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ORIGINAL REPORT

Epidemiology and Clinical outcome of Low Birth Weight infants followed up over a 12 month period at the "Mère-Enfant" University Hospital Centre (UHC) of Libreville.

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Abstract

Introduction: Low birth weight (LBW) is a key indicator of newborn health and a global public health concern. The objective of this study was to contribute to improving the care of LBW.

Subjects and methods: Cohort study conducted over a period of 18 months (January 2019 - July 2020) at the "Mère-Enfant" University Hospital Centre of Libreville. All newborns with a birth weight (BW) < 2500 g were included. Sociodemographic and clinical data of a mother-infant were studied.

Results: 1260/9035 births of LBW (14.0%) were observed, and 300 among them were included. The sex ratio was 1, with an average BW of 1908.6 ± 483.3 g, of which 79.3% accounted for low BW. The mean gestational age was 34 ± 12 with 75.3% due to prematurity. During the 1st year of life, the overall proportion of pathologies encountered decreased with age and respiratory pathology was the main one observed in general. Re-hospitalization was observed in 16.3% of cases and the main reason was malaria (59.2%). The overall mortality rate was 27.0% and the risk factors for death included ; extreme low BW (OR = 50.5 (95% CI [14.7; 173.4]; *p<0.001*)), extremely preterm (OR 46.5 (95% CI [13.2; 163.1]; *(p<0.001*)), resuscitation at birth (OR 9.9 (95% CI [5.1, 19.5]; *p<0.001*)), male gender (OR 1.8 (95% CI [1.1 to 3.0]; *p = 0.027*)). The predictor of death was perinatal asphyxia (OR 5.9 (95% CI,3.25, 10.5); *p<0.001*)).

Conclusion: LBW is a public health problem at the UHCME-JEF with harmful consequences. Many efforts remain to be done to reduce LBW levels and improve their survival.

Keywords: Low Birth Weight, Clinical outcome, "Mère-enfant" UHC, Libreville-Gabon.

Introduction

Low birth weight (LBW) is defined by the World Health Organization (WHO) as birth weight (BW) below 2500 g, regardless of gestational age[1] and generally applies only to live births[2]. This is not to be confused with intra-uterine growth retardation (IUGR) which is defined as a birth weight below the 10th percentile of the reference curves[3]. This weight limit has been used for nearly a century[4] and categorizes neonates into low birth weight (LBW) where the BW is 1500 g to <2500 g; very low birth weight (VLBW) with BW 1of 000 g to <1500 g and the extremely low birth weight (ELBW) defined by a BW <1000 g[5]. BW is an easily accessible measure, particularly in a low-resource milieu, it is a key indicator of newborn health and a major factor in neonatal morbidity and mortality[2,6]. LBW may be secondary to preterm delivery, intra-uterine growth retardation, or a combination of both conditions[3]. According to Barros et *al.*, each of these conditions contributes about half to the occurrence of LBW[7]. This is a global public health problem as UNICEF estimates that 16% of children are born with low birth weight globally[6]. This represented more than 20 million newborns worldwide in 2015, corresponding to one in seven newborns, with a large majority (90%) of these births taking place in developing countries, especially in South Asia and Africa[8]. This category of newborns is 20 times more likely to die than those with normal birth weight[4]. In addition, they also have a higher risk of morbidity, stunting during childhood, poor cognitive development, as well as the occurrence of chronic diseases such as cardiovascular disease and diabetes in adulthood[3,9,10]. Early detection and management would improve the prognosis of these newborns[11].

The absence of recent data in Gabon on this major public health problem, the vulnerability of these newborns, and the resulting morbidity-mortality, motivated the realization of this study whose purpose is to contribute to improving the care of LBW in our country.

Patients and methods

This is a longitudinal prospective study that took place over a period of 19 months (January 1st, 2019, to July 31st, 2020) in the neonatal medicine department (capacity for 1500 admissions on mean per year) of the University Hospital Centre "Mère-Enfant" - Jeanne Ebori Foundation (UHCME-JEF), a level 3 hospital, located in Libreville, the political capital of Gabon.

The study population included all newborns at the UHCME-JEF during the study period (January 1st, 2019, to July 31st, 2020). We have included all newborns with a BW <2500 g whose parents have consented. Those who have been lost to follow-up (all parents who no longer came for consultation or who no longer answered our calls) have not been retained.

Data collection

After birth and after obtaining informed consent from the parents, data of newborns of BW <2500 g were collected on a standardized data collection sheet. They were then followed up by pediatricians at a regular interval (1 month, 3 months, 6 months, 9 months, and 12 months) over a 1-year period.

We collected mothers' socio-demographic data, antenatal data (number of consultations, pathologies intercurrent with the pregnancy, etc.) and types of delivery (mode of delivery, gestation at delivery). These data were collected by interviewing mothers and reviewing mothers' obstetrical records. In newborns, we studied the clinical parameters (anthropological parameters, adaptation to birth), becoming immediately after birth (hospitalized or not). Also, during the 1st year of life, we collected data on mortality, the evolution of anthropological parameters, and acquired pathologies.

Statistical analysis

The data was recorded on Epi Info 7.2.2. We performed a descriptive analysis to determine sample characteristics and estimated the prevalence of LBW newborns. Quantitative data were expressed as average and standard deviation for gestational age, age of mothers, and anthropometric parameters of newborns. We calculated the median for the length of hospitalization and documented the age at death. We compared medians by the Mann-Whitney test. Qualitative data were expressed in frequency, to compare them we used the chi-square test. We created univariate logistic regression analyses (odd ratio) to measure the relationship between children's

and parents' parameters with low birth weight. The variables were chosen for their statistical significance in the descriptive and comparative results, but also following the relevance based on the literature. We then performed a multivariate analysis to determine the predictor of death.

The threshold of statistical significance was set at $\alpha < 0.05$ for a bilateral test. The confidence intervals of the odd ratios were calculated using the Miettinen method. The analysis was performed using CDC Epi Info 7.2.2 and the online statistical analysis software P-value (https://www.pvalue.io/fr/).

Results

Prevalence

During the study period (January 1st, 2019, to July 31st, 2020), 9035 births were recorded at the CHUMEFJE, among them, 1260 had LBW, corresponding to a prevalence of 14.0%. Among the 1260 LBW newborns, 250 were stillborn, 310 parents did not give their consent and 400 were lost during follow-up. We were able to include 300 infants delivered to 236 mothers in our study.

Characteristics of mothers

Table I shows the socio-demographic and obstetric characteristics of mothers of studied neonates. The age of mothers ranged from 15 to 45years with a mean of 27.7 (± 6.2) years. The median age was 28 years, with Q1 at 23 years and Q3 at 31years. The proportion of single mothers was 45.3%. In 63.5% of cases, the number of antenatal contacts was less than or equal to 4, and in 82.3% of cases, antenatal care was carried out by midwives. 51% of studied Mothers were poor and the main illnesses in pregnancy were malaria (18.0%), hypertension (16.7%), and vaginal infection (12.0%). In 79.0% of cases, childbirth was vaginal.

Table I: Socio-demographic and clinical characteristics of mothers

Maternal parameters	Number (n=236)	Percent (%)
Age (years)		
<20 years	26	11,0
20 - 35 years	178	75,4
>35 years	32	13,6
Lv of Ed		
Illiterate	4	1,7
Primary	21	8,9
Secondary	117	49,6
Academic	94	39,8
Profession		
In operation	74	31,4
Students	90	38,1
Without a profession	72	30,5
Marital status		
Bachelor	107	45,3
As a couple	129	54,7
Pregnancy followed (contacts)		
None	11	4,7
≤ 4 contacts	150	63,5
> 4 contacts	75	31,8
Parity		
Primiparous	77	32,6
Paucipare	122	51,7
Multiparous	37	15,7
Type of Pregnancy		
Unique	172	7 2.9
Twin	61	2 5.8
Multiple (>2)	3	1.3
Pathologies during Pregnancy		
No	103	4 3.6
Malaria	43	1 8.2
HBP	39	16.5
Vaginal infection	28	1 1.9
Urinary tract infection	23	9.7

*HBP = high blood pressure

General characteristics of newborns of LBW

Table II shows the characteristics of LBW neonates.

Extreme low birth weight babies (< 1000g) accounted for 5.3% of the cohort. The mean gestational age (GA) was 34 ± 12 weeks, with a range from 23 to 41 weeks. The median GA was 34 weeks with a Q1 of 32 weeks and a Q3 of 36 weeks. In 75.3% of cases (n = 226), newborns were premature. The mean birth weight was 1908.6 g ± 483.3 g with a range of 630 g to 2480 g. The median was 2060 g with a Q1 of 1580 g and Q3 of 2300 g. Low birth weight (1500- < 2500g) newborns constituted 79.3% of the cases. The mean cranial perimeter (CP) was 29.9 cm ± 2.6 cm and ranged from 20 to 35 cm. The median of CP was 30 cm with a Q1 at 29 cm and Q3 at 32 cm. The mean length was 44.2 cm ± 4.5 cm, with extremes ranging from 26 to 58 cm. The median was 45 cm with a Q1 at 42 cm and a Q3 at 47 cm. The sex ratio was 1. IUGR (BW< 10th percentile according to GA) was observed in 12.0% of the cases (n=36). Of these, 27 (75.0%) had asymmetric IUGR and 9 (25.0%) had symmetric IUGR. Large gestational age (> 90th percentile BW GA) was observed in 2.7% of the cases (n=8). Resuscitation at birth was performed in 13.0% of cases (n=39). On the first day of life, breast milk was the exclusive feed in 5.3% of all newborns. Hospitalization immediately after birth was observed in 48.7% (n=146). In 26.7% of cases, the reason for hospitalization was a neonatal infection (Figure 1). The average length of hospitalization was 9.6 days ± 8.2 days, with extremes ranging from 2 to 60 days. The median was 7 days with a Q1 at 4 days and Q3 at 15 days.

Table II: Characteristics of LBW Newborns

Parameters	Actual (n=300)	Percentage (%)
Gestational age (AS)		
< 28	15	5,0
28 ≤ AG < 33	61	20,3
33 ≤ AG < 37	150	50,0
AG ≥ 37	74	24,7
Mode of delivery		
low channel	186	78,8
Cesarean section	50	21,2
Sex		
Masculine	150	50,0
Feminine	150	50,0
Birth weight (g)		
< 1000	16	05,3
1000 ≤ p < 1500	46	15,4
1500 ≤ P < 2500	238	79,3
Resuscitation at birth		
Yes	39	13,0
No	261	87,0
Hospitalization at birth		
Yes	146	48,7
No	154	51,3
Type of milk on Day_1 of life		
Breast milk	16	5,3
mixed	273	91.0
Artificial	11	3,7

Evolution of PPN newborns during the 1st year of life

❖ **Childhood pathologies presented during the first year of life**

The proportion of newborns followed up to the age of 12 months was 73% (n=219). Among them, 61.6% (n=135) had a childhood illness. Respiratory pathologies (nasopharyngitis, bronchopneumonia, etc.) were more prevalent in all age groups except at the age of 3 months where the proportion of digestive pathologies (constipation, gastroenteritis, dietary error, regurgitation, and misdirection) was higher (20.5%). The overall proportion of pathologies encountered during growth decreased with age. At 1 year old, 76.2% of infants presented no pathology (Table III).

Table III: Distribution according to the pathologies encountered during the first year of life

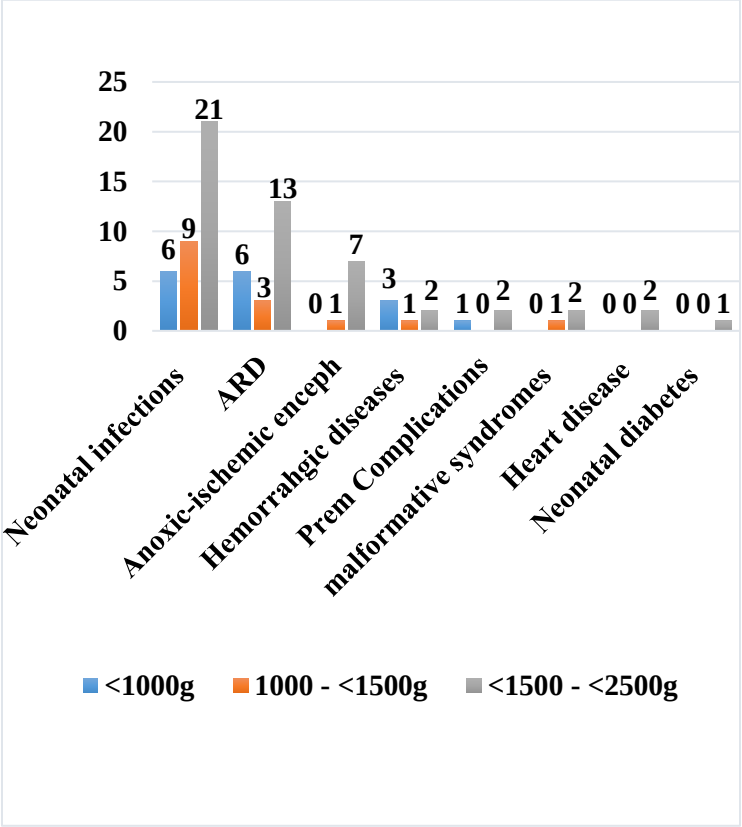
PTH	1M		3M		6M		9M		12M	
	n	%	n	%	n	%	n	%	n	%
SKN	04	1,8	03	1,4	02	0,9	02	0,9	07	4,5
DGT	38	17,3	45	20,5	15	6,8	19	8,7	09	4,2
MAL	01	0,5	05	2,3	09	4,2	06	2,7	14	6,4
RSP	82	37,4	30	13,7	28	12,8	25	11,5	19	8,7
NO	94	43	136	62,1	165	75,3	167	76,2	170	76,2

❖ **Re-hospitalization during the first year of life**

During the first year of life, 49/146 (33.6%) infants were re-hospitalized. Of these 49 infants, 8 had a second admission (readmission) still in the neonatal period. Malaria was the reason for re-hospitalization in 59.2% (n=29) of the cases, followed by pathologies of the digestive system (26.5%, n=13), haematological conditions (10.2%, n=5) and bronchopneumonia (4.1%, n=2).

❖ **Mortality rate**

The overall mortality rate was 27.0% (n=81). Among them, 61 (75.3%) died during the neonatal period (49 during the first hospitalization (hospitalization just after birth and 8 at home), and 20 (24.7%) outside the neonatal period. All deaths occurred during the first two months of life and 72.8% of the cases (n=59) occurred in the early neonatal period (≤ 7 days). The mean age of deceased newborns was 6.7 days ± 7.7 with extremes ranging from 1 to 60 days. The median was 4 days with a Q1 at 3 days and Q3 at 8 days. A 100% mortality was observed for newborns with a birth weight < 1000 g (n=16). Among them, 9 had died in hospital and 7 at home. Neonatal infections were the cause of death in 44.4% of cases (Figure 2).



***ARD** Acute Respiratory Distress

Figure 2: Cause of death of newborns from LBW

❖ **Risk factors for death of newborns from LBW**

The risk factors for death observed in our study were:

- Birth weight < 1000g (death n=19, survival n=0): OR 50.5 (95% CI [14.7 to 173.4], p<0.001),
- GA< 28 AS (death n=15, survival n=0): OR 46.5 (95% CI [13.2 to 163.1], p<0.001)

- Reanimation at birth (death n=28, survival n=11): OR 9.9 (95% CI [5.1 to 19.5], $p<0.001$)
- Maternal level of education (illiterate) (death n=4, survival n=0): OR 8.5 (95% CI [1.3 to 57.6], $p=0.027$)
- Perinatal asphyxia (death n=32, survival n=22): OR 5.9(95% CI [3.3 to 10.5], $p<0.001$)
- Male (death n=49, survival n=101): OR 1.79 (95% CI [1.1 to 3.0], $p=0.027$)

After logistic regression, perinatal asphyxia was the predictor of death with an OR of 1.27 and a *p<0.01* (Table IV).

Table IV: Multivariate Analysis of Predictors of Death

Parameters		**Odds-Ratio**	***P***
Gest.Age (classes)	33 - 36 *vs* ≤33	0.263 [0.0741; 0.842]	0,03
	>36 *vs* ≤33	0.109 [0.0234; 0.466]	<0.01
Perinatal asphyxia		1.27 [1.06; 1.51]	<0.01
Weight		1.01 [1.00; 1.01]	<0.001
Resuscitation	yes *vs* no	0.216 [0.0591; 0.742]	0,017
Sex	male vs female	0.335 [0.143; 0.739]	<0.01

Discussion

Study limitation

The context of the COVID-19 pandemic as well as the health measures taken has created certain obstacles to the optimal conduct of this survey, in particular the unique nature, the lack of patient attendance during outpatient follow-up, and the low adherence of parents to the study. Nevertheless, the results obtained have made it possible to identify useful data, which can contribute to the improvement of the management of newborns of LBW in our health centers.

Frequency of LBW

The frequency of the LBW at the UHCME-JEF during the study period was 14.0%. This frequency is similar to that observed in Gabon globally in 2004 (14.0%)[12], close to that estimated in sub-Saharan Africa (13.0%)[10] and those reported by Faye in Dakar, Bwana Kangulu in Kamina, Tshinzobe in Kinshasa and Muchemi in Olkalouqui which are 14.8%, 14.3%, 13.3% and 12.3%[13,14,15,16] respectively. It is lower than those found by Alemu in Ethiopia (18.0%)[17] and Chiabi in Cameroon (20.7%)[18]. These different prevalences of LBW all remain high. This finding may be because the UHCME-JEF is a reference facility for the management of pathological pregnancies and sick newborns and on the other hand by the high rate of intercurrent pathologies in pregnancy (56.4%), dominated by infectious and vascular pathologies that are known as providers of LBW[10]. These intercurrent pathologies in pregnancy have also been reported in the studies of Faye and Chiabi[13,18]. Also, it is well established that it is in developing countries that the rate of LBW is most high[19] this is probably due to the high prevalence of prematurity and intercurrent pathology to pregnancy that they record.

Maternal characteristics

The proportion of mothers aged between 20 and 35 years was the most observed with a median of 28 years. This result is comparable to those found by Bwana Kangulu et *al.* in DRC[14], Demmouche et *al.*[20], Alemu et *al*[17]. in Ethiopia, and Kamala et *al*[21]. in Tanzania. This can be explained simply by the fact that this age group is the preferred period for procreation in women[22].

Only 34.3% have an income-generating activity. This result is similar to those of Alemu and Ranaivo which find 34.3 and 39.5% [17.23] respectively. In the study by Faye et *al.* in Senegal, a low socio-economic level was observed in 57.2% and 65.6% of the cases respectively[13]. In Kamala et *al.* in Tanzania, mothers living in semi-urban areas were 23.0% more likely to give birth to a newborn with LBW than those living in urban areas[21]. It is well established that socioeconomic status is a risk factor for preterm birth and therefore for LBW[24].

Characteristics of newborns of LBW

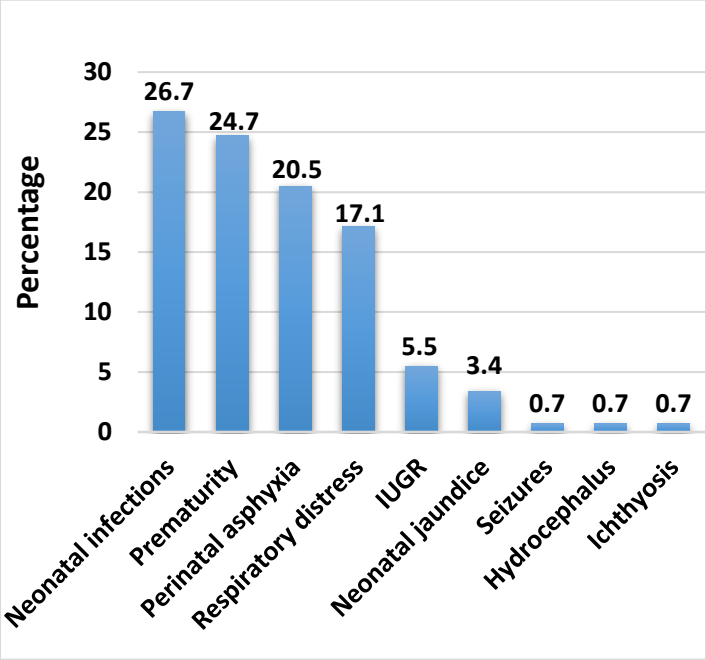
The sex ratio was 1. These results differ from those of Faye et *al.* in Senegal, Bwana Kangulu et *al.* in DRC, Chiabi et *al*. in Cameroon, and Hassoune et *al.* in Morocco, which find a female predominance[13,14,18,25]. Bandyopadhyay et *al.* in India find a male predominance

(54.2%) with no impact on the future of newborns of LBW [26]. The average GA was 34± 12 weeks in our study, with a proportion of preterm infants of 75.3% dominated by the mean prematurity (50%). These results are comparable to those forwarded by Faye, Chiabi and Bandyopadhyay who found a rate of preterm infants of 85.6%, 79.6% and 78.2% respectively with an average GA of 34 SA and a higher proportion of average prematurity[13,18,26]. This is not surprising because prematurity is one of the main causes of LBW[7,10]. This high rate of average prematurity also justifies the fact that the average birth weight in our study was 1908.6 g ± 483.3 g with a greater proportion of newborns with LBW (BW between 1500 and 2500 g). This observation is also made by Faye, Chiabi and Bandyopadhyay[13,18,26]. The proportion of IUGR was 12.0% in our study, which is different from those observed by Faye et *al.* in Senegal, Hassoune S et *al.* in Morocco, and Bandyopadhyay et *al.* in India which found respectively 53.0%, 71.1% and 21.8% [13,25,26]. This difference may be due to the nutritional status of mothers which is rather satisfactory in our context. Indeed, in developing countries, it is said that LBW is more often secondary to IUGR, due to malnutrition, while it is more frequently linked to prematurity in developed countries[7].

The outcome of the newborns of LBW

-Hospitalization of newborns with LBW at birth

The proportion of newborns with LBW hospitalized immediately after birth was 48.7%, with neonatal infection as the first reason for hospitalization followed by prematurity and asphyxiation. This observation is not surprising because these pathologies are the main providers of LBW. In Faye's study, nearly 40% of patients had poor adaptation at birth and in hospital, the main pathologies observed were neonatal infection (54.1%), respiratory distress (41.8%), and jaundice (35.7%)[13].



***IUGR= Intrauterine growth restriction

Figure 1: Reason for hospitalization of LBW newborns at birth

Childhood pathologies presented during the 1styear of life and hospitalization

Respiratory pathologies had a higher proportion than other pathologies during the one-year period, regardless of the age group except at the age of 3 months, when the proportion of digestive system pathologies was dominant. In a study on the determining factors of the hospitalization of children under 3 months at the Angondjé University Hospital in Gabon in 2018, it was observed that 24.0% of patients were hypotrophic newborns (weight < 2500g), that respiratory, infectious and digestive pathologies constituted the 3 main diagnoses observed [27]. Although the fact that there are still many unknowns about the consequences of low birth weight, it is well established that this segment of the population has susceptibility to being more affected by childhood pathologies, especially those of the respiratory system and even during adulthood[3,28].

These pathologies observed during the first year of life led to re-hospitalization in 16.3% of cases. Malaria was the 1st reason for re-hospitalization, followed by digestive pathologies and hematological pathologies. Kardum et *al.* report a re-hospitalization rate of 4.0% with the main

causes being respiratory tract infections (29.5%), jaundice (13.7%), and urinary tract infections (9.5%)[29]. In the studies by Kuissi Kamgaing and Quaresma, low birth weight was a factor in re-hospitalization[27,30], and Kuint et *al.* note that in children with VLBW, the number of morbidities and their severity are associated with excessive risks of re-hospitalization during childhood and adolescence[31].

- **Mortality rate and a risk factor for mortality of newborns of LBW**

Our mortality rate is close to that observed by the Directorate of Statistics at the national level (24.0%)[32] and that observed by Bandyopadhyay et *al.* in India (23.5%) with sepsis, respiratory distress syndrome, and asphyxia at birth as the main causes of morbidity and mortality[26]. It is well established that these different pathologies are strongly linked to neonatal mortality. Our mortality rate is slightly lower than that found by Chiabi et *al.* in Cameroon, Ouédraogo and *al.* in Burkina Faso, who observe mortality of 37.7% and 30.6% respectively[18.33]. In our study, we observed a mortality of 100% for newborns under 1000g. This rate may be biased by the high number of patients not included. However, other authors have made the same observation about the very high mortality rate of newborns from ELBW23,[34,35,36]. This high mortality rate of newborns of LBW is well known and described in the literature [5,12] and can be explained by the functional immaturity of the organs, the immune system and the fragility of the mechanisms of control of homeostasis in this segment of the population. Especially when complications such as infection, respiratory distress, and asphyxiation are added. However, in our context, the lack of required materials (CPAP, etc.), the lack of control over the management of the risk of nosocomial infection and the lack of sufficient qualified staff in the delivery room and hospital wards contribute significantly to increasing this mortality. Nevertheless, it is said that BW is a major determinant of survival[5].

Conclusion

LBW is a major problem due to its high prevalence and mortality rate in our hospital. Neonatal infections, respiratory distress and the consequences of perinatal asphyxia were the main causes of death. PN < 1000g, GA < 28 WA, resuscitation at birth, educational level (illiterate) of the mother, perinatal asphyxia and male sex were the risk factors associated with death. Improving the technical platform with adequate equipment, a sufficient number of staff and a good infection control policy will improve the survival of low birth weight newborns in our hospital structure.

Contribution of the authors:

- KKE: initiated the study, wrote the manuscript
- MRS: to perform statistical analyzes
- MGEAM, LMA, MMNE and KMR, KL: collected the data
- BM, LBP: did the proofreading,
- AS: supervised all the work

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