Infant 2;) Pars supra-occipitalis with an inverted V-shaped inferior border with a vertical division or pseudo-suture, outside view (top), inside view (middle), and pars lateralis and pars basilaris (bottom) of Infant 3.

decubitus position with an east-west orientation. There was no associated material culture, except for two buttons made of bone possibly associated with clothing present on the Infant 3. The burial practices given to these individuals are similar to those of the other non-adults in the necropolis (Fig. 1).

Based on dental development, the estimated age at death for Infants 1 and 2 is approximately 4.5 months, while Infant 3 presents a slightly earlier dental developmental stage, circa 1.5 months (AlQahtani et al., 2010). In the first two individuals, the incisors show the beginning of root formation, while in the third, the crown is still completing its calcification. Long bone development is consistent across all three individuals, with age-at-death estimates based on the femur—the bone with the least amount of error—ranging from 1.7 to 2.5 months (Cardoso et al., 2014). It is interesting to note that the long bone development is almost identical for the three individuals although there is a slight deviation from the dental age (Tables 1 and 2).

A distinct feature observed is the absence of the cranial vault, with no significant postcranial skeletal anomalies (Table 3). All three crania exhibit a flexed cranial base angle and a verticalized *pars basilaris*, likely caused by the deformation of the sphenoid body and greater and lesser wings. The squamous part of the occipital bone is composed only of the *pars supra-occipitalis*, with a non-developed *pars interparietalis*. A premature fusion of the *pars lateralis* with the *pars supra-occipitalis* was observed in Infant 1, along with an early fusion of the greater wings with the sphenoid body. The abnormal thickening and shortening of the lesser and greater wings further accentuate this structural impact, suggesting significant early cranial malformation. The superior border of the *pars supra-occipitalis* in Infants 1 and 2 displays an inward folding. Additionally, the inferior margin of the *pars supra-occipitalis* exhibits a semi-circular shape, with a well-defined form in the first, and a narrower, inward-folded margin in the latter. In contrast, Infant 3 reveals an inverted V-shaped inferior border with a vertical division or pseudo-suture and a decreased thickness (Figs. 2 and 3).

The *pars basilaris* is elongated and narrow in the three infants and the *pars lateralis* is shortened and narrow with short condylar and jugular limbs. The temporal bones, including the *pars petrosa*, are shortened, with reduced zygomatic processes and a diminished squamous part. (Figs. 4 and 5). The parietal bones appear to be absent in Infants 1 and 3. In Infant 2, the right parietal is present, while the left was not identified, likely due to fragmentation. The bone is extremely underdeveloped, with pronounced narrowing and elongation. It appears flattened, distorted, and small in size, lacking parietal eminence and positioned nearly horizontally (Irurita et al., 2015; Mathews, n.d., Fig. 6.

The frontal squama is absent, leading to a diminished frontal bone with a horizontal orientation, and a posteroinferior and lateral deviation. The form of expression is identical in Infants 1 and 2, with a more pronounced curvature in Infant 3. Facial morphology alterations are most pronounced in the zygomatic bone, with a rhomboid shape, and shortened frontal and temporal processes significantly thickened in Infants 1 and 2 (Fig. 7).

In addition, alterations in the maxilla and dentition were observed in Infants 2 and 3. Both present a premature fusion of the hemimaxilla, and Infant 3 also shows a gemination/fusion of the two central incisors, sharing a single alveolus – single maxillary central incisor (Cohen, 2006; Soxman et al., 2019), positioned in a plane as though it were projected forward relative to the lateral incisors (Figs. 8 and 9)

A slight asymmetry in the upper limbs is observed in Infant 1, the left limb is marginally thinner than the right, particularly in the ulna and radius. Although there are some taphonomic alterations, these bones also exhibit a straight configuration with less defined curvatures than typically expected, particularly at the distal extremity (Fig. 10).

Infant 3 displays more pronounced postcranial morphological variations. The superior articular facets of the atlas exhibit a pronounced elongated shape. The clavicles are asymmetric, with the left measuring

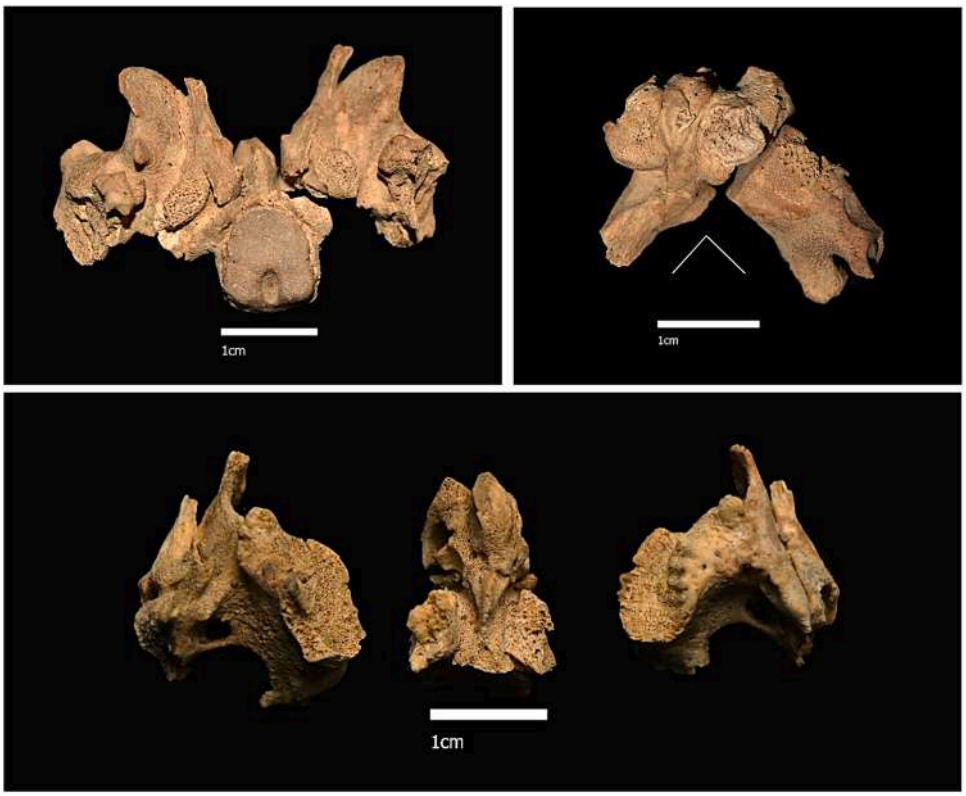

Fig. 3. Sphenoid bone exhibiting severe deformation of the body and narrowing of the lesser and greater wings. a) Infant 1, showing premature fusion of the greater wings; b) Infant 1, with a flexed cranial base angle and verticalized pars basilaris; c) Infant 3, showing no fusion of the greater wings, narrowing of the body, and significant thickening and shortening of the greater wings.

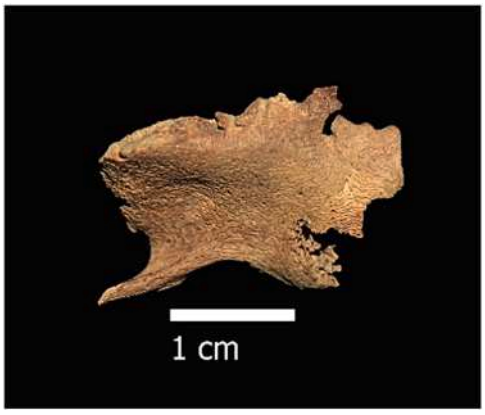

Fig. 4. Left temporal bone of Infant 1, showing a diminished squamous part and reduced zygomatic process, ectocranial view.

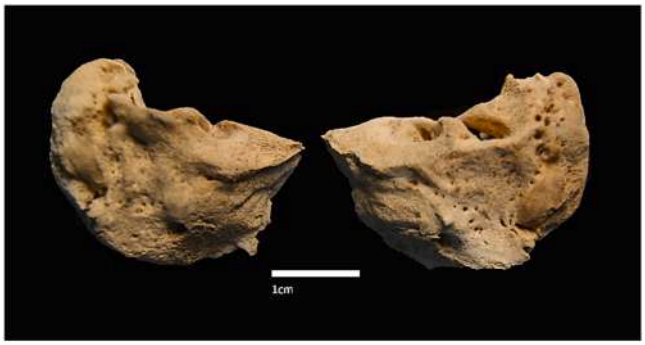

Fig. 5. Right and left pars petrosa of Infant 2, showing severe shortening and a rhomboid shape, ectocranial view.

34.7 mm and the right 43.4 mm. The scapulae exhibit an almost triangular shape, with a narrow medial border descending straight toward the inferior angle. Additionally, the pubic bones appear narrower and elongated in length (Fig. 11).

4. Discussion

Biomedical research highlights the wide range of cranial structural anomalies that can manifest in individuals with anencephaly (Munteanu et al., 2020; Berezina and Buzhilova, 2021; Schimp et al., 2021). The cranial floor and cranial vault are the most affected areas, influencing the shape and dimensions of facial bones (Irurita et al., 2015). A reduction in the cranial floor angle appears to prompt adaptive changes in adjacent structures, most notably in the positioning of the *pars lateralis*, *pars petrosa*, and temporal bones (Fields et al., 1978). These variations seemingly reflect different stages of brain development or the severity of the anomaly (Berezina and Buzhilova, 2021; Fields et al., 1978; Irurita et al., 2015; Schimp et al., 2021).

The three infants from the SDCN lack the cranial vault, and also exhibit an abnormal morphology of the occipital, sphenoid, temporal, zygomatic, and frontal bones, strongly suggesting anencephaly. These alterations are considered pathognomonic signs of the condition, e.g., Schimp et al. (2021) concur that a fetal skeleton lacking parietal bones, the squamous portions of the frontal, temporal, or occipital bones, and featuring a nearly unidentifiable prematurely fused sphenoid could be considered indicative of anencephaly. This pattern aligns with the morphological abnormalities observed in the SDCN cases. Although a parietal bone is present in Infant 2, it is significantly reduced and altered, aligning with some previously described cases (Irurita et al.,

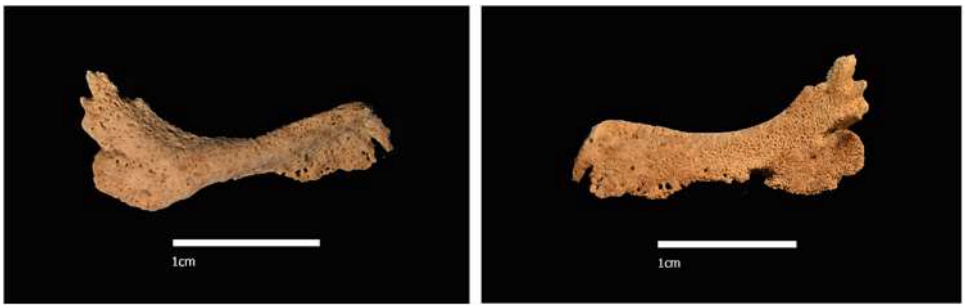

Fig. 6. Right parietal bone of Infant 2, showing extreme underdevelopment with pronounced narrowing and elongation. Left image lateral view; right image medial view.

Fig. 7. Right and left frontal and zygomatic bones of Infants 1 and 3 in anterior view. a) and b) Infant 1; c) and d) Infant 3.

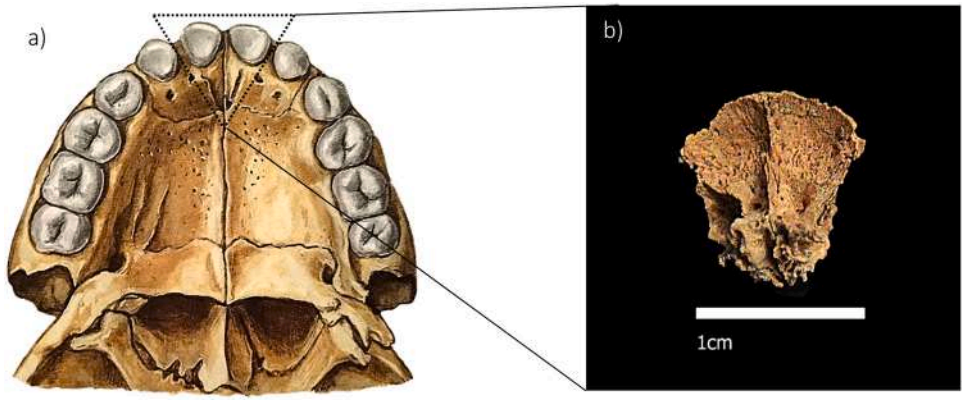

Fig. 8. Maxilla with premature fusion of the hemimaxilla of Infant 2. (a) Schematic representation of the maxilla in inferior view (adapted from Sobotta, 2006); (b) Fragment of the fused hemimaxilla of Infant 2, showing crypts for teeth 51 and 61 in inferior view.

2015; Mathews, n.d.).

One of the most striking aspects is the premature fusion of key cranial elements (Berezina and Buzhilova, 2021; Mathews, n.d.; Schimp et al., 2021). For instance, the premature fusion of the *pars lateralis* with the *pars supra-occipitalis*, typically occurring at 1–3 years of age (Cunningham et al., 2016), was observed in Infant 1, which is unusual for this age group. Similarly, early fusion of the greater wings of the sphenoid body was present. The inward folding of the superior border of the *pars supra-occipitalis* in Infants 1 and 2 adds to the cranial deformities, contrasting with the inverted V-shaped inferior border of Infant 3.

The frontal bones also show significant malformations, with the absence of the frontal squama and a posteroinferior deviation of the remaining bone. The effects extend to facial structures, particularly the zygomatic bones, further suggesting an extensive cranial disruption characteristic of anencephaly (Berezina and Buzhilova, 2021; Mathews, n.d.; Schimp et al., 2021). Additionally, a premature fusion of the maxillae was observed in two individuals. In Infant 3, this feature was more pronounced, with a single maxillary central incisor, suggesting a developmental disturbance in the maxillofacial region. A single maxillary central incisor is an etiologically diverse anomaly that can occur in various conditions, without necessarily indicating a syndromic disorder (Cohen, 2006). The postcranial skeletons of these individuals reveal relatively minor anomalies. The only noteworthy postcranial variation was the slight asymmetry of the upper limbs in Infant 1, and more pronounced asymmetry in Infant 3, particularly in the clavicles and

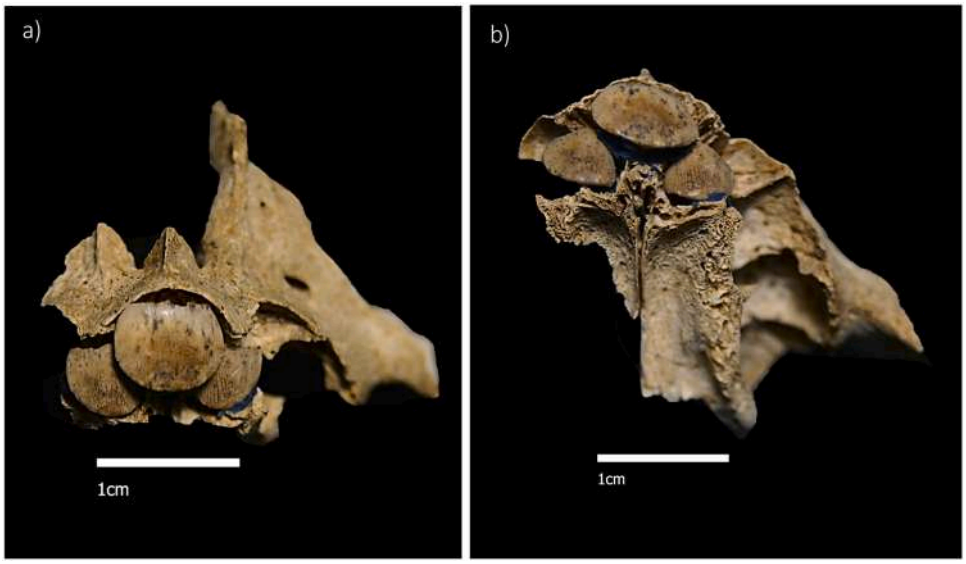

Fig. 9. Maxillae with premature fusion and a single maxillary central incisor in Infant 3. a) Maxillae in anterior view; b) Maxillae in inferior view.

Fig. 10. Forearms of Infant 1 showing slight asymmetry and a straight diaphysis. Ulnae in posterior view (left) and radii in posterior view (right).

alterations of the scapulae. These variations indicate that some cases of anencephaly may present with subtle postcranial abnormalities as well. Some anencephalic skeletons present craniorachischisis, which affects the size of clavicles and scapulae (Schimp et al.,2021). Concurrently, an asymmetry of the clavicles and an atypical morphology of the scapulae were observed in Infant 3, even though no alterations on the vertebras and in the vertebral extremities of the ribs were present.

These findings are consistent with research that documents similar patterns of cranial vault absence, premature fusion, and skeletal asymmetries in anencephalic individuals (Schimp et al., 2021). The morphological alterations observed in the SDCN infants are consistent with severe cases of anencephaly and provide further evidence of the pathological progression and structural manifestations of this condition. Moreover, Infant 3 likely suffered from a more severe form, which may have contributed to a shorter survival period. Previously documented cases suggest that the underdevelopment of the squamous portions of the occipital, frontal, and temporal bones, as well as the morphology and angle of the sphenoid-occipital synchondrosis, are the most indicative signs of this condition (Schimp et al., 2021).

Anencephaly significantly increases the risk of *in-utero* mortality, and those infants who survive birth have an even higher risk of mortality due to their exposure to the extra-uterine environment (David and Nixon, 1976; Padmanabhan, 2006). Despite this, based on dental development, the three infants from the SDCN show evidence of postnatal survival, with one surviving until the age of one month and the others approximately four months. Dental calcification, specifically the initiation of root formation in the central incisors and the development of the second molars, provides unequivocal evidence that these individuals survived birth and showed resilience to live for some period after birth. Although the dental method used to estimate age at death was developed in contemporary children, the timing and duration of tooth formation recorded in past populations are similar, indicating an insignificant effect of secular trends (Cardoso et al., 2010; Liversidge, 2015). The measurements of the long bones also suggest growth beyond 40 weeks gestation, with a slight delay relative to the dentition. However, anencephaly can result in low birth weight and growth delays that can be detected in the bones (Padmanabhan, 2006; Shewmon, 1988). The differences in long bone growth observed among the three infants should also take into account interpersonal variability (Lewis, 2007; Scheuer and Black, 2004) and the midpoint for dental age estimation that indicates an average of 6 months. Survival reports of anencephalic infants are rare, Baird and Sadovnick (1984) reported that over 40 % survived beyond 24 hours, 35 % up to three days, and 5 % up to seven days. Shewmon (1988) noted cases of infants living up to fourteen months. Obeidi et al. (2010) found that 42 % of 26 infants were born alive, with survival times ranging from 10 minutes to 8 days. These cases benefited from modern biomedical care, unlike archaeological cases. The proximity of a hospital within the same complex as the convent might suggest, albeit remotely, the possibility of some form of medical care for these infants. However, no historical records have been found to support the idea that such care was provided to young individuals.

The differential diagnosis of anencephaly must take into account other conditions with similar skeletal alterations, including a) amniotic band syndrome, particularly when the band traverses the head, as it affects the skull asymmetrically leading to cranial deformities, and amputations are common in other parts of the body; b) acardioacephaly, marked by the absence of the cranium; c) severe microcephaly, abnormally small size of the skull that maintains the bones of the vault; d) encephalocele, a birth defect in which brain tissue protrudes from the skull (usually like a sac) most commonly occurring in the occipital region, it is often associated with hydrocephalus and other

Fig. 11. Postcranial morphological variations observed in Infant 3. a) Atlas with elongation of the superior articular facets (left side), compared to the atlas of an individual with the same dental development (right side); b) Pubis with a narrow and elongated form, anterior view; c) Scapulae with a triangular and narrow shape, anterior view.

brain malformations and retains some cranial integrity. The prognosis varies, with some cases being compatible with life depending on the extent of brain involvement; such as exencephaly, the presence of brain tissue with an absence of the calvaria, is considered a transitional stage in the spectrum of anencephaly, where the brain initially forms but degenerates andholoprosencephaly, a complex congenital brain malformation characterized by the incomplete division of the prosencephalon into distinct right and left hemispheres, often accompanied by varying degrees of craniofacial abnormalities (Berezina and Buzhilova, 2021; Dubourg et al., 2007; Lemire et al., 1981; Mikayilli et al., 2020; Palamenghi et al., 2021; Palamenghi et al., 2021; Shewmon, 1988). Anencephaly cases that exhibit facial characteristics shared with holoprosencephaly have been documented in the literature (Cohen, 2006; Lemire et al., 1981). Furthermore, the occurrence of both anencephaly and holoprosencephaly within the same family suggests a potential genetic link between these brain anomalies in certain cases (Cohen, 2006; Lemire et al., 1981; Salari et al., 2022). Exencephaly is often regarded by researchers as an earlier developmental stage of anencephaly due to the strong similarities between the two conditions. The primary distinction lies in the presence of brain tissue in exencephaly, regardless of the lack of a complete cranial vault (Berezina and Buzhilova, 2021; Irurita et al., 2015). In the cases under study, it is impossible to know whether brain tissue was preserved, but the near-total loss of the cranial vault proves the high severity of the condition and leads to anencephaly.

Environmental factors have long been associated with the incidence of anencephaly. Data from urbanized, industrial regions indicate a higher prevalence of neural tube defects in areas of higher population density (Pleydell, 1960). Maternal health also plays a critical role, with studies linking infections during early pregnancy to a heightened risk of congenital anomalies, particularly during the first trimester (Pleydell, 1960; Salari et al., 2022). The vulnerability of fetal development at this stage underscores the complex interplay of environmental and maternal factors in the occurrence of anencephaly (Aguilar-Garduno et al., 2010). The population that lived between the 17th to the beginning of the 19th century in central Lisbon faced numerous challenges, including malnutrition, epidemics, developing industrialization and natural disasters such as the 1755 violent earthquake (Araújo, 1995; Barbosa and Godinho, 2001). Consequently, health and social conditions were difficult, especially for pregnant women, who are physiologically more vulnerable (Barreiros, 2014).

Interestingly, and despite the presence of a conspicuous congenital anomaly, archaeologically perceived funerary rites given to these infants did not deviate from the standard burial rites in any way distinct. The SDCN appears to conflate individuals from distinct social strata, serving as a common resting place for very young children bonded by their early age at death.

Archaeological cases of anencephaly are rare, with most available data deriving from clinical studies and medical collections (Dudar, 2010; Mathews, n.d.). An instance of anencephaly has been identified in a fetus from the Elmbank Pioneer Cemetery, in Toronto, Canada (Dudar, 2010). Two other fetal cases were identified in the Roman village of Kellis in Egypt's Dakhleh Oasis (Dupras et al., 2003; Mathews, n.d.). Other comparable pathological features were observed in the earliest recorded archaeological case of an anencephalic fetus, detailed in a report by the Royal Academy of Sciences by Saint-Hilaire (1826) and Brothwell & Powers (1968). The three presented cases from the same necropolis represent a remarkably rare occurrence, particularly given their exceptional state of preservation and completeness. These examples provide crucial evidence of the full manifestation of anencephaly during a historical period before modern biomedical interventions. Such findings offer invaluable comparative data for the identification of similar cases in other archaeological contexts. The analysis of anencephaly in skeletal remains from past populations also contributes to a deeper understanding of the condition's diverse morphological features and manifestations in historical communities.

5. Conclusions

The analysis of three infants from the SDCN offers a rare and valuable glimpse into the occurrence of anencephaly in a historical population. The distinct cranial and facial morphological alterations—particularly the absence of the cranial vault and premature fusion of key cranial elements—strongly support the diagnosis of anencephaly. Evidence of brief postnatal survival underscores the resilience of these individuals despite the severity of their congenital malformation and the lack of modern biomedical care. Identifying such cases in archaeological contexts deepens our understanding of the morphological diversity of anencephaly in past populations and enriches broader research into developmental disruptions associated with congenital anomalies. These findings provide essential data for recognizing similar cases in other archaeological contexts.

CRediT authorship contribution statement

Lourenco Marina: Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Cunha Eugénia:** Writing – review & editing, Validation, Supervision, Methodology. **Curate Francisco:** Writing – review & editing, Validation, Supervision.

Funding

The first author of this paper was funded by Fundação para a Ciência e Tecnologia through a PhD grant (reference 2020.07068.BD, DOI 10.54499/2020.07068.BD, https://doi.org/10.54499/2020.07068.BD). This work was implemented at the R&D Units Center for Functional Ecology—Science for People and the Planet (CFE), with the reference UIDB/04004/2020, and Research Centre for Anthropology and Health (CIAS), with the reference UIDB/00283/2020, both financed by the FCT/MCTES through national funds (PIDDAC).

Declaration of Competing Interest

We have no conflicts of interest to disclose.

Acknowledgments

The authors would like to thank Era Arqueologia S.A.

References

Aguilar-Garduno, C., Lacasana, M., Blanco-Munoz, J., Borja-Aburto, V.H., Garcia, A.M., 2010. Parental occupational exposure to organic solvents and anencephaly in Mexico. Occup. Environ. Med. 67 (1), 32–37. https://doi.org/10.1136/oem.2008.044743.

AlQahtani, S.J., Hector, M.P., Liversidge, H.M., 2010. Brief communication: the London atlas of human tooth development and eruption. Am. J. Phys. Anthropol. 142 (3), 481–490. https://doi.org/10.1002/ajpa.21258.

Araújo, A., 1995. A morte em Lisboa: Atitudes e representações 1700-1830. Editorial Notícias, Coimbra.

Baird, P.A., Sadovnick, A.D., 1984. Survival in Infants with Anencephaly. Clin. Pediatr. 23 (5), 268–271. https://doi.org/10.1177/000992288402300505.

Barbosa, H.; Godinho, A. 2001. Crises de mortalidade em Portugal desde meados do século XVI até ao início do século XX. Universidade do Minho. Núcleo de Estudos de População e Sociedade (NEPS).

Barreiros, B.P.F. (2014). Concepções do corpo no Portugal do século XVIII: sensibilidade, higiene e saúde pública. Universidade NOVA de Lisboa (Portugal).

Barron, S., 2016. Anencephaly: an ongoing investigation in Washington State. AJN, Am. J. Nurs. 116 (3), 60–66. https://doi.org/10.1097/01.NAJ.0000481286.16720.6e.

Bello, S.M., Thomann, A., Signoli, M., Dutour, O., Andrews, P., 2006. Age and sex bias in the reconstruction of past population structures. Am. J. Phys. Anthropol. 129 (1), 24–38. https://doi.org/10.1002/ajpa.20243.

Berezina, N., Buzhilova, A., 2021. Rare cases of rare diseases: re-examining early 20th century cases of anencephaly from the collection of the Moscow State University, Russia. Int. J. Paleopathol. 34, 12–19. https://doi.org/10.1016/j.ijpp.2021.05.008.

Bergman, J.E.H., Perraud, A., Barišić, I., Kinsner-Ovaskainen, A., Morris, J.K., Tucker, D., Wellesley, D., Garne, E., 2024. Updated EUROCAT guidelines for classification of cases with congenital anomalies. Birth Defects Res. 116 (2), e2314. https://doi.org/10.1002/bdr2.2314.

Brothwell, D.R., Powers, R., 1968. Congenital malformations of the skeleton in earlier man. In: Brothwell, D.R. (Ed.), The Skeletal Biology of Earlier Human Populations. Pergamon Press, Oxford, pp. 173–204.

Byrne, P., Canadian Paediatric Society (CPS), Bioethics Committee, 2005. Use of anencephalic newborns as organ donors. Paediatr. Child Health 10 (6), 335–337. https://doi.org/10.1093/pch/10.6.335.

Cardoso, H.F.V., Abrantes, J., Humphrey, L.T., 2014. Age estimation of immature human skeletal remains from the diaphyseal length of the long bones in the postnatal period. Int. J. Leg. Med. 128 (5), 809–824. https://doi.org/10.1007/s00414-013-0925-5.

Cardoso, H.F.V., Heuzé, Y., Júlio, P., 2010. Secular change in the timing of dental root maturation in Portuguese boys and girls. Am. J. Hum. Biol. 22 (6), 791–800. https://doi.org/10.1002/ajhb.21084.

Cohen, M.M., 2006. Holoprosencephaly: clinical, anatomic, and molecular dimensions. Birth Defects Res. Part A: Clin. Mol. Teratol. 76 (9), 658–673. https://doi.org/10.1002/bdra.20295.

Cunningham, C., Scheuer, L., Black, S., 2016. Developmental juvenile osteology. Academic press.

David, T.J., Nixon, A., 1976. Congenital malformations associated with anencephaly and iniencephaly. J. Med. Genet. 13 (4), 263–265. https://doi.org/10.1136/jmg.13.4.263.

Dubourg, C., Bendavid, C., Pasquier, L., Henry, C., Odent, S., David, V., 2007. Holoprosencephaly. Orphanet J. Rare Dis. 2 (1), 8. https://doi.org/10.1186/1750-1172-2-8.

Dudar, J.C., 2010. Qualitative and quantitative diagnosis of lethal cranial neural tube defects from the fetal and neonatal human skeleton, with a case study involving taphonomically altered remains. J. Forensic Sci. 55 (4), 877–883. https://doi.org/10.1111/j.1556-4029.2010.01382.x.

Dupras, T.L., Breach, T., Tocheri, M., Molto, J.E., Sheldrick, P., 2003. A naturally mummified fetus from Roman period Egypt. In: Tempe (AZ). Paleopathology AssociationProceedings of the Paleopathology Association'S Annual Meeting, 2003, p. 4. April 22 –23.

Fields, H.W., Metzner, L., Garol, J.D., Kokich, V.G., 1978. The craniofacial skeleton in anencephalic human fetuses. I. Cranial floor. Teratology 17 (1), 57–65. https://doi.org/10.1002/tera.1420170113.

Funayama, C.A.R., Pfeifer, L.I., Ramos, E.S., Santucci, P.Z., Gomy, I., Neto, A.M.A., 2011. Three-year-old child with meroacrania – Neurological signs. Brain Dev. 33 (1), 86–89. https://doi.org/10.1016/j.braindev.2010.02.001.

Garol, J.D., Fields, H.W., Metzner, L., Kokich, V.G., 1978. The craniofacial skeleton in anencephalic human fetuses. II. Calvarium. Teratology 17 (1), 67–73. https://doi.org/10.1002/tera.1420170114.

Irurita, J., Alemán, I., Viciano, J., López-Lázaro, S., Botella, M.C., 2015. Alterations of skull bones found in anencephalic skeletons from an identified osteological collection. Two case reports. Int. J. Leg. Med. 129 (4), 903–912. https://doi.org/10.1007/s00414-014-1123-9.

Lemire, R.J., Cohen, M.M., Beckwith, J.B., Kokich, V.G., Siebert, J.R., 1981. The facial features of holoprosencephaly in anencephalic human specimens. I. Historical review and associated malformations. Teratology 23 (3), 297–303. https://doi.org/10.1002/tera.1420230304.

Lewis, M.E., 2007. The bioarchaeology of children: Perspectives from biological and forensic anthropology. Cambridge university press.

Liversidge, H.M., 2015. Controversies in age estimation from developing teeth. Ann. Hum. Biol. 42 (4), 397–406. https://doi.org/10.3109/03014460.2015.1044468.

Mathews, S. n.d. Diagnosing Anencephaly In Archaeology: A Comparative Analysis Of Nine Clinical Specimens From The Smithsonian Institution Nation. 108.

Mikayilli, M., Hasanov, T., Demirci Otluoğlu, G., Nacitarhan, D.E., Toktaş, Z.O., Çolak, A., 2020. Congenital lateral encephalocele—case report. Child'S. Nerv. Syst. 36 (12), 3119–3122. https://doi.org/10.1007/s00381-019-04436-1.

Munteanu, O., Cîrstoiu, M.M., Filipoiu, F.M., Neamţu, M.N., Stavarache, I., Georgescu, T. A., Bratu, O.G., Iorgulescu, G., Bohîlţea, R.E., 2020. The etiopathogenic and morphological spectrum of anencephaly: a comprehensive review of literature. Rom. J. Morphol. Embryol. 61 (2), 335–343. https://doi.org/10.47162/RJME.61.2.03.

Obeidi, N., Russell, N., Higgins, J.R., O'Donoghue, K., 2010. The natural history of anencephaly: the natural history of anencephaly. Prenat. Diagn. 30 (4), 357–360. https://doi.org/10.1002/pd.2490.

Padmanabhan, R., 2006. Etiology, pathogenesis and prevention of neural tube defects. Congenit. Anom. 46 (2), 55–67. https://doi.org/10.1111/j.1741-4520.2006.00104.x.

Palamenghi, A., Biehler-Gomez, L., Mattia, M., Breda, L., Cattaneo, C., 2021. A probable case of holoprosencephaly with cyclopia in a full-term fetus from a modern skeletal collection. Int. J. Paleopathol. 33, 25–29. https://doi.org/10.1016/j.ijpp.2020.12.003.

Palamenghi, A., Biehler-Gomez, L., Mattia, M., Breda, L., Cattaneo, C., 2021. The challenging diagnosis of cranial congenital anomalies in a newborn from an Italian 20th century documented skeletal collection. Int. J. Osteoarchaeol. 31 (2), 309–315. https://doi.org/10.1002/oa.2952.

Pleydell, M.J., 1960. Anencephaly and other congenital abnormalities. BMJ 1 (5169), 309–315. https://doi.org/10.1136/bmj.1.5169.309.

Reis, F., 2001. Os expostos em Santarém. A acção social da Misericórdia (1691-1710). Lisboa. Edições Cosmos.

Saint-Hilaire, G., 1826. Note sur un monstrehumain, trouv´e dans les ruines de The`bes en´ Egypte; par M. Passalacqua. Bulletin des Sciences M´edicales 7, 105–108.

Salari, N., Fatahi, B., Fatahian, R., Mohammadi, P., Rahmani, A., Darvishi, N., Keivan, M., Shohaimi, S., Mohammadi, M., 2022. Global prevalence of congenital anencephaly: a comprehensive systematic review and meta-analysis. Reprod. Health 19 (1), 201. https://doi.org/10.1186/s12978-022-01509-4.

Santana, M.V.M.D.C., Canêdo, F.M.C., Vecchi, A.P., 2016. Anencefalia: conhecimento e opinião dos médicos ginecologistas-obstetras e pediatras de Goiânia. Rev. Bioética 24 (2), 374–385. https://doi.org/10.1590/1983-80422016242138.

Scheuer, L., & Black, S.M. (Eds.). (2004). The juvenile skeleton. Elsevier Academic Press.

Schimp, J., Dornia, C., Fanghänel, J., Proff, P., Blanck-Lubarsch, M., Weingärtner, J., Kirschneck, C., 2021. Morphometric characteristics of anencephalic skulls – a comparative study. Ann. Anat. - Anat. Anz. 233, 151607. https://doi.org/10.1016/j.aanat.2020.151607.

Shewmon, D.A., 1988. Anencephaly: selected medical aspects. Hastings Cent. Rep. 18 (5), 11. https://doi.org/10.2307/3562217.

Siebert, J.R., Kokich, V.G., Warkany, J., Lemire, R.J., 1987. Atelencephalic microcephaly: craniofacial anatomy and morphologic comparisons with holoprosencephaly and anencephaly. Teratology 36 (3), 279–285. https://doi.org/10.1002/tera.1420360302.

Sobotta, J., 2006. Sobotta: atlas de anatomía humana, Vol. 1. Médica Panamericana.

Soxman, J.A., Wunsch, P.B., Haberland, C.M., 2019. Anomalies of Crown Size. In: Soxman, J.A., Wunsch, P.B., Haberland, C.M. (Eds.), Anomalies of the Developing Dentition. Springer International Publishing, pp. 7–14. https://doi.org/10.1007/978-3-030-03164-0_2.

Van Allen, M.I., Kalousek, D.K., Chernoff, G.F., Juriloff, D., Harris, M., McGillivray, B.C., Yong, S., Langlois, S., Macleod, P.M., Chitayat, D., Friedman, J.M., Wilson, R.D., McFadden, D., Pantzar, J., Ritchie, S., Hall, J.G., 1993. Evidence for multi-site closure of the neural tube in humans. Am. J. Med. Genet. 47 (5), 723–743. https://doi.org/10.1002/ajmg.1320470528.

Van Gool, J.D., Hirche, H., Lax, H., De Schaepdrijver, L., 2018. Folic acid and primary prevention of neural tube defects: a review. Reprod. Toxicol. 80, 73–84. https://doi.org/10.1016/j.reprotox.2018.05.004.