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Neurodevelopmental Outcome of Newborns Aged More than 34 Weeks Gestational Age Managed for Birth Asphyxia in Douala (Cameroon): A Single Hospital-Based Study

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Abstract

Background: Perinatal asphyxia is a common cause of mortality and of morbidity including motor and neurodevelopmental abnormalities. The aim of this study was to evaluate the post-hospital outcome of neonates treated for perinatal asphyxia at the Douala Gynaeco-Obstetric and Pediatric Hospital (DGOPH) in Cameroon. **Patients and Methods:** We conducted a hospital-based cross-sectional study with both a retrospective and prospective data collection, conducted over a period of 3 months and involving neonates above 34 weeks of gestational age who were managed for perinatal asphyxia at DGOPH from August 2015 to February 2020. Socio-demographic, perinatal, motor, nutritional and neuro-developmental out-of-hospital data were recorded. The assessment of the child's psychomotor development was evaluated through gross motor skills, fine motor skills, language and social contact. We calculated the development quotient (DQ) by dividing the developmental age (DA) by the actual age (RA) of the patient. The data were entered and analyzed using excel and Stata version 15 software. **Results:** Among the 58 newborns included in our study, males were the most represented (59%). The mean age was 36.5 ± 14.16 months (Extremes: 12 months and 66 months).

The majority of patients were born at term (79%), had a birth weight between 2500 and 4000 grams (69%), were resuscitated (95%), and had an Apgar score < 7 at the 5th minute of life (67%). SARNAT stages II and III counted for 48%. Neurodevelopmental abnormalities were found in 25.5% of patients with gross motor delay (mainly tetraparesis) representing 23.5%, fine motor delay 27.5%, impairment in social contact 31% language speech delay. The majority of the children had a normal development quotient (78.4%). **Conclusion:** The short-term and long-term outcome of newborns who experienced perinatal asphyxia in our setting is marked by numerous impairments in developmental milestones leading to disability.

Keywords

Perinatal Asphyxia, Newborn, Neurological Outcome, Cameroon

1. Introduction

Perinatal asphyxia (PA) is defined by the World Health Organization (WHO) as the failure to establish or initiate normal breathing at birth [1]. It combines clinical and biological criteria such as cardiorespiratory and neurological depression (APGAR score < 7 at 5th minute of life), and evidence of acute hypoxia responsible for severe acidemia (arterial blood pH < 7 and/or a base deficit ≥ 12 mmol/l) and likely to be associated with neurological sequelae [2].

According to WHO in 2017, between 4 and 9 million newborns develop asphyxia annually [3]. It is higher in resource-limited countries (20 cases per 1000 live births) than in developed countries (2 cases ‰ live births). The incidence varies according to the health level of countries. It is the third leading cause of neonatal mortality worldwide (23%) after prematurity (28%) and neonatal infections (26%) [4].

Furthermore, survivors of PA are either free of disability or can develop numerous multi-organ abnormalities requiring specialized follow-up [3]. Birth asphyxia can lead to hypoxic-ischemic encephalopathy (HIE) which can in turn lead to neurological sequelae such as cerebral palsy, seizures, visual and hearing impairments, abnormal language development and social contact [5].

In Cameroon, Koum *et al.* in 2018 had a hospital proportion of PA of 22.9%, with 100% HIE. After 5 years, delayed language acquisition was the most represented neurodevelopmental abnormality (27%), followed by gait abnormalities (14.0%) and cerebral palsy (10%) with quadriplegia as the most common type [2]. The high incidence of PA and the severity of the neurological sequelae made us interested in studying the post-hospital outcome of newborns treated for PA at the Douala Gynaeco-Obstetric and Pediatric Hospital (DGOPH).

2. Materials and Methods

The study was conducted in the neonatology Department of the DGOPH, a pediatric referral center in Cameroon. With a population of 3.7 million and a birth rate of 36.8 per 1000 inhabitants, Douala is one of the two main cities in the country.

The DGOPH was created in 2015, and the neonatology department has been operational since August 1st, 2016 with 02 neonatology units: internal (for newborns born at DGOPH) and external (for newborns born out of DGOPH). During this study, the newborns admitted to the service came from both the maternity of DGOPH, and other health structures in the city of Douala and the rest of the country. The unit has 17 incubators, 2 radiant tables, a tunnel and ramps for phototherapy, electric syringes, 2 transport mechanical ventilators, one Continuous Positive Airway Pressure therapy (CPAP) machine. The medical staff is composed of one paediatricic neonatologist, one neuropaediatrician, four paediatricians and two general practitioners. The paramedical staff is composed of seventeen nurses. We receive around 500 newborn babies a year, at least 40% of whom are premature.

Our study obtained an ethical clearance N˚2587CEI-Udo/04/2021/T from the Institutional Ethics Committee of the University of Douala.

It was a hospital-based cross-sectional study, with both a retrospective and prospective data collection, conducted over a period of 3 months and involving infants with a gestational age ≥ 34 weeks who were managed for neonatal asphyxia at DGOPH from august 2015 to February 2020. We excluded patients with incomplete medical records and those whose parents/guardians refused to participate.

The first phase of the study was retrospective and date were extracted from the medical records of the newborns. We collected socio-demographic data of the newborn and their mother (age, sex of the child, telephone contact, maternal marital status, maternal economic situation); perinatal and natal data (gestational age, mode of delivery, Apgar score at the 5th minute of life, notion of resuscitation); hospitalization data (diagnosis according to SARNAT, primitive reflexes, tonus disorder, presence of convulsions or coma), neuroimaging (transfontanellar ultrasound , brain CT scan), EEG data and duration of hospitalization.

The second phase was prospective: we called back the parents/guardians to book an appointment with them and the child at the pediatric outpatient department of HGOPED for a medical review. During this phase, an informed consent was obtained from the participants and the infants were examined. The evaluation of the infant's nutritional status was based on current weight and height while the assessment of the child's psychomotor development was evaluated trough gross motor skills, fine motor skills, language and social contact. For the scoring of the Denver II score, we focused on the child's acquisitions at the time of our assessment. For each item of the Denver II test, the infant needed to realize at least three items to the left or right of the line. From this we obtain the real developmental age of a child. Finally, we calculated the development quotient (DQ) which is the quotient obtained by dividing the developmental age

(DA) by the real age (RA) of the patient [DQ = (DA/RA) × 100]. From this calculation, the developmental level was classified as high (DQ > 120), normal (DQ: 85 - 119), borderline (DQ: 70 - 84), mildly retarded (DQ: 50 - 69), moderately retarded (DQ: 35 - 49), severely retarded (DQ: 20 - 34), very severely retarded (DQ < 20).

For the assessment of the nutritional status, we measured their weight using a scale (unit in kg) and their height was taken using the stadiometer (unit in cm). The weight/height index equivalent was obtained from WHO Z scores. This index, represented by a dot on the chart, was compared to the WHO reference curves present and then classified as follows: normal (between −1 and 1), at risk of malnutrition (between −1 and −2), moderately emaciated (<−2), severely emaciated (<−3). Overweight risk (between 1 and 2), overweight (>2). This concerned children with an age ≤ 60 months. Concerning the BMI/age index, we calculated the BMI by dividing the child's weight by the square of its height. This index, represented by a dot on the diagram was compared to the WHO reference curves present and then classified as follows: normal weight (between 3th and 97thpercentile), underweight (<3th percentile), and overweight to obese (≥97th percentile). These included children of all age groups.

The data were entered and analyzed using excel and Stata version 15 software which allowed us to bring out the different numbers and percentages. Qualitative variables were expressed as numbers and frequencies while quantitative variables were expressed as mean ± standard deviation and median (interquartile range). P-value < 0.05 was considered significant and the strength of the association was given as an odds ratio with 95% CI.

Operational Terms

Perinatal asphyxia (PA): is defined by the World Health Organization (WHO) as a failure to establish or initiate normal breathing at birth. It combines clinical and biological criteria such as cardiorespiratory and neurological depression (Apgar score < 7 at 5th minutes of life), and evidence of acute hypoxia responsible for severe acidemia (arterial blood pH < 7 and/or a base deficit greater than or equal to 12 mmol/l and likely to be associated with neurological sequelae [2].

Hypoxic-ischemic encephalopathy (HIE): Neurological picture occurring in the first week, secondary to oedema with cerebral hypertension and variably associating signs of central nervous system depression, signs of damage to the cortical, sub-cortical and spinal motor pathways, signs of damage to the brainstem with or without multi-visceral damage [2].

Prematurity: birth occurring before 37 completed weeks of amenorrhea, *i.e.* before the 259th day calculated from the first day of the last menstrual period. According to the WHO classification of prematurity, we considered: very premature if born less than 28 weeks of gestation (WG), extreme prematurity from 28 to 31 WG ans 6 days, moderate prematurity from 32 to 36 WG and 6 days [6].

Denver Developmental Screening Test II (DDST II) was developed in 1967 and updated in 1992. It allows health professionals to assess the development of psychomotor skills in children from birth to 6 years of age. It is also used to identify children whose cognitive and behavioural development deviates significantly from that of others [7].

Malnutrition is defined as deficiencies, excesses or imbalances in a person's energy and/or nutritional intake [8].

Wasting is a reduction or loss of body weight for height due to a recent nutritional deficiency

Body mass index (BMI) is defined as weight in kilograms divided by height in meters squared (kg/m^2), and is usually used to determine overweight and obesity.

Psychomotor development: the maturation of the child's brain through motor skills and psychological progress (intelligence, language, affectivity, etc.) [8].

3. Results

Of 1624 neonates hospitalized during our study period, 277 were managed for neonatal asphyxia. This study included 58 participants, 7 (12%) of whom died (**Figure 1**).

3.1. Characteristics of the Study Population

The current average age of the children was 36.5 ± 14.16 months with extremes of 13 and 66 months. The age range between 36 and 42 months was the most represented (n = 12; 21%). Males were the most represented (n = 34; 59%) with a sex ratio of 1.41. The average maternal age was 27.36 ± 5.20 months. The majority of mothers were between 25 and 30 years of age (n = 21; 36%), married (n = 34; 34%), employed (n = 39; 67%).

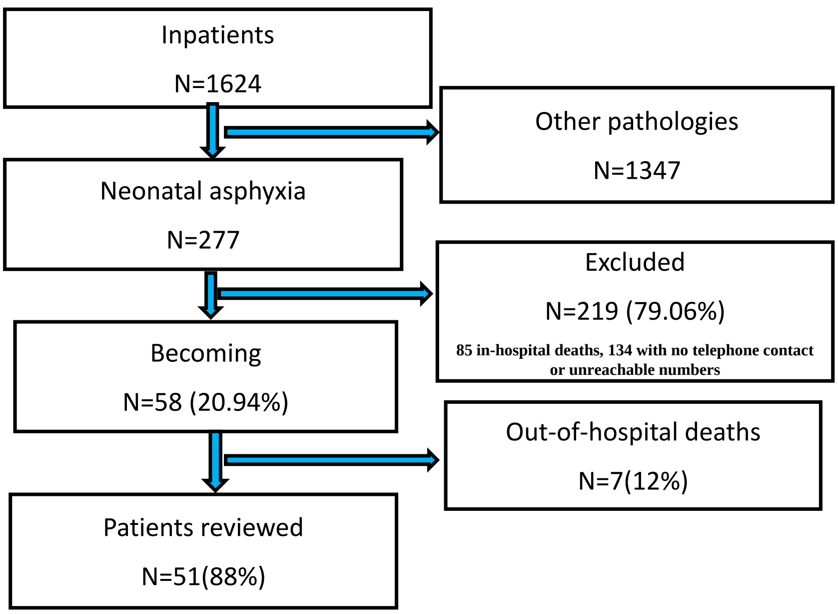

Figure 1. Flow chart of participants.

3.2. Perinatal and in-Hospital Birth History of the Study Population

Perinatal asphyxia was mostly found in full-term babies (79%) and only a minority in post-term babies (9%). Survivors of neonatal asphyxia with an Apgar score < 7 at the 5^{th} minute of life represented 67% of participants (Table 1).

Seizures accounted for 46.55% of early perinatal neurological signs. SARNAT I HIE (n = 30; 52%) was the dominant clinical form. Electroencephalographic abnormalities were found in 33% of patients who were able to perform an EEG. Abnormal brain ultrasound was found in 57%. Almost half of the patients had a neonatal hospital stay between 7 and 14 days (Table 2).

Current nutritional status of the study population

On the 51 children reviewed, the current nutritional status of 47 was assessed with the weight-for-height index because their age was ≤60 months. We observed that 8.5% were at risk of wasting (Table 3). Assessment using the BMI/age index showed us that more than half of the participants had a normal body build (n = 44; 86%). Underweight was found in 10% and overweight in 4%.

3.3. Current Motor Evolution of the Study Population

Motor disorders were found in 10 (20%) of the children reviewed. They were mainly dominated by tetraparesis (n = 9; 18%), followed by monoparesis (n = 1; 2%) (Figure 2).

Table 1. Distribution of participants according to perinatal history.

	Number (N = 58)	Proportion (%)
Gestational Age (in weeks)		
34 GA to 36 GA + 6 days	7	12
37 GA to 41 GA+ 6 days	46	79
≥42 GA	5	9
Mode of delivery		
Spontaneous vaginal delivery	36	62
Instrumental vaginal delivery	1	2
Caesarean section	21	36
Apgar < 7 at 5^{th} minute		
Yes	39	67
No	19	33
Birth weight (in grams)		
[1500 - 2500[	13	22
[2500 - 4000[	40	69
[4000 et plus]	5	9
Resuscitation		
Yes	55	95
No	3	5

Table 2. Distribution of participants according to postnatal findings or features.

Postnatal findings	Number (N)	Proportion (%)
SARNAT STAGE		
SARNAT I	30	52
SARNAT II	17	29
SARNAT III	11	19
Early neurological signs		
Primitives reflexes	58	100
Seizure	27	47
Tonic abnormality	51	88
EEG[a]	**12**	**21**
Normal	8	67
Abnormal	4	33
BUS[b]	**14**	**24**
Normal	6	43
Anormal	8	57
Length of hospital stay (in days)		
<7	18	31
7 à 14	28	48
15 à 21	6	10
≥22	6	10

[a]Electroencephalogram, [b]Brain ultrasound.

Table 3. Current weight/height index of survivors in the study population.

Weight/Height (Z score)	Number (N = 47)	Proportion (%)
<−1	4	8.5
<0	4	8.5
≥0	18	38
≥1	16	34
≥2	5	11

3.4. Assessment of the Neurodevelopmental Evolution of the Study Population

Gross motor delay was observed in 13 participants (25.5%). The age group most represented with this delay was [12 - 18[months (n = 4; 8%). The delay in social contact was observed in 14 participants (27.5%). The most represented age group with this was [30 - 36[months (n = 3; 6%) (Table 4). Age influenced the quality of the participants' social contact ($p = 0.00766$).

Among the survivors in our study, 16 (31%) had a language delay. Participants with language delay were equally aged between [12 - 18[months and [30 - 36[months (n = 5; 31% each).

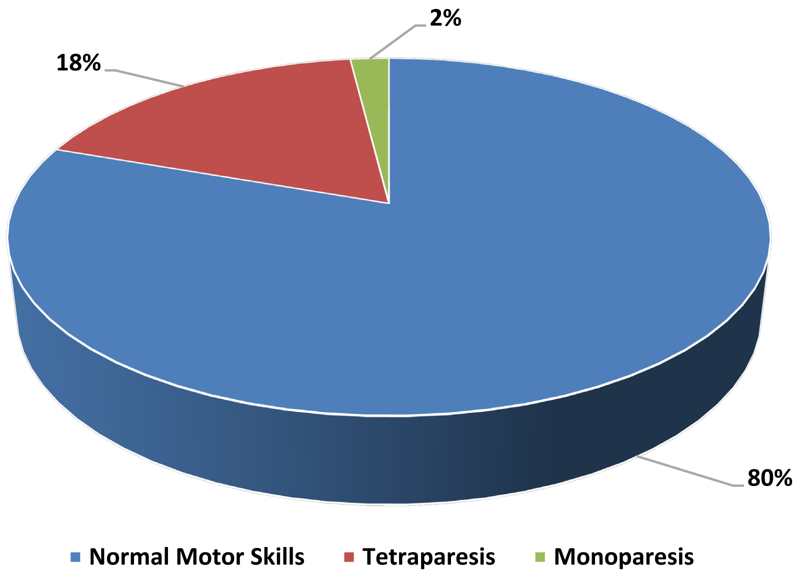

Figure 2. Distribution according to the motor functions and their abnormalities in the study population.

Table 4. Distribution of current normal motor skills and their abnormalities in the study population.

Age (month)	Normal gross motor skills (N = 38)	Delayed gross motor skills (N = 13)	Relative risk (RR) (95% CI)
[12 - 36[	19	6	1.040 (0.755 - 1.433)
[36 - 66[	19	7	0.891 (0.347 - 2.287)
Total	38	13	**1.167 (0.330 - 4.122)**

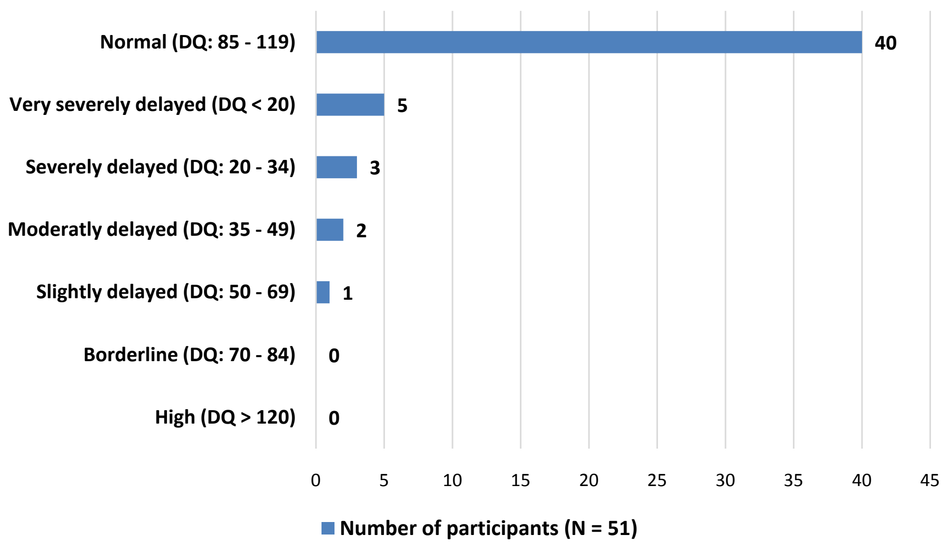

Figure 3. Distribution of participants according to the development quotient.

Fine motor delay was observed in 12 survivors (23.5%). The age range most represented with this delay was [48 - 54[(n = 3; 25%).

Developmental delay was observed in 11 survivors (21.5%), with very severe delay predominating in the [30 - 36] month age group and severe delay equally represented in the [12 - 18], [48 - 54] and [60] age groups. [48 - 54[and [60 - 66] months. Developmental delay was mild (50 - 69) in 1 survivor (2%); moderate (35 - 49) in 2 (4%); severe (20 - 34) in 3 (6%) and very severe (<20) in 5 (10%).

The mean developmental quotient was 83.43 ± 31.29 with extremes of 10 and 107. The majority of survivors had a normal developmental quotient (85 - 119) (**Figure 3**).

4. Discussion

Among the 58 newborns included in our study, males were the most represented (59%). The mean age was 36.5± months (Extremes: 12 months and 66 months). The majority of patients were born at term (79%), had a birth weight between 2500 and 4000 grams (69%), were resuscitated (95%), and had an Apgar score < 7 at the 5th minute of life (67%). SARNAT stages II and III accounted for 48%. Neurodevelopmental abnormalities were found in 25.5% of patients with gross motor delay (mainly tetraparesis) representing 23.5%, fine motor delay 27.5%, impairment in social contact 31% language speech delay. Majority of children reviewed had a normal development quotient (78.4%).

In our sample, the male gender was the most represented (59%). This trend was also observed by Koum *et al.* in Cameroon 2018 and Pili in France 2013 with respectively 61% and 68.42% [9] [10]. This was not expected as no predisposition of any sex to neonatal asphyxia was found in the literature.

The mean age of the children was 36.5 months. This result was lower than that of Perez *et al.* in Switzerland 2013 who found a mean age of 11.2 years [11]. This could be explained by the difference in the methodology used. In his study, the age of patients included was not limited.

The average maternal age was 27.36 years. This result was similar to that of Pili in France in 2013 and Hayakawa *et al.* in Japan in 2013, who found respectively 30 years and 31 years [10] [12]. However, in Senegal Thiam *et al.* reported a lower frequency of 17.2 years [13]. This difference could be explained by early adolescent pregnancy and high level of illiteracy as well as the low economic level.

The majority of mothers in our study population were married. This result was similar to that of Bayih *et al.* in 2021 in Ethiopia [14]. More than half of the mothers in the study population were employed (67.24%). This result was higher than that of Bayih *et al.* who found 41.2%.

Perinatal asphyxia occurred after caesarean section and instrumental deliveries at 36% and 2% respectively. The caesarean section rate was close to that of Woday *et al.* in 2018 in Ethiopia who found 35.5% caesarean section [15]. Pili in France and Thiam *et al.* in 2017 in Senegal reported high frequencies of 52.6% caesarean sections and 39.5% instrumental deliveries in France and 52.3% caesarean sections and 5.2% instrumental deliveries in Senegal respectively [10] [13]. Furthermore, a high rate of instrumental delivery was reported by Banu *et* *al.* in Bangladesh in 2015 (93.6%) [16]. It follows that the practice of deliveries varies in both developed and resource-limited settings.

Children of neonatal asphyxia who had an Apgar score < 7 at 5eme minute of life were 67%. This result was closed to the one reported by *Koum and al.* in Cameroon, 63.70% [9]. A lower rate was reported by Thiam *et al.* in Senegal, 42.6% [13]. Whereas a high rate was reported by Halloran *et al.* in Zambia in 2009, 86% [17]. This disparity could suggest that there was no emphasis on the use of the Apgar score. Indeed, not all the study population had an Apgar score < 7 at 5th minute of life but had been diagnosed with neonatal asphyxia. This was probably due to the fact that in others studies the Apgar score was not systematically used to do the diagnosis therefore bringing some bias in the initial evaluation of newborn.

Perinatal asphyxia was found in 95% of neonates resuscitated at birth. This result was similar to those of Koum *et al.* in Cameroon and Thiam *et al.* in Senegal who found 91.40% and 100% respectively [9] [13]. These results reflect the shortcomings of neonatal resuscitation in our contexts.

According to SARNAT Classification in our study, 52% of newborns presented grade 1 HIE. This was consistent with results found by Koum K *et al.* in Cameroon and Thiam *et al.* in Senegal [9] [13]. Kumar and Dipangkar in 2016 in India, Agnani in France in 2019 and Ouédraogo *et al.* in Burkina Faso in 2015 reported respectively SARNAT III stage (44%) and SARNAT II grade (69.2%) then 45% of SARNAT II [4] [18]. This difference in the grading of HIE probably results from the cohort of each study.

Seizures were found in 46.5% of participants. This result was similar to Pili in France in 2013 and Mwakyusa *et al.* in Tanzania in 2008 who reported 47.36% and 41.7% respectively [4] [10] [19]. The other hand a low rate was reported by *Begum et al.* in Bangladesh in 2006 and *Halloran et al.* 2009 in Gambia respectively 35% and 26% [16] [17].

Electroencephalographic abnormalities were found in 33% of newborns who were able to perform EEG. This result was lower than that of *Pili* who reported 84.21% of abnormal EEGs before the 7th day of life [10]. These results could be explained by the fact that most of our newborns have EEGs after several days, usually when they are stabilized enough to be transported to the EEG lab safely, since we don't dispose bedside EEG.

The nutritional status of asphyxiated children with an age ≤ 60 months showed 8.1% risk of wasting. These results were lower than those of Kone *et al.* in 2011 in Mali who found in non-asphyxiated children 12% wasting with 4.4% severe wasting, and 35.7% risk of wasting [20]. This could be explained by the fact that in our study, we had a low number of children compared to Mali. This could be explained by the fact that in our study, we had a low number of children compared to Mali.

Overweight was found in 4% of survivors. This result was lower than that of Skinner *et al.* in America in 2018 who found 26% overweight and 15.7% obesity in non-asphyxiated children [21]. This could be explained by dietary habits varying between the Occident and sub-Saharan Africa.

Motor abnormalities were found in 20% of the survivors with tetraparesis being the most represented abnormality. This result was higher than that of Koum *et al.* who reported 8% of motor anomalies with quadriplegia as the most represented anomaly [9].

Psychomotor developmental abnormalities detected by the Denver score in survivors of perinatal asphyxia showed: 25.5% gross motor delay, 23.5% fine motor delay, 27.5% social contact delay, 31.4% language delay. This was similar to those of Adhikari and Seshagiri in Nepal in 2016 who found 29.4% gross motor delay, 18.2% fine motor delay, 17.1% socialization delay, 19.2% language delay using the Denver II score [5]. In contrast, Aly *et al.* in Egypt in 2005 found a lower rate using the Denver II score, *i.e.* 8.3% gross motor delay, 4.2% fine motor delay, 4.2% language delay [22]. Furthermore, higher rates were reported by Shehu *et al.*, in Nigeria in 2020 who found 50% gross motor delay, 40.9% fine motor delay, 27.3% language delay using the Denver II score [23]. Furthermore, a rate of language delay close to our results was reported by Nguefack *et al.* in Cameroon in 2017 in healthy children without perinatal asphyxia assessed with the Denver II score (33.3%) and an advance on the other items of this score [24]. This could be explained by the fact that screening for sequelae in infants at risk was not systematic. As a result, the implementation of appropriate treatment by the specialist was delayed. Furthermore, the results of Nguefack *et al.* in 2017 in Cameroon obtained on children who had not suffered from neonatal asphyxia showed that more than half of these children had advanced acquisitions for their age in relation to the Denver II score. They therefore suggest laboration of a neurodevelopmental assessment adapted for Africa.

The development quotient of the asphyxiated revealed that 21.5% were having developmental delay. This result was close to that of Boskabadi *et al.* Iran in 2015 who found a rate of 28.18% developmental delay [25].

5. Limits

The initial collection of data during the retrospective phase with a lack of information, especially contact with parents, explains our low sample size. The short duration of the prospective phase limited the number of patients included.

6. Conclusion

The short-term and long-term outcome of newborns who experienced perinatal asphyxia in our setting was marked by impairments in developmental milestones leading to disability. A good follow up of pregnancies and a proper management in the first minutes of life can help prevent some of these. An early management of infants with developmental delay may lead to better results and thus, the creation of a rehabilitation unit for these children could be of great help for them.

Conflicts of Interest

The authors declare that they have no competing interest.

Author Contributions

DNN, DCKK and DE designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. DLNM and DNN designed the data collection instruments, collected the data. DE, YDF and DCKK critically reviewed the manuscript for important intellectual content. DNN, DE and DCKK coordinated, and supervised data collection. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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