Scientific Research Publishing

Open Journal of Pediatrics, 2023, 13, 934-946
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Outcome of Very Premature Newborns in a Referral Hospital in a Resource-Limited Setting

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How to cite this paper: Njinkui, D.N., Enyama, D., Fokam, Y.D., Pongo, V.E., Ekoube, C.E., Tchouamo, A.A.S., Ndombo, P.O.K. and Koum, D.-C.K. (2023) Outcome of Very Premature Newborns in a Referral Hospital in a Resource-Limited Setting. *Open Journal of Pediatrics*, **13**, 934-946.
https://doi.org/10.4236/ojped.2023.136103

Received: November 2, 2023
Accepted: November 26, 2023
Published: November 29, 2023

Abstract

Background: In Cameroon, prematurity is considered among the first cause of neonatal mortality and the main cause of sequelae in children under 5 years old. Although some local teams have studied the causes of neonatal deaths, the survival of the very preterm babies in our context remains poorly known. **Patients and Methods:** We conducted a hospital-based cross-sectional study with both a retrospective and prospective data collection, covering a period of 5 years and 8 months, including 120 participants who presented with very preterm birth. Socio-demographic, anamnestic, and outcome features were studied. The assessment of the child's psychomotor development was evaluated trough 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. Qualitative variables were expressed as numbers and percentages and quantitative variables as means ± standard deviations. **Results:** At the clinic, 23.8% of the children developed cerebral palsy, 3.1% had cerebral palsy with mental delay, and 6.6% had praxis disorders. Hearing impairment was observed in 6.3% of the survivors, visual impairment in 9%, and swallowing disorders in 7.6%. The mean developmental quotient was (89.98 ± 19.7) with a median of 93. A delay in developmental milestones was observed in 10.8%, speech disorder in 57%, severe malnutrition in 7.7%. The mortality rate was 48.5%. **Conclusion:** Very preterm birth is associated with a higher risk of neonatal death. Cognitive and motor disorders should not be underestimated. The harmonised management of very premature babies is highly recommended in our context for early di-

agnosis of sequelae.

Keywords

Very Preterm Birth, Cerebral Palsy, Psychomotor Development, Sensory Development

1. Introduction

Preterm birth is defined by the World Health Organization (WHO) as all births before 37 completed weeks of gestation age (WGA) or fewer than 259 days since the first day of a woman's last menstrual period. Preterm birth can be further subdivided into extremely preterm (<28 weeks), very preterm (28 - <32 weeks), and moderately preterm (32 - <37 completed WGA). According to WHO, 15 million children are born prematurely each year, which represents more than one in ten children. Out of the 132 million births worldwide each year, about 4 million newborns will die during the first 28 days of life [1] [2].

In most industrialized countries, prematurity has increased over the last three decades. Over 60% of preterm births occurred in sub-Saharan Africa and South Asia where 9.1 million births (12.8%) annually are estimated to be preterm [2]. In Cameroon, Njom Nlend *et al.* (2014) revealed a hospital prevalence of prematurity of 7.6% [3]. While prematurity-induced lethality remains high in low-income countries, significant progress has been made in reducing prematurity-induced lethality in advanced countries, both in late preterm and extreme preterm births [4] [5]. Nearly one million children die each year worldwide due to complications of prematurity [6]. Many of the survivors suffer lifelong disabilities, including learning, neurological, motor, and sensory impairments.

Although some local teams have studied the causes of neonatal deaths, the survival of the very premature baby in our context remains poorly known. Survival rates show striking inequalities from country to country. The aim of our study was therefore to evaluate the outcome of these very premature babies.

2. Materials and Methods

The study was conducted in the neonatology department of the Douala Gynaeco-Obstetric and Pediatric Hospital (DGOPH). Douala is the economic capital of Cameroon located on the country's coast. With a population of 3.7 million and a birth rate of 36.8 per 1000 inhabitants, it is one of the two largest cities in the country, along with Yaoundé as the political capital.

DGOPH was established in 2015, and the neonatology department functional since August 1, 2016, with two neonatology subunits: internal (for newborns born in DGOPH) and external (for newborns born out of DGOPH). The newborns admitted in this study were from the maternity ward of the DGOPH as well as from other health facilities in the city of Douala and the rest of the coun-

try. The unit has 17 incubators, 2 neonatal radiant warmers, a tunnel and ramps for phototherapy, 6 electric syringe pumps, 2 mechanical transport ventilators, and a continuous positive airway pressure (CPAP) machine. The medical staff consists of a neonatologist, a child neurologist, four general pediatricians, and three 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.

Approval was obtained from the ethics committee of University of Douala and research approval was obtained from the Institutional Committee on Ethics and Research for Human Health (ICERHH) of the DGOPH. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

It was a hospital-based cross-sectional study, with both a retrospective and prospective data collection carried out during a period of 5 years and 8 months, from 1st January 2015 to 1st September 2020. All premature newborn files who were admitted to DGOPH during the study period were retained for the study. We included all very preterm babies (gestational age between 28 and 32 weeks' amenorrhoea) alive or died during our study period, followed up at least 6 months after discharge. We excluded patients with no consent form given by the parents or guardians or refusal to participate declared by the parents or guardian and incomplete records.

Data collection was done with each child accompanied by his/her parent/guardian meeting the inclusion criteria. The questionnaire was pre-tested on a sample of 05 children. The interview began with an information note to the participant. The interviewer then took care to explain carefully the instructions until the participant understood them correctly. The participant was then given an informed consent form in which the aims and objectives of the study were detailed. After that, the investigator administered the questionnaire in a face to face.

Maternal socio-demographic characteristics such as gestational age, sex, mother's age, and place of residence, were collected from each candidate's medical file. Concerning the socio-economic level, we collected the information in person by asking the parents directly and we categorized the average monthly income of the family into three groups;

Band 1: less than 100,000 CFA francs, which reflects a low economic level;

Band 2: 100,001 - 300,000 CFA francs, which reflects an average economic level;

Band 3: above 300,000 CFA which reflected a good economic level.

The anamnestic data were collected mostly from the medical records. The data on the development were assessed in three ways: For the sensory level, we first explored the follow-up booklet to notice whether the child has been followed for a particular visual and auditory impairment and then we proceeded to a pure clinical evaluation. For neurodevelopment: we used the follow-up and the different clinical findings of the child to detect and assess motor and praxis disord-

ers. The developmental quotient assessment was done according to the four elements of psychomotor development described in the DENVER II test, which were gross motor, fine motor, language, and social interaction. We focused on the child's acquisitions at the time of our assessment. For each item of the DENVER test, we administered at least three items completely for the left side of the line corresponding to the child's actual age, and for those across the line, we observed the patient doing the desired item (e.g. standing, walking, throwing the ball, riding a tricycle). If the child was unable to complete the items in the first stage, further items were administered to the left until the child passed three consecutive items, and then to the right of the age line until the child missed three consecutive items. The ages corresponding to the lines from which the child missed three consecutive items represent the developmental age (DA). At the end, we calculated the developmental quotient (DQ) which is the ratio of the developmental age (DA) and the actual age (AA) of the patient (DQ = DA/AA * 100). Developmental level was therefore classified as high (above 120); normal (85 - 119), borderline (70 - 84), mildly retarded (50 - 69), moderately retarded (35 - 49), severely retarded (20 - 34) and very severely retarded (below 20).

Nutritional status was assessed using the WHO growth charts for preterm infants.

Data analysis enabled us to produce statistics which results are expressed in the form of diagrams and/or frequency tables grouping the number of cases observed and their percentages. The data were entered into a digital application KOBOCOLLECT and then exported to EXCEL 2016 and the analyses were carried out using SPSS (Statistical Package for the Social Sciences) software version 26.0. Categorical variables were expressed as numbers and percentages and quantitative variables as means ± standard deviations.

3. Results

During our study period, we had 1624 newborns admitted to the neonatal department, of which 198 were very premature, we included 120 in our study. The other 78 were not analyzed due to various technical constraints (Unworkable records, parents unreachable by phone, etc.). Of the 120 very premature babies studied, 55 died during hospitalisation and 65 survived. This gave an inclusion rate of 60.60% which represents an admission rate of 12.20% (**Figure 1**).

3.1. Characteristics of the Study Population

The most represented birth age was between 31 - 32 WGA with a proportion of 42.50% (**Table 1**). The sex ratio was 76 boys for 44 girls. For the patient seen for follow-up, the mean age of our study population was 35 months ±15 with extremes ranging from 6 to 73 months; and a median of 38 months. Children aged (35-48) months were the most represented (46.2%) (**Figure 2**). The age of the mothers was between 15 and 20 years in 59.1% and over 35 in 23.4% of cases. Among them, 62.5% were in couples and more than half (52.5%) had a relatively

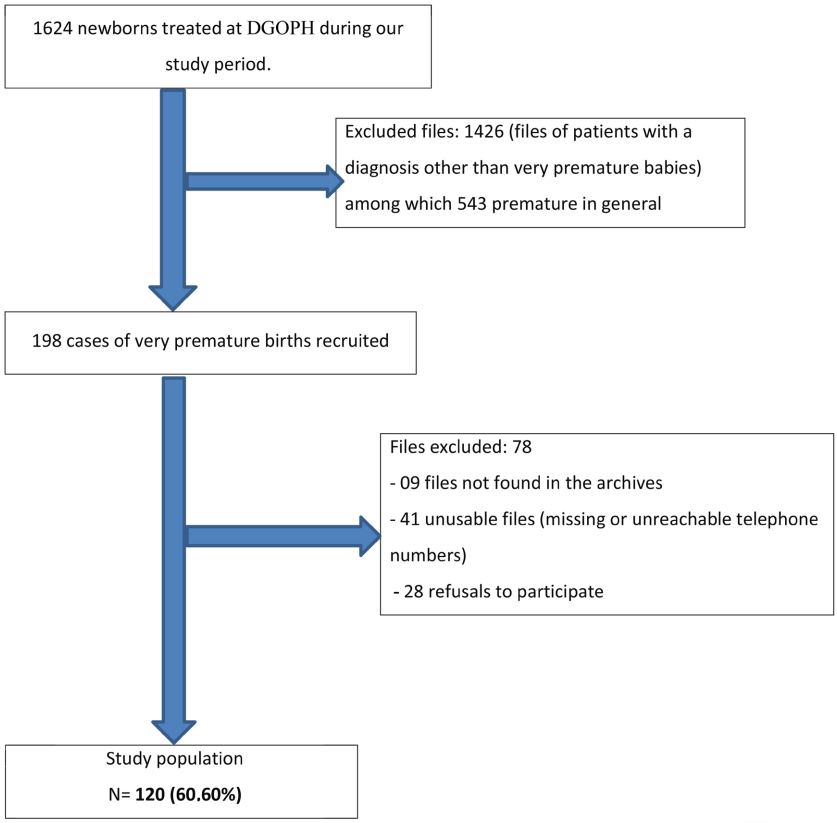

Figure 1. Diagramme of FLOW.

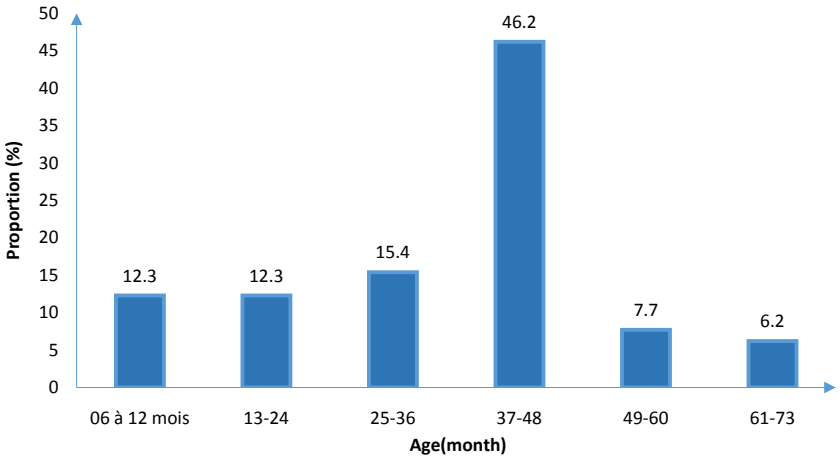

Figure 2. Distribution of very premature babies by current age.

Table 1. Proportion of very premature births in the source population.

Gestational age (GA)	Numbers	Proportion %
28SA à 28 WGA + 6 days	29	24.2
29SA à 29 WGA + 6 days	20	16.7
30SA à 30 WGA + 6 days	20	16.7
31SA à 32 WGA	51	42.5
TOTAL	120	100

low economic and educational level (Table 2). In our series, 91.7% of the very premature babies had a birth weight of less than 1500 g, most of them born via vaginal delivery (83%).

3.2. Neurodevelopmental Evolution of Very Premature Babies

When we re-evaluated the 65 survivors, we found that 15 (23.8%) children developed cerebral palsy (CP) of the spastic diplegic type, 2 had cerebral palsy with mental delay, and 5 had various praxis disorders (Table 3). Gross motor skills were abnormal in 9 (13.8%) children, and fine motor skills were abnormal in 14 (21.5%) children. Language disorders were present in 28 (43%) children. Social interaction was abnormal in 18 (27.7%) children.

3.3. Psychomotor Development

Gross motor skills were abnormal in 9 (13.8%) of the 65 children reassessed. Fine motor skills were abnormal in 14 (21.5%) children. Language disorders were present in 28 (43%) children. Social interaction was abnormal in 18 (27.7%) children. In our study, the majority, 57 (87.60%) children had a normal developmental quotient (Table 4).

3.4. Sensorial Development

In terms of sensory outcome, 6 (9%) children developed severe visual problems (blindness, strabismus, reduced visual acuity) (Table 5).

Table 2. Distribution of very premature babies according to maternal age, parents economic situation, educational level and marital status.

Variables	Number n (120)	Proportion (%)
Age (years)		
[15 - 20]	71	59.1
[21 - 30]	21	17.5
[31 - 35]	11	9.1
[36 - 40]	10	8.4
[>41]	7	5.9
Marital status		
Single	45	37.5
Married/Couple	75	62.5
Educational level		
None	12	10.0
Primary	18	15.0
Secondary	60	50.0
University	30	25.0
Economic situation		
<100,000 XAF	63	52.5
100,001 - 300,000 XAF	44	36.7
>300,000 XAF	13	10.8

Table 3. Distribution of very premature babies according to motor and praxis disorders.

Variables	Effectif	Proportion (%)
Minor IMOC (n = 65) (spastic diplegia type)		
Yes	15	23.8
No	50	76.2
Cerebral palsy (n = 65)		
Yes	2	3.1
No	63	96.9
Ideo-motor dyspraxia (n = 65)		
Yes	5	6.2
Non	60	93.8
Dressing dyspraxia (n = 65)		
Yes	4	6.8
No	61	93.2
Visual-constructive dyspraxia (n = 65)		
Yes	4	6.8
No	61	93.2

Table 4. Distribution of development quotients in the study population.

Development quotient	Number	Proportion (%)
>120 (high)	1	1.6
(85 - 119)	47	72.3
(70 - 84)	10	15.3
(50 - 69) (normal)	4	6.1
(35 - 49)	2	3.1
(20 - 34) (boderline)	0	0.0
<20 (severe)	1	1.6
Total	65	100

Table 5. Distribution of very premature babies by sensory outcome.

Variables	Number	Proportion (%)
Visual impairment (n = 65)		
Yes	6	9.0
Non	59	91.0
Hearing impairment (n = 65)		
Yes	4	6.3
Non	61	93.7
Swallowing disorder (n = 65)		
Yes	5	7.6
Non	60	92.4

3.5. Growth in Height and Weight

According to the nutritional assessment, among the 65 very premature babies, 5 (7.7%) had severe malnutrition, and 18 (27.7%) were wasting (Table 6).

Table 6. Distribution of the study population by BMI/age index.

Z-score (BMI/age)	Number	Proportion (%)
>2	2	3.1
[2; 1[	22	33.8
[1; 0]	12	18.5
]0; −1]	6	9.2
]−1; −2]	13	20.0
]−2; −3]	5	7.7
<−3	5	7.7
Total	65	100

3.6. Mortality Rate

Out of the 120 very premature babies included, 55 (45.8%) died during hospitalization.

4. Discussion

In our series, we noticed a clear male predominance with 76 very premature males (63.3%). These results are similar to those of Nguefack *et al.* (2020) in Cameroon [7]. Gestational age between [31 - 32 WGA] was more represented (42.5%), Linstrom *et al.* (2007) found 34% of premature babies between 29 - 32 WGA, 36% between 33 - 36 WGA, against 39% at term [8]. This difference could be explained by the fact that in this study the evaluation was made on late and moderate prematurity, contrary to ours, which was targeted at very premature babies. The current mean age of our study population was 35 months ± 15 with extremes of 6 and 73 months. Children aged [35 - 48] months were the most represented (46.2%). Differences are observed in the study conducted by Nguefack *et al.* (2020) who found a mean age of 25 ± 19.5 months and the most represented age group was children [12 - 23] months (34%) [7]. The age of the mothers in our study was between 15 and 20 years in 59.1% of cases and over 35 in 23.4% of cases. Half of the mothers had a relatively low economic and educational level; these results are similar to those found in a study conducted by Balaka *et al.* (2002) in Togo [9], with extreme ages at 32%, low socio-economic level at 51%, and low educational level at 39%. On the other hand, differences are observed in the study by Ancel *et al.* (2015) in France [10], which found extreme ages at 16%; low socio-economic level at 43%; and low level of education at 6%. This difference could be explained by the socio-economic frontier between Western countries and countries with limited resources such as Togo and Cameroon. The DGOPH is a hospital located at the top of the health pyramid in

Cameroon. It acts as a hospital of last reference for unstable sick newborns and therefore for very premature babies. However, many bottlenecks persist in the management of very premature babies in our hospitals. Concerning the technical platform: non-invasive ventilation, classic or high-frequency mechanical ventilation, administration of surfactant, and parenteral nutrition, all this is not available in this department. However, these are strong levers in the care of very premature babies. Furthermore, the transfer of newborns is not organized. There has indeed been a perinatal network in the city of Douala since 2016 which links child health professionals to facilitate the care and transfer of newborns. However, after 5 years, it is clear that this network is still poorly used. The consequences are transfers in totally inappropriate conditions in non-medicalised vehicles that do not comply with any standards for neonatal transport [11].

We found that 50 (76.2%) were free of cerebral palsy and 15 (23.8%) had spastic cerebral palsy. This result is lower than that of Arnaud C. *and al* in 2008 [12] who showed that very premature babies have a 41.4% chance of developing cerebral palsy and that the number of children with cerebral palsy with two affected subsystems decreases with increasing gestational age. The Epipage study in 2008 found a prevalence of cerebral palsy of 9% (95% CI 7 - 10) in 1812 formerly very premature children [13]. This difference could be explained by their larger sample size than ours. French cohorts have shown that the risk of cerebral palsy is around 6% - 8% for children born before 33 WGA and 1% for moderate preterm infants [14]. Deforge *et al.* (2009) found 6.6% of praxis disorders. It appears that children born at term have better results than very premature babies for all the tests (except for analogical reasoning and less than 28 WGA) [15]. Children born before 28 WGA performed worse on all tests than children between 28 and 32 WGA, implying that prematurity has a negative impact in the praxis domain, the more important it is.

Based on the Denver score, the most affected psychomotor development element in our series was language with 43% of language delays, followed by delays in social development at 27.7%, then delayed fine motor skills at 21.5%, and gross motor skills at 13.8%. These results are similar to those of Nguefack *et al.* (2020) [7] who also found a predominance of language disorders among the disorders, as well as Ballot *et al.* (2012) [16]. Despite different proportions, they also found that the most affected developmental element was language (9.4%), followed by cognition (8.5%) and motor skills (7.6%). On the other hand, Nepomnyaschy *et al.* in the United States in 2012 [17] found a preponderance of delayed social development, while Eickmann *et al.* (2012) in Brazil found motor skills to be the most affected component [18]. It is difficult to accurately assess the incidence of language impairment in preterm infants due to the conflicting results of different studies.

The majority, *i.e.* 72.3% of children had a normal developmental quotient, these results are similar to those of Nguefack and Ballot who found a normal DQ in the majority [7] [16]. The children in the EPIPAGE cohort, free of neurological or sensory deficiencies, had a higher proportion of intellectual deficiencies

(DQ below 70) in premature infants and this risk is 8% in children born at less than 33 years of age [12].

The visual disorders (blindness, strabismus, reduced visual acuity) found in our study are similar to the findings of Fierson (2018) [19]. Indeed, 40% to 50% of children born before 31 weeks of gestational age will present one of the stages of premature retinopathy, and 7% to 8% will acquire a severe visual impairment. The Epicure study by Blond *et al.* (2003) found that 2% of the premature babies in the cohort were blind or only perceived light [20]. The observed difference could be explained by the fact that our sample was not very representative and the unavailability of a rest camp in our hospital.

In our study 6 (3%) children had developed hearing problems (deafness). The work of Ancel *et al.* (2010) found cases of deafness between 0.4% and 3% of children born before 26 - 28 WGA [10]. This difference could be explained by the much larger cohort size and the methodological difference. Severe malnutrition was found to be 7.7% - these results are similar to those of Alain Ahishakiye *et al.* (2019) in Rwanda. With a sample almost similar to ours, they show that preterm and/or low body weight children were more likely to be developmentally delayed, and the main predictor of developmental delay was growth retardation [21]. The very premature baby should be able to benefit from essential investigations in the unit. The neonatology unit should therefore have a dedicated mobile X-ray and ultrasound machine, and systematic ophthalmological and auditory evaluation. These investigations can allow early detection and management of pathologies that often go unnoticed. This specific care context can lead to increased morbidity, consequent mortality, and more or less severe sequelae.

We found a mortality rate of 45.8% which, despite its increase, is decreasing according to the studies carried out by Njom lend *et al.* (2016) who found nearly 64% of deaths in very premature babies [22]. This indicates the gap that remains to be bridged in reducing mortality through good monitoring of pregnancies, improved neonatal transfers, technical facilities, and continuous capacity building.

5. Limits

The frequencies reported in our study are probably underestimated due to our small sample size, especially since we excluded several files from our study, because they were either not found or incomplete, in addition to the refusal of some parents to participate.

6. Conclusion

Very preterm birth is associated with a higher risk of neonatal death. Psychomotor sequelaes are significant. In our settlement, the key elements of the prevention are amelioration of antenatal care, promotion of deliveries of very premature babies in reference hospitals, and harmonization of protocols for the

management of very premature babies. This will therefore permit the early detection of most of the complications which will be adequately managed to improve the outcome.

Author Contributions

DNN, DCKK, and DE designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. VEP and DNN designed the data collection instruments and 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 agreed to be accountable for all aspects of the work.

Acknowledgements

The authors would like to thank the medical staff in the departments of paediatrics and neonatology, gynaecology and obstetrics, and the DGOPH archives who created an environment conducive to the realization of this study.

Conflicts of Interest

The authors declare that they have no competing interests.

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