ORIGINAL ARTICLES

Anterior fontanelle closure time in 684 healthy Portuguese children

Idade de encerramento da fontanela anterior em 684 crianças portuguesas saudáveis

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ABSTRACT

Introduction and Aim: The timing of anterior fontanelle (AF) closure may be a useful marker for early disease detection. However, the few published studies on this topic have reported significant differences in the normal age ranges of AF closure between countries. The aim of this study was to report AF closure time in the Portuguese population during the last two decades.

Methods: This was a 21-year retrospective observational study of healthy Portuguese children conducted from January 1999 to December 2019. Data on the age of AF closure were collected by a single pediatrician during outpatient child visits at specific ages (1, 2, 4, 6, 9, 12, 18, 24, 30, and 36 months) and during unscheduled visits due to appointment changes or illness. Clinically closed AF was defined as the absence of a depressible fontanelle on physical examination. AF closure time was calculated as the mean age between the age of the last palpable AF and the age of the first clinically closed AF.

Results: A total of 684 children (gestational age ≥37 weeks, birth weight ≥2500 grams) were evaluated, of whom 364 (53.2%) were boys. The mean ± 1 standard deviation (SD) age of AF closure was 14.3 ± 4.9 months (range 2–33 months). The 2.5th and 97.5th percentiles, representing ± 2 SD of AF closure time, were 6 and 25 months, respectively. Other percentiles were P5 - 7 months, P25 - 11 months, P50 - 14 months, P75 - 16 months, and P95 - 22 months. Noteworthy, 0.6% and 3.1% of children had a closed AF at three and six months, respectively, while 2.9% still had an open AF at 24 months. AF closure occurred earlier in males than in females (13.6±4.7 vs. 15.1±5.0, p <0.001). A statistically significant difference was found in the mean ± 2 SD of the gender comparison (p=0.045).

Conclusions: This study showed a normal distribution of AF closure age in Portuguese children. The acknowledgment of age-related variations in AF closure timing in different populations is important to raise clinicians' awareness for timely suspicion and detection of pathologic cases and the need for clinical study.

Keywords: child; cranial fontanelle; development; growth; pediatrics

RESUMO

Introdução e Objetivo: O tempo para o encerramento da fontanela anterior (FA) pode ser um indicador útil na deteção precoce de doença. Os escassos estudos publicados sobre o tema evidenciam a existência de diferenças significativas entre países na definição do intervalo de idades normal para o encerramento da FA. O objetivo deste estudo foi determinar o intervalo de idades de encerramento da FA na população

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portuguesa ao longo das últimas duas décadas.

Métodos: Estudo observacional, retrospetivo, com a duração de 21 anos, efetuado em crianças portuguesas saudáveis entre Janeiro de 1999 e Dezembro de 2019. Foram recolhidos dados relativos à idade de encerramento da FA por um único pediatra em contexto de consulta de saúde infantil realizada em idades específicas (1, 2, 4, 6, 9, 12, 18, 24, 30 e 36 meses) e de consultas não programadas devido a reagendamentos ou situação de doença aguda. Foi definida FA clinicamente encerrada como ausência de fontanela anterior depressível no exame objetivo. A idade de encerramento da FA foi calculada como a idade média entre a idade da criança na última palpação da FA aberta e a idade na consulta em que se objetivou o seu encerramento.

Resultados: Um total de 684 crianças (idade gestacional ≥37 semanas, peso ao nascimento ≥2500 gramas) foram avaliadas, 364 (53%) das quais do sexo masculino. A idade média de encerramento da FA ± 1 desvio-padrão (DP) foi de 14.3 ± 4.9 meses (variação 2−33 meses). Os percentis 2.5 e 97.5, correspondentes a ± 2 DP do tempo de encerramento da FA, foram 6 e 25 meses de idade, respetivamente. A distribuição das idades de encerramento foi ainda caracterizada pelos seguintes percentis: P5 - 7 meses, P25 - 11 meses, P50 - 14 meses, P75 - 16 meses e P95 - 22 meses. Aos três e seis meses de vida, 0.6% e 3.1% das crianças, respetivamente já tinham a FA encerrada, enquanto aos 24 meses de idade, 2.9% mantinham-na aberta. O encerramento da FA foi significativamente mais precoce no sexo masculino do que no sexo feminino (13.6±4.7 vs. 15.1±5.0, p <0.001) e a média ± 2 DP da comparação entre os sexos também foi estatisticamente diferente (p=0.045).

Conclusões: Os resultados deste estudo sugerem uma distribuição normal na idade de encerramento da FA num grupo de crianças portuguesas. Ter conhecimento de variações relacionadas com a idade de encerramento da FA em diferentes populações é importante para sensibilizar os clínicos para a deteção precoce de estados patológicos e para determinar a necessidade de prosseguir o estudo clínico.

Palavras-chave: crescimento; criança; fontanela craniana; pediatria

INTRODUCTION

Careful examination of fontanels should be part of the routine physical examination of infants, as it provides clinicians with valuable clues to assess brain development disorders, calvarial ossification, and others.[1-3] Fontanels are soft spaces between the bones of the skull that are essential for the overlap of the cranial bones during delivery and for accommodating brain growth during the first years of life.[1,2] The anterior fontanel (AF) is usually defined as a curved, rhomboid, nonmineralized fibrous membrane in the cranial vault at the convergence of the coronal, sagittal, and metopic sutures in the developing fetus and infant.[1,2] AF usually varies in size at birth in healthy newborns, and some studies have suggested a positive correlation with gestational age.[1-3] Abnormal AF size and/or an inappropriate AF closure time could be a useful sign leading to early diagnosis of several disorders.[1-6]

In order to use fontanels as an indication of morphogenetic changes, it is important to determine the normal population range of AF closure time, which may help clinicians to decide on additional investigations.[1-6] However, pediatric textbooks assume different limits for the normal range and quote each other endlessly. For example, Gripp *et al*.[3] defined normal AF closure at 12 ± 4 months of age (without mentioning age limits), and Zorc *et al*.[6] between 4 and 26 months of age.

The few published studies on this subject report significant differences in the normal age range of AF closure among countries.[4,5,7-13] Only two American (1950 and 2014) and two European (1954 and 1986) studies were found on this subject.[7,9,11,12] The latter is one of the most cited in the literature, despite having included only 111 infants born at term.[1,12,13]

The aim of this study was to describe the age range of AF closure in healthy Portuguese children and compare it with international studies.

METHODS

This was a retrospective observational study conducted in a pediatric outpatient clinic over 21 years (from January 1999 to December 2019), using data from a comprehensive database created and maintained for health surveillance purposes. Children's inclusion criteria comprised the absence of any medical condition, gestational age ≥37 weeks, and birth weight ≥2500 grams.

A single pediatrician was responsible for assessing AF closure as part of routine physical examination during regular follow-up visits at specific ages, including 1, 2, 4, 6, 9, 12, 18, 24, 30, and 36 months. In addition, other AF assessments were performed at unscheduled time points when appointments were rescheduled or in the event of acute illness.

Clinically closed AF was defined as the absence of a depressible orifice corresponding to AF. The age of the last palpable AF and the age of the first clinically closed AF were recorded. The mean age between these two ages was defined as AF closure time. The largest difference between these two assessments was three months in the

first year of life and six months in the second and third years of life.

A two-sample t-test was used to compare the means and medians derived from female and male children. In addition, a chi-square goodness-of-fit test was used to determine whether there was a statistically significant difference in the expected counts for each level of a variable (months) compared to the observed counts. The study hypotheses were as follows: H0a (null hypothesis): There is no difference between the distribution of cases in Portugal and other studies; H1a (alternative hypothesis): There is a significant difference between the distribution of cases in Portugal and other studies. Similarly, H0b (null hypothesis): The distribution of cases in Portugal follows a normal distribution; H1b (alternative hypothesis): The distribution of cases in Portugal does not follow a normal distribution.

RESULTS

A total of 684 healthy Portuguese children, of whom 364 (53.2%) were boys, were included in this study. The participants were predominantly of Caucasian ethnicity, living in the central region of Portugal, with parents of middle or high socioeconomic level. The mean ± standard deviation (SD) age of AF closure was 14.3±4.9 months, ranging from 2 to 33 months. At three months of age, 0.6% of children (n=4, two boys and two girls) already had closed AF, a percentage that increased to 3.1% (n=21, 15 boys and six girls) at six months of age. Conversely, 2.9% of children (n=20, six boys and 14 girls) did not have AF closure until 24 months of age, including two children (one boy and one girl) who did not have AF closure until 33 months of age. The 2.5th and 97.5th percentiles, representing ± 2 SD of AF closure time in this cohort, were 6 and 25 months (**Figure 1**).

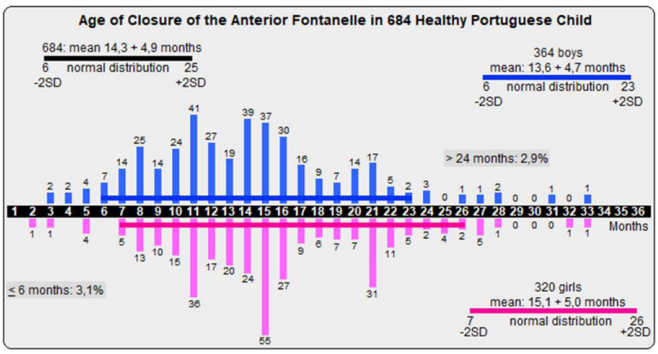

Figure 1- Age of anterior fontanelle closure in 684 healthy Portuguese children

The age distribution of AF closure was additionally characterized by the following percentiles: P5 - 7 months, P25 - 11 months, P50 - 14 months, P75 - 16 months, and P95 - 22 months.

The mean ± SD of AF closure time was significantly earlier in males compared to females (13.6±4.7 vs. 15.1±5.0, p <0.001). A statistically significant difference was also found between genders in the mean ± 2 SD of AF closure time (p=0.045). In the group of 364 boys, ± 2 SD was found at six and 23 months of age, whereas in the group of 320 girls, ± 2 SD was found at seven and 26 months of age. The detailed results are shown in **Figure 1**.

DISCUSSION

This study aimed to characterize the timing of AF closure in a cohort of healthy Portuguese children. The results showed a mean ± SD age of AF closure of 14.3 ± 4.9 months and a gender difference in AF closure time, which was significantly earlier in males compared to females.

The gender differences found in this study are in line with the results reported by Acheson et al. (1954), who found a mean age of AF closure of 16 ± 3 months in boys and 18 ± 8 months in girls in the Oxford area.[7] In addition, the study's results add to the current literature by confirming a significant gender difference in the age of AF closure. On average, the age of AF closure in females was 1.5 months later than in males, which is consistent with the trend observed in previous studies reporting 1.1 to 2.5 months later in females compared to males.[4,7,11,12] This reinforces and extends the existing evidence indicating a time difference in AF closure between genders, and supports the growing body of evidence suggesting that differences in brain structure and maturation between genders may underlie variations in AF closure timelines.[4]

Table 1 provides a comparative overview of the mean AF closure age reported in eight clinical studies involving more than 100 healthy children. Of note, this study's results indicate that the AF closure age tends to be lower in the Arab population than in the American, European, and Chinese populations. This observation highlights the potential influence of regional or ethnic factors on AF closure time.

Although head computed tomography (HCT) is the gold standard for assessing AF closure, it has limitations for routine clinical use, including cost, availability, and radiation risk. Mathur *et al*. found that 91.3% of Indian children experienced AF closure before 24 months, attributing the delay to the prevalence of malnutrition in this population.[10] Interestingly, two recent studies using HCT for AF assessment found comparable results, reinforcing its reliability.[12,13] In a 2014 retrospective American study, 464 children younger than 24 months were assessed for other clinical purposes (trauma, headache, seizures, neurological examination changes, mental status changes, etc.) using HCT, and AF closure was recorded. All children with conditions affecting cranial growth, neurologic development, and/or prematurity were excluded from the cohort.[12] In this study, 90% of the children had already closed AF, highlighting the diagnostic ability of HCT for multiple clinical purposes.[12] Similarly, a study in New Zealand (NZ) evaluated 163 children under four years of age (116

Mãori/Pasifika and 47 NZ European) and found that 90% of Pasifika children had HCT evidence of AF closure at 24 months, although all were considered clinically closed.[13] These findings are consistent with previous results and suggest a potential genetic influence on the variation in AF closure across populations, although socioeconomic factors and health conditions cannot be excluded.[4,5,10,13] The observed ethnic differences in age of AF closure underscore the complexity of factors influencing cranial development. While genetic factors may contribute, socioeconomic variables and health conditions are also likely to play a role, as suggested by several authors.[4,5,10,13] Ethnic diversity therefore emerges as a critical consideration in understanding the nuanced timelines of AF closure, shedding light on the multifaceted nature of this developmental process.

When comparing the published series for statistical significance, the null hypothesis a) was not rejected in the American and Swiss studies, as no significant differences were found (p=0.19 and 0.11, respectively). The British study can be considered non-significant at the 1% level. These results are consistent with the similarity of lifestyles and living conditions in these Western countries. The null hypothesis b) was also not rejected, as the data suggest that AF closure time in children follows a normal distribution.

Although this study provides valuable insights into the clinical aspect of AF closure, it is important to acknowledge the existing limitations. First, the assessment of AF closure was based solely on clinical criteria without including radiological closure in the analysis. This omission may limit the comprehensiveness of the study findings and the comparability of its results with those of other studies that have included radiological assessment of AF closure. All AF assessments in this study were performed by a single designated pediatrician, which ensured consistency and minimized interobserver variability. However, the assessment based on the expertise and judgment of a single individual should also be considered when interpreting the study results.

Table 1 - Comparative analysis of AF closure in eight published series*

Year Ref	Country	Number	3 M	6 M	12 M	18 M	24 M	30 M	33 M	Median age and ± 1 SD	p-value
1950 [9]	USA	1677		2,7%	41.6%	91.3%	99.9%	100%		13.5	0.1997#
1954 [7]	UK	530		0.5%	25.8%	72.3%	91.5%	98.5%	>99.5%	16.3 / 18.8	0.0162&
1986 [11]	Switzerl.	111	1.0%	7.5%	38.0%	70.0%	96.0%	100%		13.8	0.0044
1994 [10]	India	445			40.0%	71.4%	91.3%				0.1179#
2015 [5]	Iran	550			77.0%	100%					2.984E-15
2017 [8]	China	104.147	0.1%			≈70%	>98%		>99%	14.5	1.841E-12
2018 [4]	Turkey	321	11.0%	32.0%	81.0%	96.0%	100%			9.7 ± 5.0	2.457E-76
2020	Portugal	684	0.6%	2.9%	38.2%	80.8%	97.1%	99.4%	100%	14.3 ± 4.9	0.2020##

** Only studies with clinical evaluation of AF closure in more than 100 term infants were included*
 # Not significantly different from the Portuguese distribution of cases (chi-square goodness of fit test applied)
& Not significantly different from the Portuguese distribution of cases at 1% (chi-square goodness of fit test applied)
Not significantly different from normal distribution values (chi-square goodness of fit test applied)

CONCLUSION

The results of this study support the hypothesis of normal variability in the age of AF closure in different populations. Knowledge of the variation in AF closure time for each population is crucial for early detection of pathological processes and to avoid overestimation of early or late AF closure in healthy children with normal head growth.

AUTHORSHIP

*Ricardo Craveiro Costa - Writing – original draft; Writing – review & editing; Formal analysis.

*Joana Rosmaninho Salgado – Writing – original draft; Conceptualization; Investigation; Supervision and Validation.

*Daniela Oliveira – Writing – original draft; Formal analysis; Methodology.

Francisca Mendes – Writing – original draft; Formal analysis.
Alexandre Mendes – Methodology; Software; Formal analysis.
Manuel Salgado – Conceptualization; Investigation; Data curation; Supervision and Validation.

Note: * - these authors had an equal contribution to the article elaboration

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