

Concordance factors in craniosynostosis twins: a meta-analysis and case report

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Introduction: Craniosynostosis is a condition where the cranial sutures close prematurely. It is influenced by both genetics and environment. This paper focuses on craniosynostosis in twins, which is an understudied area. It presents a case report of male identical twins and conducts a meta-analysis based on 34 articles to understand the factors affecting concordance in twins who have craniosynostosis. The study considers factors such as zygosity, gender, genetic syndromes, and the type of synostosis.

Material and methods: A meta-analysis was conducted on 105 twin pairs (210 patients) identified from studies carried out between 1963 to 2023. The eligible studies, based on PICO criteria, included case reports and case series focusing on twins with craniosynostosis. A systematic literature search was conducted on PUBMED and Mendeley platforms to gather data on gestational age, zygosity, genetic syndromes, affected sutures, and concordance.

Results: The report is about two identical twin brothers who had sagittal and metopic suture synostosis. They were treated successfully with cranial remodeling surgery. In a meta-analysis of 105 twin pairs (210 patients), a total of 25.9% showed concordance. The study found a significant difference in concordance between monozygotic (45.3%) and dizygotic (7.3%) twins. The analysis also revealed that twins with scaphocephaly had a higher degree of concordance than those with trigonocephaly (46.7% vs. 18.9%, respectively). The study did not find any significant correlation between gender, the presence of genetic syndromes, and concordance.

Conclusion: This investigation highlights the complex interplay of genetic and environmental factors in craniosynostosis in twins. The higher concordance in monozygotic twins emphasizes the genetic basis. These findings validate existing literature and provide new insights.

Keywords: craniosynostosis, meta-analysis, case report, neurosurgery

INTRODUCTION

Craniosynostosis consists of the premature closure of one or more cranial sutures. It is classified according to the suture where the closure occurred and may or may not be linked to genetic syndromes [1]. It is estimated that the incidence of craniosynostosis is 1 case in 2100 - 2500 live births, with the main type of craniosynostosis being scaphocephaly, caused by the closure of the sagittal suture and accounting for around 39% of cases, followed by trigonocephaly, caused by the closure of the metopic suture and accounting for 19% of cases [1,2].

Research indicates that genetic factors play a significant role in the development of craniosynostosis, with studies associating mutations in genes such as Axin2, FUZZY, FGFR1, and ERF, among others, with a greater likelihood of developing the disease. In addition, intrauterine factors, such as fetal growth restriction and macrosomia, and maternal lifestyle habits during pregnancy, such as smoking

and drug use, influence the development of craniosynostosis. Other factors such as multiple pregnancies, male gender, race, and age are also positively correlated with the development of this condition [3,4,5,6].

Craniosynostosis can be classified as non-syndromic, when patients only have cranial alterations, or syndromic, in cases where there are extracranial alterations. More than 100 genetic syndromes, such as Apert, Saethre-Chotzen, and Crouzon syndromes, are also related to an increased likelihood of developing this condition.

In addition to aesthetic manifestations, such as the abnormal shape of the head and facial anomalies, the restriction of cerebral growth in craniosynostosis can also result in increased intracranial pressure. This, in turn, can trigger symptoms such as nausea and headaches. Affected children can show motor deficits, seizures and experience delays in motor and language development. These symptoms highlight the complexity and impact of craniosynostosis on



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the child's central nervous system and overall development, making early treatment and multidisciplinary approaches essential for these children [7,8].

Twins, regardless of the presence or absence of genetic syndromes, have an increased likelihood of developing craniosynostosis. Notably, twins account for approximately 6.9% of craniosynostosis cases, although they make up only 2.3% of live births. This increased incidence among twins suggests a contribution of shared genetic and environmental factors during intrauterine development to the onset of this condition [10,11].

In cases where twins with craniosynostosis have the same type of suture closure, they are classified as concordant. On the other hand, in cases where only one of the twins has craniosynostosis or when both have it, but of different types, they are classified as discordant. This classification is useful for understanding the similarity or dissimilarity in the development of craniosynostosis between twins and assessing the influence of genetic and environmental factors on the expression of the disease.

To date, the issue of concordance of craniosynostosis in twins has been poorly explored, with most studies restricted to case reports. This study presents the report of a pair of twins with craniosynostosis, accompanied by a meta-analysis that assessed the concordance of this condition in monozygotic and dizygotic twins. This approach seeks to provide a more comprehensive and systematic analysis of the prevalence and concordance patterns of craniosynostosis in different types of twins, contributing to a deeper understanding of the genetic mechanisms in the development of this condition.

MATERIALS AND METHODS

Research Question and Study Eligibility Criteria. The guiding question for this study was "What factors affect concordance in twins with craniosynostosis?". The types of studies included were case reports and case series. Articles that did not specify the type of craniosynostosis or type of zygosity were excluded from this meta-analysis. The twins were considered to be concordant when they both had synostosis of the same suture and the concordance factors were defined as the epidemiological and genetic characteristics that could have influenced the development of the same type of craniosynostosis in both twins.

To identify the relevant studies for this review, the population-intervention-comparator-outcome (PICO) framework was used. The population chosen to answer this question were twins, monozygotic or dizygotic, with or without genetic syndromes, and at least one of them had craniosynostosis. The intervention/comparison made was between twins of different zygositys, different sexes, and

with or without genetic syndromes. The outcome analyzed was the concordance or not of the type of craniosynostosis. Literature Search.

An electronic literature search was carried out by two researchers independently on the PUBMED, and Mendeley platforms, limiting the studies searched to the years 1963 to 2023. The terms used were "Twins" and "Craniosynostosis". Only publications available in English were included in this meta-analysis. Study Selection.

Two researchers performed the stages of identifying eligible studies and screening independently. In cases where there was disagreement, a third researcher resolved the issue. The process of selecting, including, and excluding studies is explained in detail in Table 1.

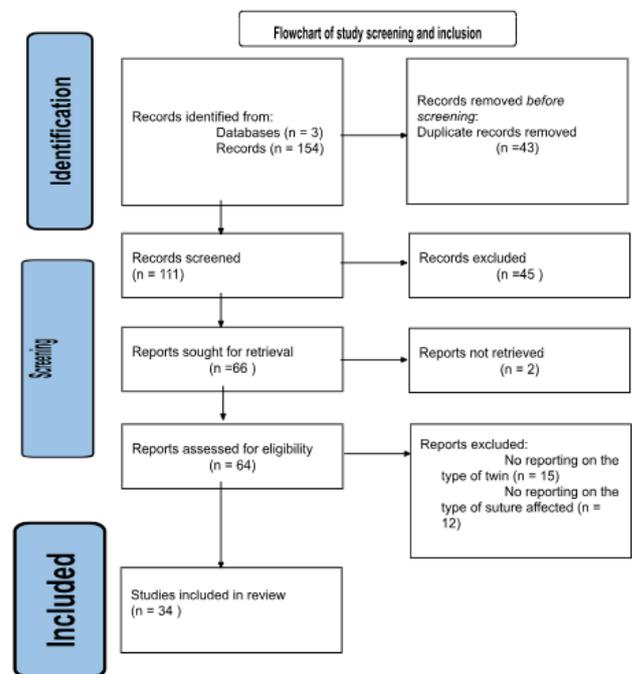


Table 1- Flow chart

Data collection.

In all the studies that were considered eligible, data was collected on gestational age, gender, type of twinning, presence or absence of genetic syndromes, affected sutures, and concordance or not between the twins. The information collected from the studies is summarized in Table 2 (attached to the article).

Statistical analysis

The statistical tests used were Pearson's chi-square, Fisher's exact test, percentage, mean and standard deviation. SPSS software was used to carry out these tests and data management.

RESULTS

This meta-analysis synthesized data from 34 articles including case reports and series, covering 105 twin pairs or 210 patients with craniosynostosis.

Case report.

Two identical male twins, born as the result of an unplanned first pregnancy, to a 28-year-old mother and a 29-year-old father who denied any consanguinity, were referred to the service due to a history of an abnormal skull shape, which was initially identified during the last month of pregnancy through an ultrasound scan.

A CT scan of the skull confirmed the diagnosis of craniosynostosis, with one twin exhibiting synostosis of the sagittal suture and the other showing synostosis of the metopic suture. Magnetic resonance imaging of the skull was conducted, ruling out other cranial malformations. Additionally, genetic tests were performed, excluding the presence of genetic syndromes associated with craniosynostosis.

At 7 months of age, both patients underwent cranial remodeling surgery, and they progressed post-operatively without any complications. (See figure 1)

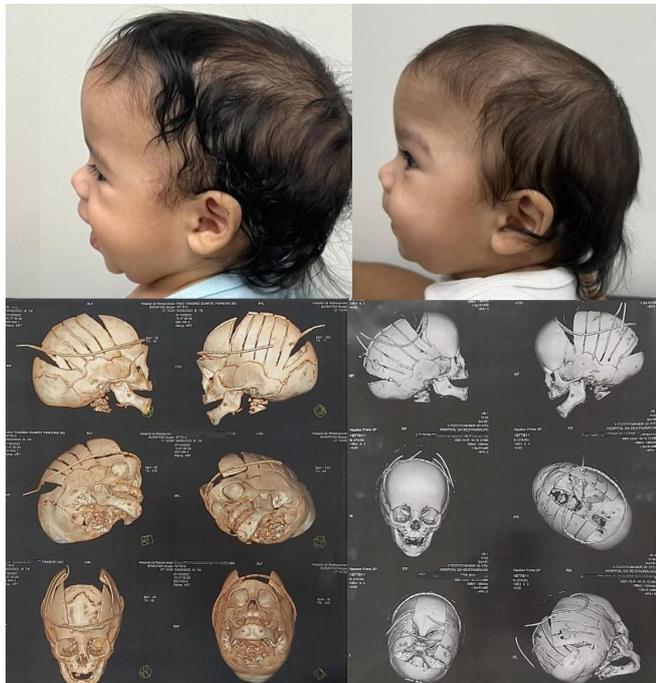


Figure 1 - pre operative pictures of the patients and post operative CT scan

Patient characteristics.

A total of 210 individuals were identified, corresponding to 105 pairs of twins. The average maternal age was 28.1 years (n=17; range, 21 to 36 years; SD 4.5) and the gestational age of these children was 35.1 weeks (n=26; range, 28 to 40 weeks; SD 3). 9 pairs of twins were born between 37-40 weeks, 9 between 35-36 weeks, 8 below 35 weeks and in 82 the gestational age was not reported.

The 105 pairs had the type of zygosity recorded, with 53 (50.4%) being dizygotic and 52 (49.6%) monozygotic. We identified 19 (17.6%) cases in which both twins were male, 15 (13.9%) in which both were female, 4 (3.7%) in which one was male and the other female and 67 (64.8%) cases the sex of the twins was not specified. Excluding the unidentified, the incidence in men was 55% (42/76) and 45% in women (34/72). (See Table 3)

Table 3: Patient characteristics

Table 3: Patient characteristics	n (%)
Twins types	
Monozygotic	52 (49,6)
Dizygotic	53 (51,4)
Twins sex	
Both male	19 (17,6)
Both female	30 (27,8)
Male/Female	4 (3,7)
Not mentioned	70 (64,8)
Suture affected	
Sagittal	67 (31,0)
None	65 (30,0)
Metopic	43 (20,6)
Coronal	9 (4,1)
Bicoronal	9 (4,1)
All	4 (1,8)
Lambdoid and bicoronal	4 (1,8)
Lambdoid	3 (1,3)
Lambdoid and coronal	2 (0,9)
Lambdoid, coronal and sagittal	2 (0,9)
Genetic syndrome	
With	14 (13)
Without	30 (27,8)
Not mentioned	64 (69,2)
Concordance	
Yes	28 (25,9)
No	80 (74,1)

With regard to genetic syndromes, they were present in 14 pairs (13%), absent in 30 pairs (27.8%) and no information was found on their presence in 64 (59.2%) pairs (See Table 4).

In relation to the type of suture with synostosis, 66 (31.0%) individuals had synostosis of the sagittal suture, 64 (30.0%) had no synostosis of any suture, 42 (20.6%) had synostosis of the metopic suture, 9 (4.1%) of the unilateral coronal suture, 9 (4.1%) of the bilateral coronal suture, 4 (1.8%) of all the sutures, 4 (1.8%) of the lambdoid and bicoronal suture, 3 (1.3%) of the lambdoid suture, 2 (0.9%) of the lambdoid and coronal suture and 2 (0.9%) of the lambdoid, bicoronal and sagittal suture. Considering only individuals with craniosynostosis, patients with sagittal suture synostosis accounted for 44%, metopic synostosis for 28.4%, unilateral coronal synostosis for 5.9% and bicoronal synostosis for 5.9%. The general analysis found that 26

Table 4.1 - Results of agreement on suture type between pairs of twins.

Type of Twins	Accordance Between Peers			p Value
	Present n (%)	Absent n (%)	Total n (%)	
Monozygotic	24 (45,3)	29 (54,7)	53 (100,0)	$p^{(1)} < 0,001^*$
Dizygotic	4 (7,3)	51 (92,7)	55 (100,0)	
Total	28 (25,9)	80 (74,1)	108 (100,0)	

(*) Significant association at 5%.

(1) Pearson's Chi-square test.

Table 4.2 - Results of agreement on the type of suture between pairs of twins with and without genetic syndromes.

Genetic Syndrome	Accordance Between Peers			p Value
	Present n (%)	Absent n (%)	Total n (%)	
With	8 (57,1)	6 (42,9)	14 (100,0)	$p^{(2)} = 0,393$
Without	13 (43,3)	17 (56,7)	30 (100,0)	
Grupo total	21 (47,7)	23 (52,3)	44 (100,0)	

(1) In 64 pairs the information was not recorded

(2) Pearson's Chi-square test.

Table 4.3 – Results of agreement on the type of suture between pairs of twins with the same gender.

Gender of peers	Accordance Between Peers			p Value
	Present n (%)	Absent n (%)	Total n (%)	
Both male	11 (57,9)	8 (42,1)	19 (100,0)	$p^{(2)} = 0,300$
Both female	6 (40,0)	9 (60,0)	15 (100,0)	
Total	17 (50,0)	17 (50,0)	34 (100,0)	

(1) In 4 pairs, the genders were mixed, and in the remaining 70 pairs, the gender was not recorded.

(2) Pearson's Chi-square test.

Table 4.4 – Assessment of agreement according to the most frequent types of sutures affected.

Type of Suture	Accordance Between Peers			p Value
	Present n (%)	Absent n (%)	Total n (%)	
With trigonocephaly	7 (18,9)	30 (81,1)	37 (100,0)	$p^{(2)} = 0,015^*$
With scaphocephaly	14 (46,7)	16 (53,3)	30 (100,0)	
Total	21 (31,3)	46 (68,7)	67 (100,0)	

(*) Significant association at 5%.

(2) Pearson's Chi-square test.

Table 4.5 – Assessment of agreement between sutures according to the type of twins with trigonocephaly.

Type of Twins	Accordance Between Peers			p Value
	Positive n (%)	Negative n (%)	Total n (%)	
Monozygotic	5 (33,3)	10 (66,7)	15 (100,0)	$p^{(2)} = 0,095$
Dizygotic	2 (9,1)	20 (90,9)	22 (100,0)	
Total	7 (18,9)	30 (81,1)	37 (100,0)	

(2) Fisher's Exact Test.

Table 4.6 – Assessment of agreement between sutures according to the type of twins with scaphocephaly.

Type of Twins	Accordance Between Peers			p Value
	Positive n (%)	Negative n (%)	Total n (%)	
Monozygotic	13 (50,0)	13 (50,0)	26 (100,0)	$p^{(2)} = 0,602$
Dizygotic	1 (25,0)	3 (75,0)	4 (100,0)	
Total	14 (46,7)	16 (53,3)	30 (100,0)	

(2) Fisher's Exact Test.

(25.9%) of the twins agreed on the type of suture and 79 (74.1%) disagreed.

According to the analysis of twin pairs, it was found that 45.3% of monozygotic twins had concordance while only 7.3% of dizygotic twins had concordance. The difference between the two was statistically significant.

The study also examined the relationship between concordance and genetic syndrome. It included 44 twin pairs, out of which 14 had a genetic syndrome. Among these 14 patients, 8 (57.1%) were concordant while 6 (42.9%) were discordant. Among the patients without syndromes, 13 (43.3%) had concordance while 17 (56.7%) were discordant. However, no statistically significant differences were found between these two groups.

The analysis of concordance and the gender of twins included 34 patients. It was found that the agreement between male twin pairs was 57.9%, whereas the agreement between female twin pairs was 40%. Despite the numerical difference, no statistical significance was found between them.

Out of the 37 patients with trigonocephaly, only 7 (18.9%) had concordance. Whereas, out of the 30 patients with scaphocephaly, 14 (46.7%) had concordance. This difference in concordance between the two groups was statistically significant.

Despite the difference in concordance between monozygotic and dizygotic patients in general, there was no significant difference when comparing the two groups in the trigonocephaly and scaphocephaly groups.

Refer to Table 4 for more information.

DISCUSSION

Craniosynostosis is a condition in which one or more cranial sutures close prematurely, leading to negative clinical and aesthetic effects. Both genetic and environmental factors contribute to its development, and the primary goal of this research is to evaluate the influence of genetic factors on this condition.

Excluding syndromes and genetic mutations, certain factors increase the risk of developing craniosynostosis. These factors include maternal lifestyle habits during pregnancy such as cocaine and tobacco use, as well as restrictions on fetal growth. A study conducted by Sanchez-Lara et al. involving 675 individuals with craniosynostosis revealed that nulliparity, macrosomia, and multiple

gestation (twins) were associated with a higher risk of craniosynostosis [3,12,13,14].

According to the study, scaphocephaly and trigonocephaly were found to be the most common types of craniosynostosis, accounting for 44% and 28.4% of cases, respectively. These results support a previous publication by Boulet SL et al. Which studied 216 individuals with non-syndromic craniosynostosis, and also found scaphocephaly to be the most prevalent type (39%), followed by trigonocephaly (19%) [2].

The literature widely reports a higher incidence of craniosynostosis in males, ranging from 62% to 73%, a figure similar to that found in this study. However, although gender was a relevant factor for the incidence of the condition, it was not relevant for the concordance between twins. This observation is in line with the results of the study by Lakin GE, et al [2,11,15].

The influence of genetic factors on the development of craniosynostosis is evident when observing that the general level of concordance between twins was 25.9%; however, when concordance was analyzed taking zygosity into account, this figure was 45.3% for monozygotic individuals, while dizygotic individuals showed a substantially lower concordance of only 7.3%. As well as being numerically significant, this difference was also statistically significant.

The results of this study support the findings of two other relevant studies in the field. Lajeunie E et al. discovered a higher level of agreement in monozygotic twins (35%) compared to dizygotic twins (2%). On the other hand, Lakin GE et al. observed an agreement of 60.9% among monozygotic twins and 5.3% among dizygotic twins. These consistent results reinforce the significant association between zygosity and agreement in the occurrence of craniosynostosis. It highlights the significant influence of genetic factors on the development of the condition and the agreement between twins [11,15].

Among the genetic syndromes associated with craniosynostosis, such as Pfeiffer and Crouzon, this study also explored the relationship between the presence of these syndromes and concordance between twins. Although agreement in individuals with genetic syndromes (57.1 %) was numerically higher than overall agreement (25.9 %), statistical tests indicated that this difference was not relevant. A possible explanation for this result may lie in the limited number of pairs in which information on the presence or absence of genetic syndromes was available, being substantially lower than those in which this information was not available (44 pairs vs. 64 pairs, respectively).

In the study by Lakin GE, et al., a numerically higher concordance value was also observed between twins with the syndrome (78.60 %) compared to those without (21.70 %). However, similar to the present study, no statistical relevance was found in these figures [11].

Concordance was also influenced by the type of synostosis, with twins with scaphocephaly showing significantly higher concordance than those with trigonocephaly (46.7% vs. 18.9%, respectively). It is interesting to note that in the study conducted by Lajeunie E et al., the results were the opposite, with greater agreement among twins with trigonocephaly [11].

Despite the correlation previously highlighted between zygosity and concordance, analyzing the possible difference in concordance between monozygotic and dizygotic twins with trigonocephaly revealed no significant relevance to this association. The same was true for twins with scaphocephaly. These results suggest that although there is an influence of zygosity on concordance, this association may vary depending on the specific type of synostosis, indicating an additional complexity in the factors that determine the clinical expression of craniosynostosis in twins.

Although genetic factors have a strong influence on the development of a condition, the role of environmental factors cannot be ignored. This is evident from the fact that if only genetic factors were responsible, we would expect a 100% agreement among monozygotic twins and 50% among dizygotic twins. However, the results of this and other studies show that this is not the case. Hence, environmental factors play a fundamental role in the development of the condition.

A study conducted by Xu J, et al. has reinforced the importance of environmental factors in the development of craniosynostosis. The study reported the case of two monozygotic sisters who shared a mutation in the axin 2 gene, which is associated with the condition. However, only the sister who remained in a breech position during pregnancy developed craniosynostosis. This highlights the significant impact of specific environmental factors, such as fetal position, on the development of the condition [6].

CONCLUSION

Our investigation into craniosynostosis, particularly in twins, has uncovered valuable insights. The study, which includes a meta-analysis and a case report of identical male twins, highlights the significant genetic influence on craniosynostosis, which is notably higher in monozygotic twins. The type of synostosis was identified as a significant factor affecting concordance patterns, while gender and

genetic syndromes did not exhibit a statistically significant impact.

This research describes the complex interplay between genetics and environmental factors, emphasizing the importance of managing craniosynostosis. The findings not only advance our understanding of this condition but also provide a solid foundation for future research, particularly in the unique context of twins.

DISCLOSURES

Ethical approval

The studies involving human participants were reviewed and approved by the Ethics and Research Committee of the Hospital da Restauração de Pernambuco, which is affiliated to CONEP (National Commission for Ethics in Research), which is part of the Brazilian government's Department of Health. The patient was informed and provided written informed consent to the publication of his case anonymously. Reference number of the hospital's ethics committee: 5198.

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

The patient gave consent to use his information and images for publication.

Conflict of interest

The authors declare no conflicts of interest with respect to the content, authorship, and/or publication of this article.

The authors report no conflict of interest

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CONTRIBUTIONS

-Artur Henrique Galvao Bruno Da Cunha: Conceptualization, Formal Analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing

-Pedro Lucas Negromonte Guerra: Writing – original draft, Writing – review & editing

-Renata Raizza Monterazzo Cysneiros: Writing – original draft, Writing – review & editing

-Inaê Caroline Silveira da Silva: Writing – original draft,
Writing – review & editing

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Table 2- Included studies

Study	Gestational age	Type of twins	Twins sex	Suture involved	Genetic syndrome	Concordant sutures?
Keith J, et al. (1968) ¹⁶	38 weeks	Monozygotic	Male	Sagittal/Sagittal	None	Yes
Loffredo A, et al. (1977) ¹⁷	Not mentioned	Monozygotic	Female	Oxycephaly/Oxycephaly	Crouzon	Yes
Woon KC, et al. (1980) ¹⁸	36 weeks	Monozygotic	Male	Bicoronal and lambdoid Bicoronal and lambdoid	None	Yes
David DJ, et al. (1991) ¹⁹	36 weeks	Monozygotic	Male	Sagittal, coronal and lambdoid/ Sagittal, coronal and lambdoid	None	Yes
Keusch C, et al. (1991) ²⁰	26 weeks	Monozygotic	Not specified	Sagittal/None	None	No
Marini R, et al. (1991) ²¹	32 weeks	Monozygotic	Male	Sagittal/Sagittal	None	Yes
Yasuda S, et al. (1993) ²²	38 weeks	Monozygotic	Female	Oxycephaly/ Oxycephaly	Crouzon	Yes
Satoh, K. et al. (1999) ²³	34 weeks	Dizygotic	Male and Female	Metopic/Metopic	None	Yes
Williamson-Kruse L, et al. (1995) ²⁴	40 weeks	Dizygotic	Male	Sagittal/Sagittal	Pfeiffer	Yes
Franceschini P, et al. (1998) ²⁵	Not mentioned	Monozygotic	Female	Coronal/None	Baller-Gerold syndrome	No
Van Nesselrooij BP, et al. (1998) ²⁶	Not mentioned	Monozygotic	Male	Sagittal/None	None	No
Cruysberg JR, et al. (1999) ²⁷	37 weeks	Monozygotic	Female	Sagittal/Metopic	None	No
Lajeunie E et al. (2000) ²⁸	Not mentioned	Monozygotic	Female	Sagittal/Sagittal	Crouzon	Yes
Tubbs RS, et al. (2002) ²⁹	Not mentioned	Monozygotic	Female	Sagittal/Sagittal	None	No
Funato N, et al. (2005) ³⁰	Not mentioned	Monozygotic	Female	Coronal and lambdoid Coronal and lambdoid	Crouzon	Yes
Lajeunie et al. (2005) ¹⁵	Not mentioned	17 Monozygotic 47 Dizygotic	Not specified	41 Sagittal 30 Metopic 57 None	Not specified	7 Yes 57 No
Rogers GF, et al. (2005) ³¹	37 weeks	Dizygotic	Male and female	Lambdoid/Lambdoid	None	Yes
Van Aalst, et al. (2005) ³²	Not mentioned	A: Monozygotic B: Dizygotic	A: Not specified B: Not specified	A: Sagittal/Sagittal B: Coronal/None	A: None B: None	A: Yes B: No
Breugem CC, et al. (2008) ³³	36 weeks	Monozygotic	Male	Bicoronal/Metopic	Apert	No
Kohan E, et al. (2008) ³⁴	36 weeks	Monozygotic	Male	Sagittal/Sagittal	None	Yes
Sher S, et al. (2008) ³⁵	37 weeks	Monozygotic	Female	Bicoronal/Coronal	Crouzon	No
Butzelaar L, et al (2009) ³⁶	Not mentioned	Monozygotic	Not specified	Bicoronal/Coronal	None	No

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Escobar LF, et al. (2009) ³⁷	35 weeks	Monozygotic	Female	Bicoronal/Bicoronal	Muenke	Yes
Kohan E, et al. (2008) ³⁸	36 weeks	Monozygotic	Male	Bicoronal and sagittal Bicoronal and sagittal	Pfeiffer	Yes
Lakin G, et al. (2012) ¹¹	Not mentioned	A: Monozygotic B: Monozygotic C: Dizygotic D: Dizygotic	A: Male B: Male C: Male/female D: Male/female	A: Coronal/None B: Sagittal/Sagittal C: Sagittal/None D: Metopic/None	A: None B: None C: None D: None	A: No B: Yes C: No D: No
Watson CC, et al. (2014) ³⁹	37 weeks	Dizygotic	Female	Bicoronal/Lambdoid	None	No
Hove HD, et al. (2016) ⁴⁰	33 weeks	Monozygotic	Male	Sagittal/Bicoronal	None	No
Magge S, et al. (2017) ⁴¹	32 weeks	Monozygotic	Female	Metopic/None	None	No
Dap M, et al. (2018) ⁴²	Not mentioned	Monozygotic	Not specified	Coronal/Coronal	Apert	Yes
Farooq S, et al. (2020) ⁴	A: 29 weeks B: 34 weeks C: 36 weeks D: 29 weeks	A: Monozygotic B: Dizygotic C: Monozygotic D: Monozygotic	A: Male B: Male C: Female D: Male	A: Metopic/Metopic B: Metopic/Sagittal C: Sagittal/Sagittal D: Metopic/Metopic	A: None B: None C: None D: None	A: Yes B: No C: Yes D: Yes
Xu J, et al. (2021) ⁶	28 weeks	Monozygotic	Female	Sagittal/None	None	No
Kantaputra P., et al. (2022) ⁴³	39 weeks	Monozygotic	Not specified	Bicoronal and Lambdoid/Bicoronal	Pfeiffer	No
Barrell WB, et al. (2022) ⁵	36 weeks	Monozygotic	Female	Coronal/Metopic	None	No
Segal NL, et al. (2023) ⁴⁴	35 weeks	Monozygotic	Male	Sagittal/Sagittal	None	Yes
Present study. (2023)	37 weeks	Monozygotic	Male	Sagittal/Metopic	None	No