





# Early craniometric and neurological assessment of preterm infants: an observational study

*Avaliação craniométrica e neurológica precoce de recém-nascidos pré-termo: estudo observacional*

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## Abstract

**Introduction:** Preterm infants show greater susceptibility to positional cranial asymmetry, which was long considered an aesthetic issue but has recently been associated with delayed neurodevelopment. **Objective:** To assess the prevalence of positional cranial asymmetries and compare the neurological assessment of preterm infants with and without cranial asymmetry at discharge from a neonatal intensive care unit (NICU). **Methods:** This observational study evaluated neonates who were born from 28 to 36 weeks and six days of gestational age at their NICU discharge and at 40 weeks of corrected gestational age. Cranial symmetry was measured by a craniometer. The cranial and cranial vault asymmetry indices were used to classify deformities. Neurological assessment was performed by the Hammersmith Neonatal Neurological Examination. **Results:** Overall, 50 neonates were evaluated at hospital discharge, of whom 64% (n = 32) showed cranial asymmetry, with isolated dolichocephaly occurring the most prevalently (66%, n = 21). This study evaluated 21 neonates at term-equivalent age, 71% (n = 15) of whom showed cranial asymmetry, with only plagiocephaly and plagiocephaly with dolichocephaly occurring most often, (40%; n = 6). The groups with and without asymmetry failed to significantly differ in neurological assessment scores, 33 [IQR 31–34] vs. 33 [IQR 32–34] totals, respectively (p = 0.885). **Conclusion:** Preterm infants showed a high prevalence of positional cranial asymmetry at discharge. Neurological assessment found no significant differences in early neurodevelopment between infants with and without cranial asymmetry, suggesting that this deformity may fail to impact early neurological outcomes.

**Keywords:** Premature infants. Plagiocephaly. Skull. Neurological examination. Neonatal Intensive Care Units.

## Resumo

**Introdução:** Recém-nascidos pré-termo são mais suscetíveis ao desenvolvimento de assimetria craniana posicional, que por muito tempo foi tratada como questão estética, mas recentemente tem sido associada ao atraso no neurodesenvolvimento.

**Objetivo:** Avaliar a prevalência de assimetrias cranianas posicionais e comparar a avaliação neurológica de recém-nascidos pré-termo, com e sem assimetria craniana, na alta da Unidade de Terapia Intensiva Neonatal (UTIN). **Métodos:** Trata-se de um estudo observacional, em que foram avaliados neonatos, com idade gestacional ao nascimento de 28 a 36 semanas e 6 dias, na alta da UTIN e com 40 semanas de idade gestacional corrigida. A simetria craniana foi medida com um craniômetro e o Cranial Index e o Cranial Vault Assymetry Index foram usados para classificar as deformidades. A avaliação neurológica foi realizada pelo Hammersmith Neonatal Neurological Examination. **Resultados:** Cinquenta neonatos foram avaliados na alta hospitalar, dos quais 64% (n = 32) apresentaram assimetria craniana, sendo a dolicocefalia isolada mais prevalente em 66% (n = 21). Na idade equivalente a termo, 21 neonatos foram avaliados, dos quais 71% (n = 15) apresentaram assimetria craniana, sendo a plagiocéfalia isolada e a plagiocéfalia combinada com dolicocefalia mais prevalentes, com 40% (n = 6) cada. Os grupos com e sem assimetria não diferiram significativamente nas pontuações da avaliação neurológica, com escore total de 33 [IQR 31-34] e 33 [IQR 32-34], respectivamente (p = 0,885). **Conclusão:** Neonatos prematuros apresentaram elevada prevalência de assimetria craniana posicional na alta. A avaliação neurológica não mostrou diferença significativa no desenvolvimento neurológico dos recém-nascidos com assimetria craniana, sugerindo que essa deformidade parece não ter impacto no desenvolvimento neurológico precoce.

**Palavras-chave:** Recém-nascido prematuro. Plagiocéfalia. Crânio. Exame neurológico. Unidades de Terapia Intensiva Neonatal.

## Introduction

The liquid environment during pregnancy, with its high density and no gravity, enables fetuses to progressively develop their ability to move, to perceive and react to different stimuli, and to carry out increasingly complex explorations.<sup>1</sup> The uterine wall provides boundaries to support fetuses in a flexed and restrained position. They develop, with the support of the central nervous system

and the uterine environment, a physiological flexed position in their last gestational trimester, which is vital for the development of normal movement and body control.<sup>2</sup> Premature birth deprives newborns (NB) of this environment that facilitated their movement and exposes them to stimuli with greater intensity, such as visual and auditory ones.<sup>1</sup> This early transition to extrauterine life challenges preterm infants (PT), who struggle to maintain previously organized functioning patterns in the face of excessive stimuli in intensive care.<sup>3</sup>

Placed in various postures in neonatal care, PTs experience varying forces and pressures on their still-developing joints and muscles. These motor experiences can positively influence the development of joints and mechanoreceptors in preparation for coordinated movement. On the other hand, if NBs remain in restrictive body positions, they experience prolonged joint compression with minimal refinement of their mechanoreceptor action, which predisposes them to skeletal deformations, muscle shortening, and restricted joint mobility.<sup>4</sup> Skeletal deformities due to prolonged positioning in neonatal intensive care units (NICU) include positional cranial asymmetries, which stem from external forces on the malleable bones of neonates' skull, leading to deformities and interfering with their normal development.<sup>5,6</sup>

Positional cranial asymmetries fall into three types: plagiocephaly, characterized by the unilateral flattening of the parieto-occipital region due to the constant support of the head on one side, resulting in a parallelogram head shape that may be associated with alterations such as ear and ipsilateral frontal bone deviations or facial asymmetry in more severe cases; brachycephaly characterized by symmetrical occipital flattening and parietal enlargement due to prolonged lying with the head in the midline, resulting in a wider head with a reduced anterior diameter; and dolichocephaly, characterized by the narrowing of the skull, causing a long and narrow face due to prolonged rest on the sides of the head.<sup>5,7,8</sup>

Although a benign condition, positional cranial asymmetry (PCA) can lead to important consequences, such as musculoskeletal and postural, sensory,<sup>9-11</sup> and neurodevelopmental disorders, which the literature has widely discussed, showing it to be a risk factor for motor, sensory, and cognitive developmental delay.<sup>12-15</sup>

Despite the widely recognized relationship between PCA and neurodevelopmental delay, especially in later corrected age for premature infants, the direction of this

association remains unclear. In other words, it is impossible to know whether changes in skull shape delay neurodevelopment or whether a deficit in neurodevelopment favors the emergence of positional cranial deformities. Although PTs, due to characteristics such as muscle hypotonia, a more malleable skull, and difficulty moving against gravity, may be more susceptible to these deformities and their possible effect on neuropsychomotor development, few data exist on their early neurological and craniometric evaluation, necessitating the investigation of this topic.

Thus, this study aimed to evaluate the prevalence of PCA and to compare neurological evaluation results in PTs with and without PCA at discharge from a NICU in Paraná. This research hopes to show that PCA fails to alter the early neurological development of PTs at NICU discharge.

## Methods

Prospective data collection according to the STROBE checklist was used in this observational, analytical, cross-sectional, and compared study. This research was approved by the Human Research Ethics Committee at Hospital de Clínicas Complex of Universidade Federal do Paraná under protocol CAAE 65739022.8.0000.009, opinion 5.840.4. It was conducted in the NICU of the institution above from July to December 2023.

The following were chosen as inclusion criteria: PTs with gestational ages ranging from 28 to 36 weeks and six days of both sexes whose parents or guardians agreed to participate in this study. NBs with synostotic abnormalities in head shape or skull fracture; congenital neurological malformations, chromosomal abnormalities, and genetic syndromes (as these conditions adversely impact neurological development profiles); congenital muscular torticollis; or cervical range of motion restriction were excluded from this study. The following were chosen as exclusion criteria: transfers to another unit before discharge, incomplete craniometric or neurological evaluation at discharge, and those with cranial measurements below 80 mm, due to limitations of the measurement instrument.

Neurological evaluation was performed using the scale Hammersmith Neonatal Neurological Examination (HNNE), that draws a detailed profile of neurological status and identifies NBs and infants at risk for neurological abnormalities.

The instrument has 34 items that assess posture and tone (10 items), tone patterns (five items), reflexes (six items), movements (three items), abnormal signs (three items), and orientation and behavior (seven items). The evaluation proform consists of columns numbered from one to five. Each item is scored by circling the most appropriate column or, in case of variations, the column that is closest to what is being observed in the NB. These non-linear raw scores are converted into optimization scores. Thus, for PTs, for each item evaluated, 1 point is assigned to results within the 90th percentile and 0 points, to those in the 10th percentile. The composite optimization score for this evaluation is composed by the sum of the optimization scores for all individual items. It can range from 0 to 34, the normal range being from 30.5 to 34 for full-term infants and above 26.5 for PTs.<sup>16</sup> The instrument has been adapted and validated for the Brazilian population.<sup>17</sup> It was administered by a single evaluator, a physical therapist with experience in HNNE. It was impossible to blind the evaluator since the cranial deformities were usually visible, which made it unfeasible for the evaluator to perform their examination without observing the shape of the skull. The NBs only used diapers and were in a state of alertness during the evaluation (which took place between feedings). The items were scored and the total score was calculated after the evaluation.

Cranial symmetry was assessed by anthropometric measurements of the skull and the calculation of cranial symmetry parameters. The measurements were performed by two experienced physical therapists using a Mimos® craniometer. The length, width, and diagonal length of the skull were measured in centimeters according to the points in Chang.<sup>6</sup> A single measurement was performed directly at the anatomical reference points without intermediaries such as a band or cap between the craniometer and the NB's head. The cranial index (CI), the ratio between cranial width and length, and the cranial vault asymmetry index (CVAI), the difference between the two oblique cranial measurements divided by the longest diagonal and multiplied by 100, were calculated based on these measurements.<sup>18</sup>

CVAI was used to classify plagiocephaly, whereas CI was used to classify dolichocephaly and brachycephaly. The cut-off values in this study were based on the values in Dieks et al.'s study,<sup>19</sup> that evaluated a sample of hospitalized PTs. Thus, plagiocephaly was classified based on the CVAI into: < 3.7 = normal; 3.7-5.3 = mild; > 5.3-7.0 = moderate; > 7 = severe.

Dolichocephaly was classified as mild (CI from 74 to 77.5%), moderate (CI from 70.3 to less than 74%), and severe (CI below 70.3%). Brachy-cephaly was classified as mild (CI from 85.6 to 89.5%), moderate (CI from above 89.5 to 94.2%), and severe (CI greater than 94.2%).

In addition to neurological and craniometric evaluation, NBs' data regarding their birth and hospitalization were collected. Craniometric and neurological evaluations were performed at NICU discharge or up to three days before it if previously scheduled. The ideal corrected age for HNNE application lies at 40 weeks. However, Venkata et al.<sup>20</sup> found that early-applied HNNE showed as a reliable predicative capacity as those administered at term equivalent age (TEA), being able to be applied up to four weeks before a 40-week corrected age with the same predictive capacity for neurodevelopmental disability assessed at one year of age. Since the minimum corrected age for hospital discharge at the service in which this study was carried out equals 35 weeks, the evaluations were repeated at TEA or up to five days before or after it, applying the HNNE at the age considered ideal for evaluating PTs. The evaluation at the TEA was performed in the NICU if the NBs were still hospitalized. If they had been discharged from the hospital, their guardians were invited for a second evaluation.

The minimum sample size test was calculated on G-Power. The effect size was taken from a pilot project with 14 PTs using an 80% test power (0.8); with a total 32.3 ( $\pm$  0.75) and 31.3 ( $\pm$  1.5) HNNE score for the groups with and without positional cranial asymmetries, respectively. The bilateral test included a 0.844 Cohen's effect size and a 0.05 alpha value. Thus, a minimum of 36 NBs

equally distributed in two groups was obtained. SPSS Statistical Package was used for the statistical analyses (Chicago, IL, USA). Data distribution was analyzed by the Shapiro-Wilk test. The data are described according to their distribution as means  $\pm$  standard deviations, medians [interquartile range 25-75%], or as absolute and relative frequencies. The data were compared according to their normality using the Student's t, Mann-Whitney, or chi squared tests. An analysis of variance for repeated measures was also performed. Statistical significance was set at  $p < 0.05$ .

## Results

During the study period, 170 NBs were admitted to the chosen NICU, 81 of whom were born preterm. Of these, this study included 54. During the subsequent collection period, this research excluded three NBs since they lacked an evaluation at hospital discharge and one because they had been transferred from the service before discharge. Thus, the sample totaled 50 PTs.

This study evaluated PTs at their NICU discharge. They had a mean corrected age of 36.4 ( $\pm$ 1.3) weeks. This study followed up the PTs; 21 underwent a new assessment at TEA, with a mean of 40 ( $\pm$ 0.7) weeks. The mean gestational age and birth weight of the sample totaled 32.3 ( $\pm$  2.1) weeks and 1658.3 ( $\pm$  452.9) grams, respectively. The group with PCA statistically differed from the group without it, showing lower gestational age ( $p = 0.037$ ) and birth weight ( $p = 0.049$ ) and longer hospital stays ( $p = 0.020$ ), as shown in Table 1.

**Table 1** - Perinatal data of the newborns in the sample

Parameters	PCA group (n = 32)	NPCA group (n = 18)	p-value
<b>Number of pregnancies</b>			
First pregnancy	10 (31)	3 (17)	
2-3	16 (50)	9 (50)	0.375
> 4	6 (19)	6 (33)	
Twins	10 (31)	5 (28)	1.000
Intrauterine growth restriction	8 (25)	3 (17)	0.495
Congenital viral exposure	4 (13)	3 (17)	0.684
<b>Presentation</b>			
Cephalic	25 (81)	11 (61)	0.135
Pelvic	6 (19)	7 (39)	

Note: PCA = positional cranial asymmetry; NPCA = no positional cranial asymmetry. Data shown as n (%).

**Table 1** - Perinatal data of the newborns in the sample (continued)

Parameters	PCA (n = 32)	NPCA (n = 18)	p-value
<b>Type of delivery</b>			
Vaginal	14 (44)	5 (28)	0.260
C-section	18 (56)	13 (72)	
Difficult extraction	2 (6)	0 (0)	0.279
Resuscitation	13 (41)	6 (33)	0.610
<b>Apgar 5'</b>			
0-3	28 (88)	17 (94)	0.659
4-6	3 (9)	1 (6)	
7-10	1 (3)	0 (0)	
<b>Sex</b>			
Male	14 (44)	10 (56)	0.557
Female	18 (56)	8 (44)	
Gestational age at birth*	31.8 ± 2.1	33.1 ± 2.0	<b>0.037</b>
<b>Gestational age classification</b>			
Very Premature	12 (37)	2 (11)	0.093
Moderate	14 (44)	9 (50)	
Late	6 (19)	7 (39)	
Birth weight*	1564.2 ± 421.0	1825.6 ± 470.9	<b>0.049</b>
<b>Weight classification</b>			
Low	20 (63)	15 (83)	0.304
Very low	8 (25)	2 (11)	
Extremely low	4 (12)	1 (6)	
Head circumference at birth*	28.8 ± 2.2	29.8 ± 2.4	0.122
Corrected age at discharge**	36.9 (35.7 - 38.2)	36 (35.4 - 37.3)	0.275
Corrected age at term**	40 (39.3 - 40.8)	40.07 (39.6 - 40.3)	0.969
Post-discharge term assessment	12 (80)	4 (67)	0.517
Length of hospital stay (days)**	29 (20.5 - 56.8)	24 (15.7 - 28.5)	<b>0.020</b>
<b>Neurological comorbidities</b>			
Periventricular-intraventricular hemorrhage I	8 (25)	1 (6)	0.236
Periventricular-intraventricular hemorrhage II	1 (3)	0 (0)	
Seizure	2 (6)	1 (6)	
Periventricular leukomalacia	1 (3)	0 (0)	
<b>Respiratory comorbidities</b>			
Mechanical ventilation > 7 days	0 (0)	1 (6)	0.238
Bronchopulmonary dysplasia	4 (13)	0 (0)	
Mechanical ventilation > 7 days + bronchopulmonary dysplasia	1 (3)	1 (6)	
<b>Cardiac comorbidities</b>			
Patent ductus arteriosus	4 (13)	1 (6)	0.432
<b>Infectious comorbidities</b>			
Sepsis	4 (13)	5 (27)	0.235
Necrotizing enterocolitis	1 (3)	1 (6)	
Necrotizing enterocolitis + sepsis	0 (0)	1 (6)	

Note: PCA = positional cranial asymmetry; NPCA = no positional cranial asymmetry; IUGR = intrauterine growth restriction. Data shown as n (%), except when mean ± standard deviation (\*) or median [interquartile range 25-75%] (\*\*). Bold values indicate statistically differing data.

The two groups had no serious diagnoses that could interfere with their neurodevelopment and the neurological evaluation in this study, such as exposure to congenital viral infections, more severe brain injuries, prolonged use of mechanical ventilation, bronchopulmonary dysplasia, and infectious conditions after birth.

The prevalence of PCA at NICU discharge totaled 64% (n = 32), with isolated dolichocephaly configuring the most prevalent type. Of the 21 NBs who were assessed at TEA, 71% (n = 15) had PCA, with plagiocephaly and plagiocephaly with dolichocephaly constituting the most prevalent types.

Considering the total number of PTs who met the criteria for dolichocephaly (that is, adding those who only had dolichocephaly to those who had dolichocephaly and plagiocephaly) raises such numbers. Doing so, the prevalence of dolichocephaly increases to 91% (n = 20) at NICU discharge. All neonates with plagiocephaly had it on the right side of their faces. Table 2 shows the types and degrees of PCA in this sample at both evaluations. Severe cranial deformity occurred in only three PTs in the NICU discharge evaluation, of whom only one returned for evaluation at TEA, showing a decrease of their degree of dolichocephaly to moderate.

Of the infants who were reassessed at TEA, 16 had underwent an evaluation after discharge from the NICU, whereas five, during their hospital stay. Only two of the 15 PTs who had PCA at NICU discharge improved, no longer showing asymmetry in the evaluation at TEA. Moreover, two patients without cranial asymmetry at discharge developed some type of cranial asymmetry at 40-week corrected age (Table 3). Regarding the type of asymmetry, of the six PTs who showed no PCA at discharge and underwent the evaluation at TEA, four still had no asymmetry and two had developed plagiocephaly. Of the 15 PTs who had PCA at their NICU discharge and underwent reassessment at TEA, only one of the six who only had dolichocephaly had improved (returning without asymmetry), two still only had dolichocephaly, two had developed plagiocephaly, and one had developed brachycephaly. Of the six PTs who had dolichocephaly and plagiocephaly, four retained that combination, one returned without asymmetry and one only had plagiocephaly. The three PTs who had plagiocephaly still had it at their second evaluation.

The neurological evaluation found no difference in the scores of each category and in the total HNNE score between the groups with and without PCA at the time

of discharge from the NICU and at the reassessment at TEA (Table 4). The graphs A and B in Figure 1 show the analysis of variance for repeated measures results. Despite no statistical differences, the group with PCA showed a lower trend in total HNNE scores than the group without asymmetry at both evaluations. Only comparing total HNNE scores for the PT group and ignoring the presence of PCA obtained a statistically significant difference (p = 0.012) between the assessment at NICU discharge and that at TEA (Figure 1C).

**Table 2** - Type and degree of positional cranial asymmetry at hospital discharge (n = 32) and at term equivalent age (TEA) (n = 15)

Type of asymmetry	Discharge	TEA
Plagiocephaly on the right (POR)	3 (9)	6 (40)
Dolichocephaly (DOLI)	21 (66)	2 (13)
Brachycephaly	-	1 (7)
POR + DOLI	8 (25)	6 (40)
Total dolichocephaly	29 (91)	8 (53)
<b>Degree of asymmetry</b>		
<i>Plagiocephaly</i>		
Mild	7 (64)	9 (90)
Moderate	4 (36)	1 (10)
Severe	0 (0)	0 (0)
<i>Dolichocephaly</i>		
Mild	17 (59)	4 (50)
Moderate	9 (31)	4 (50)
Severe	3 (10)	0 (0)
<i>Brachycephaly</i>		
Mild	0 (0)	1 (100)
Moderate	0 (0)	0 (0)
Severe	0 (0)	0 (0)

Note: Data shown in n (%).

**Table 3** - Prevalence of positional cranial asymmetry (PCA) in preterm newborns at neonatal intensive care unit discharge and at the equivalent age of term

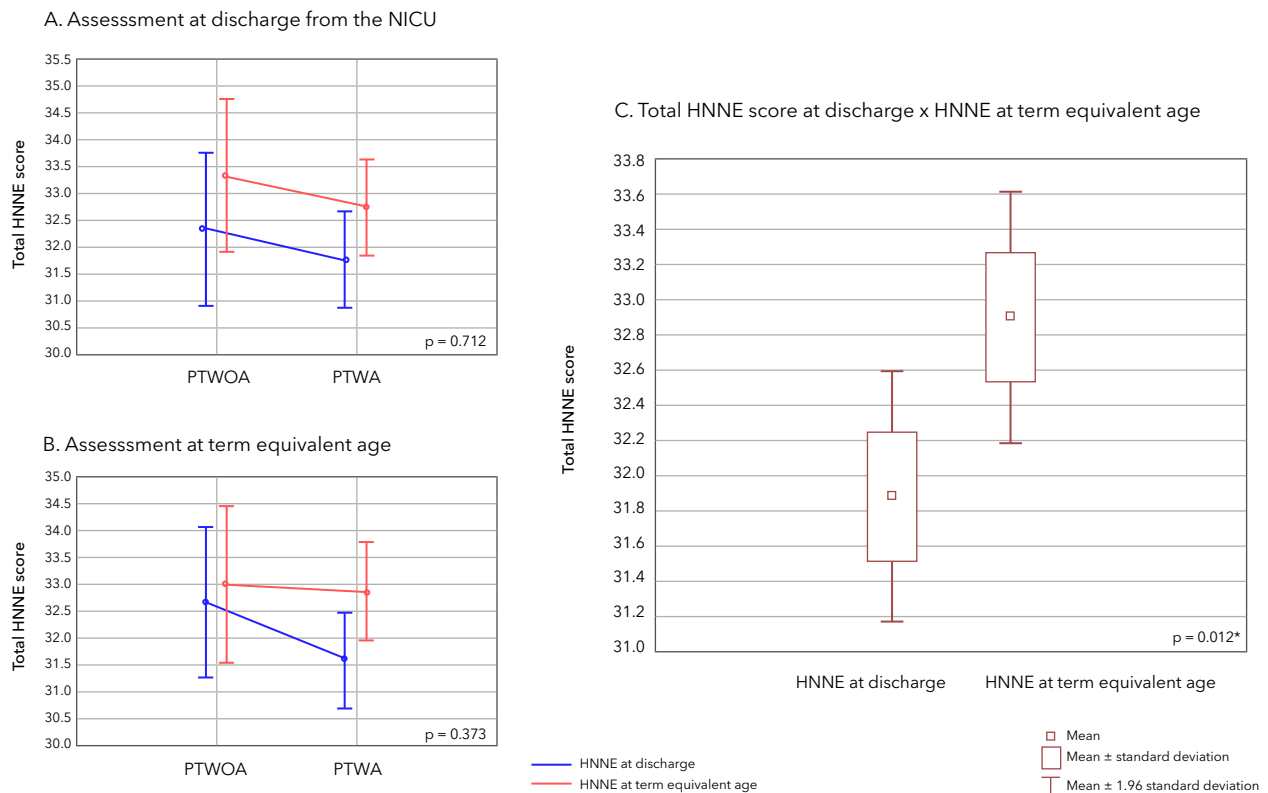
Groups	Discharge (n = 50)	Age equivalent to term (n = 21)	
		PCA	NPCA
PCA	32 (64.0)	13 (86.7)	2 (13.3)
NPCA	18 (36.0)	2 (33.3)	4 (66.7)

Note: NPCA = no positional cranial asymmetry. Data shown in n (%).

**Table 4** - Hammersmith Neonatal Neurological Examination (HNNE) scores at hospital discharge and at term equivalent age

Evaluation at hospital discharge	PCA group	NPCA group	p-value
Posture and tone	10 [10 - 10]	10 (9.7 - 10)	1.000
Tone pattern	5 [5 - 5]	5 [5 - 5]	0.453
Reflexes	6 [5 - 6]	6 [5.7 - 6]	0.651
Movement	3 [3 - 3]	3 [3 - 3]	0.893
Abnormal signs	3 [3 - 3]	3 [3 - 3]	0.453
Orientation and behavior	6 [5 - 7]	6 [5 - 7]	0.915
Total HNNE	33 [31 - 34]	33 [32 - 33]	0.885
<b>Age equivalent to term evaluation</b>			
Posture and tone	10 [10 - 10]	10 [10 - 10]	0.677
Tone pattern	5 [5 - 5]	5 [5 - 5]	1.000
Reflexes	6 [6 - 6]	6 [5 - 6]	0.519
Movement	3 [3 - 3]	3 [2.7 - 3]	0.622
Abnormal signs	3 [3 - 3]	3 [3 - 3]	1.000
Orientation and behavior	7 [6 - 7]	7 [6 - 7]	1.000
Total HNNE	33 [32 - 34]	34 [32 - 34]	0.569

Note: PCA = positional cranial asymmetry; NPCA = no positional cranial asymmetry. Data shown as median [interquartile range 25-75%].



**Figure 1** - Neurological performance of preterm infants with (PTWA) and without (PTWOA) asymmetry according to the Hammersmith Neonatal Neurological Examination (HNNE).

## Discussion

This study evaluated PTs early at their NICU discharge and found a 64% (n = 32) prevalence of PCA, of which dolichocephaly constituted the most prevalent type. This study evaluated PTs with and without PCA by HNNE. They showed no difference in results in this neurological evaluation.

The literature has described the high prevalence of positional cranial deformities in PTs, especially plagiocephaly, particularly if evaluated in late corrected gestational age. Yang et al.<sup>21</sup> evaluated a sample of 530 Chinese PTs with up to six months of corrected gestational age and found a 90% prevalence (n = 476) of cranial asymmetry, whereas Mosca-Hayler et al.,<sup>22</sup> found a 96.1% such prevalence (n = 99) in 103 Chilean PTs with corrected gestational age up to three months and 29 days. On the other hand, the literature has scarcely explored early craniometric evaluations in premature neonates still hospitalized in NICUs. Hepnar et al.<sup>23</sup> evaluated 53 PTs and followed them up during their hospitalization in an Australian tertiary NICU. They found a 66% (n = 35) prevalence of cranial asymmetries, resembling that in this study. These numbers show the importance of early craniometric evaluations during NICU stays or discharge since this environment seems to influence the development of cranial asymmetries in this population. Early assessment can find alterations and provide opportunities for changes in the routine of positioning PTs under intensive care, guidance to caregivers on repositioning, and the anticipated referral of NBs for early intervention if necessary.

The PTs with PCA in this study had significantly lower gestational age and birth weight and longer hospital stays than those without cranial asymmetry. The literature has described these findings.<sup>24</sup> Yang et al.,<sup>21</sup> evaluating the incidence of positional cranial asymmetries across gestational age ranges, also observed that PTs with lower gestational ages and birth weight have a higher incidence of deformities. On the other hand, Mosca-Hayler et al.,<sup>22</sup> analyzing several gestational ranges, found no differences in incidence in relation to prematurity degree, observing that plagiocephaly was positively associated with longer hospital stays, as in this study. These results reinforce that immaturity at birth results in a more malleable and flexible skull, muscle hypotonia, and a lower ability to actively move the head, which can cause such NBs to remain with their head in the same position for a

prolonged time. Moreover, the more premature they are the more interventions they require, such as prolonged respiratory support and longer hospital stay, favoring the emergence of cranial deformities.

The literature shows that dolichocephaly constitutes the most common type of PCA in PTs,<sup>19,25</sup> occurring in isolation in 66% (n = 21) of those evaluated at NICU discharge in this study. Considering dolichocephaly with plagiocephaly increases this prevalence to 91% (n = 29). This finding is in line with that of Dieks et al.<sup>19</sup> – who followed 26 extremely premature NBs from birth to their 40-week corrected age, finding an 80.8% prevalence (n = 21) of dolichocephaly – and Hepner et al.<sup>23</sup> – who found a 53.8% prevalence of this type of deformity. Unlike these results, Mosca-Hayler et al.<sup>22</sup> and Yang et al.<sup>21</sup> observed other forms of PCA that were more prevalent in their studies: plagiocephaly (94.2%; n = 97) and plagiocephaly with brachycephaly (48.7%; n = 258), respectively. This divergence may stem from cultural differences since Yang et al.<sup>21</sup> evaluated Chinese PTs. Moreover, the authors argue that this population tends toward a higher cranial index than the international standard. These studies evaluated PTs at corrected ages late rather than early at NICUs, showing a tendency for change in the type of deformity over time.

This study also observed this fact, albeit in a smaller proportion. Although not longitudinal, this study reassessed a portion of its sample at their TEA, finding a change in the most prevalent type of cranial asymmetry since plagiocephaly occurred in 80% (12/15) of the infants. Moreover, the two PTs without asymmetry at discharge developed plagiocephaly in the evaluation at 40-week corrected age. These findings strengthen the thought that PTs have low muscle tone and poor active movement soon after birth, making it difficult for them to change positions. Thus, they tend to keep their heads in fully lateral rest, which favors the emergence of dolichocephaly.

As development progresses and NBs acquire muscle control, the development of plagiocephaly and brachycephaly becomes more frequent due to their prolonged time in the supine position with their head centered or rotated to one of their sides. The home environment may also influence the change in the type of cranial deformity since, after discharge from the NICU, these PTs may remain in strollers and in chairs with proper positioning for a longer time, remaining longer in the supine position.

Regarding the degree of cranial asymmetry, mild cranial deformities occurred more prevalently at discharge and at the evaluation at TEA, corroborating Mosca-Hayler et al.<sup>22</sup> and Hepner et al.<sup>23</sup> and differing from Ifflaender et al.,<sup>25</sup> who evaluated PTs at NICU discharge and at three- and six-month corrected gestational age, finding moderate to severe deformity at the earlier moment, with a decrease in severity at six-month. The low prevalence of severe deformities in this study may have suffered the influence of preventive measures that were taken as routine care during the hospital stay of PTs in the service in which this study was carried out, which prioritizes changing decubitus position every three hours and encourages the kangaroo position with parents and the monitoring of head positioning. Hepner et al.<sup>23</sup> found a moderate correlation between dolichocephaly severity and time spent in the incubator, highlighting the importance of this routine surveillance of the position of PTs during their stay at NICUs.

A debate revolves around the relationship between PCA and neurological development. Studies have shown that cranial asymmetry leads to deficits in motor, cognitive, and language development.<sup>12-15</sup> However, this relationship remains controversial since the directionality of these findings remains unanswered. This study brought unprecedented results by performing a craniometric and neurological evaluation of PTs while they were still at a NICU. The HNNE (the instrument used for neurological evaluation) found that both groups showed excellent results, with no statistical differences between them in category or total scores. However, the analysis of variance showed that PTs with PCA tended toward lower HNNE scores than those without asymmetry. Fowler et al.<sup>26</sup> evaluated late corrected gestational age infants using the version of the Hammersmith Infant Neurological Examination that is indicated for children aged from two months to two years of age to compare the neurological profiles of infants with positional plagiocephaly and healthy children and found a statistically significant difference in the overall neurological scores ( $p = 0.002$ ). This difference predominantly occurred in one category, in which infants with plagiocephaly had significantly more abnormal tone than those without it ( $p = 0.003$ ). The results of this study may have reflected its limited sample size. Although this research found no statistical differences in neurological results between its groups, those with PCA were smaller and more immature, which strengthens the hypothesis that PCA may stem from PTs' gestational age.

The neurological performance of PTs – according to the HNNE and ignoring the presence of PCA – showed a statistically significant difference between the evaluation at discharge and that at TEA. Moreover, comparing the raw HNNE scores at hospital discharge with the expected responses in the original sample in Dubowitz et al.<sup>16</sup> for each item for the groups with and without asymmetry (Supplement) shows that both groups had lower-than-expected responses in posture, arm traction, ventral suspension, and all movement and visual orientation categories. These findings may reflect PTs' immaturity, who, in this sample, had a 36.4-weeks mean corrected gestational age when evaluated at discharge from the NICU.

Although the HNNE can evaluate PTs up to four weeks before their 40-week corrected gestational age with the same predictive capacity regarding neurodevelopmental disability,<sup>20</sup> Spittle et al.,<sup>27</sup> evaluating a population of late and moderate PTs and full-term infants, reported that raw HNNE scores were similar in the late and moderate PT groups but were lower and with greater variability than those for full-term infants. Other studies have also shown that PTs have lower raw and optimization scores than their full-term infant peers.<sup>28,29</sup> These findings in PTs at NICU discharge show that intensive care fails to promote an ideal environment for the complete maturation of PTs because of its stimulus poverty and that the weeks between NICU discharge and the TEA may determine their neurological maturation.

Still regarding the expected raw HNNE score, both groups remained below expectations in movement item results but PTs without cranial asymmetry tended to score within the expected range. Although this descriptive analysis has no statistical significance, these findings signal a possible relationship between low spontaneous movement and the development of PCA and may constitute a starting point for new studies that seek to better understand the relationship between neurodevelopment and positional cranial deformities in PTs.

This study provides important information on early neurological evaluation of PTs with and without PCA. Although PCA is very prevalent in this population, studies on the association between these deformities and neurodevelopment in PTs during hospital stays or discharge from NICUs remain scarce, making these results unprecedented for explaining this relationship.

This study has some limitations that may have generated biases. One such limitation refers to selection since this study ignored PTs who were born extremely

prematurely. This group, due to its gestational age below 28 weeks, generally has a longer stay in NICUs and is more susceptible to the effects of musculoskeletal system positioning, showing a higher risk for more severe positional cranial asymmetries, which may reflect itself on neurodevelopmental changes.

Another point refers to its limited sample size, which may have generated a type II error. A larger sample would increase the testing power of this study and could have shown different results in the neurological results of PTs with and without cranial asymmetry. Moreover, PTs' guardians showed poor adherence to the reassessment at the age equivalent to term, further reducing the sample size at this moment. The age at which that study evaluated PTs at discharge may have influenced neonates' poorer response to some item raw score, which prohibited comparisons with their performance in the 40-week corrected age assessment. This sample loss in the reassessment may have occurred due to financial limitations of the study population and climatic factors since the study period had low temperatures, which made it difficult for families to travel to the institution. A study with a larger number of NBs who were reassessed at 40-week corrected age could have found differing evolutions of positional cranial asymmetries and neurological profiles since the 40-week corrected age HNNE obtained results unlike the raw scores, with more immature responses in PTs than in those evaluated before term age.

Further research should include a larger number of participants, including extremely preterm neonates, standardized assessments with greater predictive capacity for long-term neurological development to be applied early in NICUs, longitudinal follow-up since PTs' admission throughout their entire hospital stay, and follow-ups to better explain the development of PCA and its influence on PTs' neurological development and to assess whether differences manifest themselves in later phases of neurological and motor development.

## Conclusion

This found a high prevalence of PCA in PTs who were evaluated early at their discharge from a NICU in Paraná. Dolichocephaly showed the greatest prevalence at discharge, whereas plagiocephaly occurred more pre-

valently in the group reassessed at the age equivalent to term. Both groups showed excellent HNNE results, with no differences between PTs with and without cranial asymmetry, suggesting that PCA fails to impact the neurological development of early-evaluated PTs.

## Authors' contributions

APBB and CMS were responsible for conceptualization, data curation, and investigation. MAG analyzed the data, APBG wrote the manuscript (general draft). All authors contributed to its review and editing. MGA and ALSF supervised this research. All authors approved the final version of this manuscript.

## Data availability statement

The data that support the findings of this study are available upon reasonable request.

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## Supplement

**Table 1** - Comparison of the expected raw score of neonates from the original UK sample with the groups with and without cranial asymmetry assessed at hospital discharge

	Normative sample* (n = 224)	Group with positional cranial asymmetry (n = 32)	Group without positional cranial asymmetry (n = 18)
Posture	202 (90.0)	16 (50.0)	5 (27.8)
Arm recoil	206 (92.0)	29 (90.6)	15 (83.3)
Arm traction	222 (99.0)	18 (56.2)	9 (50.0)
Leg recoil	204 (91.0)	25 (8.1)	15 (83.3)
Leg traction	215 (96.0)	27 (84.4)	15 (83.3)
Popliteal angle	202 (90.0)	30 (93.7)	18 (100.0)
Head control 1	211 (94.0)	30 (93.7)	16 (88.9)
Head control 2	215 (96.0)	31 (96.9)	18 (100.0)
Pull to sit	204 (91.0)	24 (75.0)	8 (44.4)
Ventral suspension	204 (91.0)	6 (18.7)	5 (27.8)
Flexor tone 1	222 (99.0)	32 (100.0)	12 (66.7)
Flexor tone 2	222 (99.0)	32 (100.0)	17 (94.4)
Leg extensor tone	206 (92.0)	31 (96.9)	18 (100.0)
Cervical extensor tone 1	211 (94.0)	25 (78.1)	15 (83.3)
Cervical extensor tone 2	224 (100.0)	31 (96.9)	15 (83.3)
Tendon reflexes	222 (99.0)	32 (100.0)	18 (100.0)
Sucking	206 (92.0)	32 (100.0)	18 (100.0)
Palmar grip	208 (93.0)	23 (71.9)	16 (88.9)
Plantar grip	220 (98.0)	32 (100.0)	17 (94.4)
Plantar placement	222 (99.0)	29 (90.6)	14 (77.8)
Moro reflex	222 (99.0)	18 (56.2)	15 (83.3)
Quantitative movement	206 (92.0)	2 (6.2)	4 (22.2)
Qualitative movement	208 (93.0)	0 (0)	1 (5.6)
Head elevation in prone	202 (90.0)	15 (46.9)	9 (50.0)
Abnormal foot and hand postures	217 (97.0)	31 (96.9)	18 (100.0)
Tremor	224 (100.0)	32 (100.0)	18 (100.0)
Fear	211 (94.0)	28 (87.5)	14 (77.8)
Eye appearance	206 (92.0)	31 (96.9)	18 (100.0)
Auditory orientation	224 (100.0)	27 (84.4)	11 (61.1)
Visual orientation	206 (92.0)	15 (40.6)	10 (55.6)
Alertness	217 (97.0)	24 (75.0)	14 (77.8)
Irritability	208 (93.0)	24 (75.0)	15 (83.3)
Consolability	220 (98.0)	30 (93.7)	17 (94.4)
Crying	206 (92.0)	27 (84.4)	15 (83.3)

Note: Bold values indicate the proportion of preterm newborns with raw scores below expectations. Data shown in n (%). \*Normative data from: Lawford HLS, Nuamah MA, Liley HG, Lee AC, Kumar S, Adjei AA, Bora S. Neonatal neurological examination in a resource-limited setting: What defines normal? Eur J Paediatr Neurol. 2020;29:71-80. <https://doi.org/10.1016/j.ejpn.2020.08.010>