PERI-INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS: THE IMPORTANCE OF SCREENING BY TRANSFONTANELLAR ULTRASOUND

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ABSTRACT

Objectives. In preterm babies, peri-intraventricular hemorrahges (PIVH) might cause various degrees of neuropsycho-motor impairment. A 4-year prospective study (2009-2012) performed in the IOMC, was aimed to determine the prevalence of different degrees of PIVH diagnosed by head ultrasound (HUS) among 160 admitted preterm babies, the associated risk factors, along with the neuro-developmental effects on a 12-month follow-up period.

Material and methods. In the above-mentioned period all admitted preterms were examined by transfontanelar ultrasound according to a standardized protocol based on Papile's PIVH classification. For those preterms included in the study a 12-month systematic neurologic follow-up was performed.

Results. PIVH grade I (45%) and II (37,5%) were the most prevalent types. Grade IV PIVH represented 4,4% from all PIVH cases. The good neurological outcome of grade I and II PIVH, was found to be statistically significant ($p < 0.01$) for both types. Severe neurological sequelae were associated with grade III and IV and a statistically significant correlation ($p<0.01$) was found only for grade IV hemorrhages.

Conclusion. Systematic HUS screenings for all preterm babies is useful for early diagnosis and PIVH staging, for neurologic outcome prediction, providing the appropriate management strategy and a well-suited parental counseling.

Key words: preterm, transfontanelar ultrasound, peri-intraventricular hemorrhage, neurological outcome

INTRODUCTION

The preterm's high susceptibility for peri-intraventricular hemorrhage (PIVH), along with the considerable number of asymptomatic cases makes head ultrasound screening (HUS) an important tool in premature babies management. Severe cases of PIVH are usually symptomatic (seizures or other neurological signs). HUS screening in preterm infants is now universally recommended due to increased reliability, and lower diagnostic rates by CT (1,2).

Although medical advances in perinatology field have been achieved, leading to a significant PIVH incidence decrease in preterm babies (50% in the '70 to 15-25% today), this condition still remains a major problem (3,4). Recent studies have shown a lower overall incidence of PIVH, and parenchymal lesions, but the prevalence of neurological sequelae remains high (5,6).

In Romania few studies have been published on preterm infants HUS screening. The aim of the study was to determine the prevalence of PIVH detected by HUS in preterm babies admitted in IOMC over period of four years, along with a 12 months follow-up for possible associated neurological sequelae.

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MATERIALS AND METHODS

The prospective study conducted between 2009-2012 in IOMC Pediatric Clinic from Bucharest included 160 patients with PIVH diagnosed by HUS screening of all preterm infants admitted in the same period. A 12 months neurological follow up of the enrolled patients was equally performed. For all subjects included in the study the Informed Consent and Ethics Committee approval were obtained.

Both Aloka SSD 5500 and GE Logiq 300 ultrasound devices were used, with 5-10 MHz frequency HUS dedicated probes. The examinations were conducted by two medical specialists using a standardized protocol. Examinations were performed on days 3-8, 14-21, then monthly for the first 3 months and then every 3 months until 1 year of age, by multiple sagittal and coronal sections through the anterior and posterior fontanelle. The diagnosis was based on the Papile and Volpe classification (7,8). Grade I hemorrhage is confined to subependymal germinal matrix (Fig.1). Grade II hemorrhage extends to the lateral ventricles, occupying less than 50% of them without ventriculomegaly. Grade III hemorrhage occupies more than 50% of the lateral ventricle volume with secondary dilation. Grade IV hemorrhage result from bleeding in both ventricular system and parenchyma, secondary to hemorrhagic venous infarcts (Fig. 2).

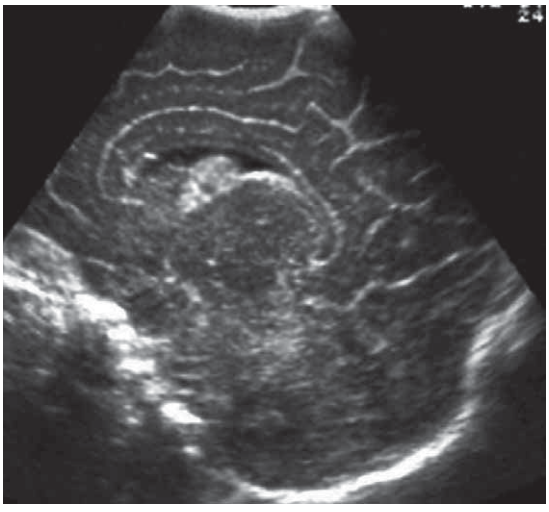

FIGURE 1. *HUS sagittal view: echogenic oval shaped homogeneous material located in thalamo-caudate groove. Normal sized lateral ventricles. Diagnostic: grade I subependymal PIVH*

Neurological examination performed by the same physician beginning with the PIVH diagnosis and every 3 months till 1 year of age, established three degrees of neurological impairments: mild - minimal axial hypotonia, medium with moderate axial hypotonia and severe with generalized hypotonia, motor

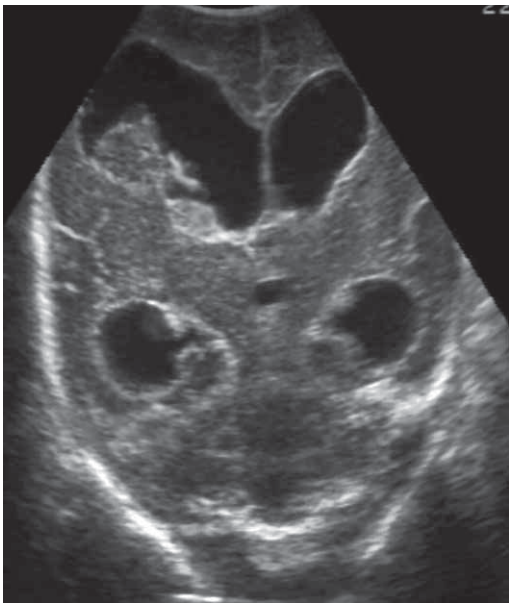

FIGURE 2. *HUS coronal view: global distention of the ventricular system, porencephalic cavity in the right frontal lobe communicating with the lateral ventricle. Diagnostic: grade IV intraventricular and parenchymal PIVH*

coordination deficiencies at age 6 months and chronic infantile encephalopathy at the age > 6 months.

We underwent statistical analysis by chi-square test (Pearson Chi Square) for independence. The test was performed to analyze risk factors influence (eg. gender, origin, gestational age (GA), birth weight (BW), Apgar score, type of birth) on variables such as PIVH or neurological sequelae severity.

RESULTS

From the 33518 admissions during the four years, 840 were preterm (2.5%) of which 160 cases were diagnosed with PIVH (0.47%). Table 1

TABLE 1. *Demographic characteristics of the study group*

Demographic characteristics	Number of cases/ procentual values
Male M/F	103 (64,4%) / 57 (35,6%)
Types of delivery:vaginal/caesarean	113 (70,6%) / 47 (29,4%)
BW < 1,000 g BW 1,000-1,500 g BW 1,500-2,000 g BW > 2,000 g	36 (22,5%) 38 (23,8%) 31 (19,4%) 55 (34,4%)
GA < 28 w GA 28-32 w GA 32-37 w	25 (15,6%) 60 (37,5%) 72 (45%)
Apgar score 8-10 Apgar score 5-7 Apgar score < 5	44 (32,4%) 58 (42,6%) 34 (25%)
Grade I PIVH Grade II PIVH Grade III PIVH Grade IV PIVH	72 (45%) 60 (37,5%) 21 (13,1%) 7 (4,4%)

PIVH prevalence in the study group was 18.68%, with values decreasing from 28.43% in the first study year to 12.5% in the last year. Boys (64.4%), along with vaginal delivery (70.6%) were dominant. 1-minute Apgar score < 7 was recorded in 67.6% cases and < 5 in 25% (Table 1). 21,42% of the severe PIVH (grade III and IV) had Apgar score <5. In the study group 53.1% of patients had GA < 32 weeks and in 46.3% the BW was less than 1500 g (Table 1). Grade I PIVH accounted for 45%, followed by grade II PIVH 37.5% (Table 2). All IV grade PIVH (4.4%) had severe neurologic outcome with major neurological sequelae and 11.1% of the PIVH III cases (13.1%) were associated with severe neurologic outcome (Table 3). In the severe neurological sequelae subgroup 66.6% had GA 32 weeks, 55.5% BW 1500 g and 42.85% 1-minute Apgar score 7. Although in the same group 11.1% had respiratory distress syndrome, 44.4% required mechanical ventilation, 22.2% had necrotizing enterocolitis and 66.6% were diagnosed with retinopathy of prematurity, no significant correlations could be established.

TABLE 2. *Association between prematurity grade and PIVH severity*

GA	Grade I PIVH	Grade II PIVH	Grade III PIVH	Grade IV PIVH
< 28 w	6 (24%)	9 (36%)	8 (32%)	2 (8%)
28-31 w	27 (45%)	22 (36,7%)	8 (13,3%)	3 (5%)
32-37 w	38 (52,8%) **p < 0,05**	27 (37,5%)	5 (6,9%)	2 (2,8%)

TABLE 3. *Association between neurological sequelae and hemorrhage grade*

Neurological sequelae	Grade I PIVH	Grade II PIVH	Grade III PIVH	Grade IV PIVH
Mild	64 (51,2%) **p < 0,05**	53 (42,4%)	8 (6,4%)	0 (0,0%)
Severe	1 (11,1%)	2 (22,2%)	1 (11,1%)	5 (55,6%) **p < 0,05**

DISCUSSION

The study's objective was to determine the prevalence of PIVH , to identify risk factors, along with a 12 months neurological follow-up of preterm infants with PIVH. According to literature data the incidence of PIVH varies from 5 to 90% depending on the study (7, 8). The observed prevalence decreased from 50% (1977) to 11.5% (1986) and 5.5% (1995), with a frequency drop of the severe forms from 70% to 23% (9). Although the studied group was relatively small, the PIVH incidence of 18.68% is consistent with the published data. Most studies show a higher incidence of PIVH in males and in those born with 1500 g, by vaginal delivery (5). Our results are concordant with literature data: the incidence of PIVH in males was 1.8 times higher than in females and vaginal delivery was 2.4 times more frequent than caesarean section (5). According to most studies perinatal hypoxia quantified by the Apgar score is a determinant of PIVH (5, 10). In the study group 1 minute Apgar score was 7 in 67.6% of cases and 5 in 25% of cases; 21.42% of severe forms of PIVH (grade III and IV) had an Apgar score 5 at 1 minute. Multiple studies demonstrate a high correlation between the prematurity degree and an increased risk for PIVH (11). Increasing the GA might be a preventive method for PIVH and periventricular leukomalacia, by this reducing the neurological impairment risk (12). The incidence and severity of PIVH inversely correlates with GA and BW and were found in 25-30% of patients with GA 32 weeks and BW < 1500g (13). In the study group 54.1% of patients had GA32 weeks and 46.3% had BW1500g. According to Papile and Volpe classification, PIVH severity was assessed into 4 grades (I-IV). The neurological impairment severity was divided into mild - moderate (grade I and II PIVH) and severe (grade III and IV PIVH). In the study cohort 45% were diagnosed with grade I PIVH. Most literature data shows similar results, around 40%, with a higher incidence in the study of Kadri et al of 52.4% (14). Grade I hemorrhage is usually an incidental finding, being generally asymptomatic (10). Grade I PIVH favorable prognosis is confirmed by most studies (10,15). Our study found a statistically significant correlation ($p < 0.01$) between grade I and II PIVH with absent or minimal sequelae and favorable neurological outcome in the first 12 months of life respectively. Literature data showed that grade I and II PIVH correlate with a mild/moderate long-term impact on neuromotor and cognitive development (16).

Most grade III and IV PIVH associate a severe neurological prognosis with major deficits (17). In the study group all PIVH IV had statistical significant correlation with severe neurological sequelae and poor prognosis ($p < 0.01$), whereas in grade III PIVH the unfavorable neurological prognosis was associated in 11.1% cases. According to published data, severe neurological impairment is found in 10-20% grade III and 57-80% grade IV PIVH (5). In our study 66.6% of infants with severe neurological sequelae were born < 32 weeks of gestation, 55.5% had a BW < 1500 g and 42.85% had an Apgar score < 7, all this data emphasizing the importance of prematurity prevention, thereby decreasing the associated risks. A limitation of the study

might be the lack of statistical correlation in the severe neurological impairment group with respiratory distress, mechanical ventilation, ulcero-necrotic enterocolitis, or retinopathy of prematurity, most likely due to the small sample size.

There are no conflicts of interest.

CONCLUSIONS

Prematurity is associated with an increased risk of morbidity and mortality. It is important to understand the pathogenesis of brain injury in preterm infants, in order to limit or even avoid their occurrence, thereby achieving an improved neurological long-term outcome. The fact that preterm infants with PIVH do not always associate long-term neurological impairments it is well recognized. Although the lack of specific treatment for PIVH limits to some extent the importance of HUS screening, this is really important in the early diagnosis and staging of PIVH and thereby in limiting the hemorrhage extension. Through this study we wanted to point out that prematurity is still a major health problem, by the associated mortality and its short and long-term complications, PIVH being one of the most significant.

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