Original Research Article

Risk factors for mortality of preterm infants in the neonatal medicine department of the 'Mère-Enfant' University Hospital Centre of Libreville

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ABSTRACT

Background: Reducing neonatal mortality of preterm infants is a public health priority in developing countries. The objective of this study was to study the risk factors for mortality of preterm infants in the neonatology department of UHCME-JEF.

Methods: A retrospective, analytical study was done over 36 months (January 2019-December 2021) in the neonatology department of UHCME-JEF. Maternal and newborn parameters were studied. All hospitalized preterm newborns were included.

Results: The prevalence of prematurity was 44.6%. The mortality rate was 18.7%. The mean age of mothers was 28.05±6.5 years. They were unemployed (69.4%) and single (73.6%). The three main causes of death were sepsis (41.7%), respiratory failure (26.0%), and anoxic-ischemic encephalopathy (15.3%). The risk factors associated with death were multiparity [p=0.001, OR=2.0, IC 95% (1.32-3.00)], pre-existing maternal diabetes [p=0.007, OR=2.4, IC 95% (1.31-4.52)], prenatal check-up not done [p=0, 024, OR=1.5 IC 95% (1.04-2.05)], GA<28SA [p<0.001, OR=1.8 IC 95% (1.24 -2.71)], Apgar <3 at the first [p=0.036, OR=1.8, IC 95% (1.21-2.76)] and fifth minute [p=0.010, OR=3.2, IC 95% (1.35-7.74)] resuscitation at birth [p=0.017, OR=1.5, IC 95% (1.04-2.05)], birth weight <1000 g (p=0.001, OR=2.8, IC 95% (1.92-4.23)], hypotonia [p=0.001, OR=1.6, IC 95% (1.23-2.32)], asphyxia [p=0.020, OR=1.7 CI 95% (1.09-2.55)], hypothermia [p<0.001, OR=2.1, CI 95% (1.56-2.86)], the presence of thrombocytopenia [p=0.001, OR=1.9, CI 95% (1.62-2.93)] and glycemic dysregulation [p=0.001, OR=2.8, CI 95% (2.09-3.73)].

Conclusions: The mortality of preterm newborns remains a major problem in our department. It is necessary to promote good surveillance of pregnancy, and correct care of premature infants in the delivery room and hospitalization.

Keywords: Prematurity, Mortality factors, UHCME-JEF, Libreville, Gabon

INTRODUCTION

Prematurity is defined as a birth occurring after 22 weeks of amenorrhea (WA) and before the 37th WA or before the 259th day of gestation.[1] According to the WHO, it affects 15 million births worldwide (i. e., one child out of 10) and in 90% of cases, these births occur in sub-Saharan Africa and South Asia.[1] The immaturity of vital functions in preterm new-borns makes them a very fragile population with multiple complications. This justifies the fact that

prematurity is the cause of approximately 1 million child deaths per year and is the leading cause of mortality in children under 5 years of age.[1]

In developing countries, an average of 12% of new-borns are premature compared to 9% in developed countries. Gabon is one of the ten countries with the highest preterm birth rate per 100 live births with a rate of 16.3%.[1] Prematurity is therefore the main reason for hospitalization in neonatology departments, the main cause of death, and the risk of lifelong sequelae.[2] The reduction of neonatal morbidity and mortality is a public health priority, particularly in developing countries. Achieving Sustainable development goal (SDG) 3 by 2030, which stipulates a reduction in neonatal mortality to no more than 12% live births, specifically depends on this.[3] For this, it is important to know contextually the factors associated with the morbidity and mortality of preterm new-borns. Hence our study aims to identify the factors finally to improve the survival rate of preterm new-borns at UHCME-JEF in particular and in Gabon in general.

METHODS

This was a monocentric, retrospective, descriptive and analytical study. It dealt with the analysis of the records of hospitalized premature new-borns. This study covered a period of 3 years from 01 January 2019 to 31 December 2021. It was conducted in the neonatal medicine department of UHCME-JEF. The study population was premature new-borns hospitalized at UHCME-JEF. All hospitalized preterm new-borns were included in this study, regardless of the cause of hospitalization. New-borns with incomplete medical records were not included. The data were collected from the hospitalization records on a standardized form. The parameters studied were maternal (age, socioeconomic and marital status, gyneco-obstetrical and medical history, data related to the follow-up of the pregnancy and delivery, as well as the cause of prematurity) and neonatal (Apgar score at birth, birth weight, sex, and evolution).

Statistically, data were collected on Excel 2016 and analyzed on SPSS 26.0. We performed a descriptive analysis to determine the characteristics of the sample and to estimate the prevalence of preterm new-borns. Quantitative data were given as mean and/or median. We also gave the minimum and maximum of the data series. Categorical variables were given as percentages, the percentages were given with a 95% confidence interval, to compare them we used the Chi-square test of independence. We created univariate analyses to measure the strength of the association between the selected sample variables with the risk of death occurrence. The association was assessed by calculating the odd ratio (OR). Confidence intervals for the OR were calculated using the Miettinen method. Variables were selected based on the statistical significance of univariate comparisons and relevance based on the literature. The threshold for significance was set at $p<0.05$ for a two-tailed test.

RESULTS

Frequency of prematurity at UHCME-JEF

During the study period, 2670 new-borns were hospitalized in the neonatal medicine department of UHCME-JEF; among them, 1191 were born prematurely, i.e. a frequency of 44.6%. In 10% of cases (n=119), new-borns came from outside of the University Hospital Centre 'Mère-Enfant'- Jeanne Ebori Foundation (CHUME FJE) outborn.

Socio-demographic characteristics of mothers

These new-borns were born to 1148 mothers. The average age of mothers was 28.05±6.5 years, with a minimum of 14 years, a maximum of 46 years, and a median of 28 years. The proportion of mothers aged 18-35 years was 79.3% (n=910) and 14.1% (n=162) over 35 years. They were unemployed in 69.4% (n=797) of cases and single in 73.6% (n=845) of cases.

Obstetrical and medical characteristics of mothers

Table 1 shows the obstetrical and medical characteristics of the mothers. In 96.3% (n=1106) of cases, the pregnancy was single, in 3.6% (n=41) of cases it was a twin and in 0.1% (n=1) of cases triple. The average number of prenatal contacts (PNC) made by the mothers was 3.32±1.7 with a minimum of 0 PNC, a maximum of 10, and a median of 3 PNC. In 4.2% (n=48) of cases, the pregnancy was not followed up and in 56.3% (n=646) of cases, the number ANC was less than 3. In 38.6% (n=443) of cases, the prenatal check-up was incomplete; it was not performed in 15.6% (n=179) of cases. Obstetrical ultrasound was not performed in 21.2% (n=243) of cases. Antenatal corticosteroid therapy was performed in 3.8% (n=44) of cases. The intercurrent pathologies observed during pregnancy were= hypertension (29.0%, n=333), PAD (26.9%, n=309) and infections (24.4%, n=280), malaria (10.1%, n=116) and diabetes (6.2%, n=71). The amniotic fluid was abnormal in (14.3%, n=164) of cases. The premature rupture of membranes (PMR) was observed in (18.5%, n=212) of cases. The time to rupture was greater than 12 h in (43.9%, n=93/212) of cases. The birth occurred at the University Hospital Centre UHCME-JEF in (90.0%, n=1033) of cases. Caesarean section was performed in (30.5%, n=350) of cases. The three main indications for caesarean section were severe preeclampsia and eclampsia (50.0%, n=175), acute fetal distress (14.9%, n=52), and the presence of dystocia (7.2%, n=25).

Causes of prematurity

Prematurity was spontaneous in 64.6% (n=742) of cases, the 3 main causes were maternal infection (43.0%, n=319), socio-economic (31.0%, n=230), and unknown cause (11.0%, n=82). It was induced in 35.4% (n=406) of cases with vascular (57.9%, n=235), adnexal (22.9%, n=93), and fetal (13.0%, n=53) as the main causes.

Characteristics of new-borns

The mean GA was 32.24±2.9 weeks (range 22-36 weeks, median 33 weeks). The mean weight was 1787±639 g (extremes 580-4050 g, median 1750 g). Low birth weight for GA was observed in 41.2% (n=491) of cases. The mean CP was 29±3.1 cm (extremes 20-34 cm, median 29 cm). The mean height was 42.7±4.9 cm (extremes 35-50 cm, median 43 cm). The sex ratio was 1.03.

Cause of hospitalization

The 3 main causes of hospitalization were spontaneous prematurity (35.7%), risk of infection (30.9%), and respiratory distress (9.5%).

Causes of death

The mortality rate in our study was 18.7% (n=223/1191). In 84.3% (n=188) of cases, death occurred between the 1st and 7th day of life. Of these, 66.8% (124/188) died before the 5th day of life. The causes of death are listed in Figure 2. When the cause of death was sepsis (n = 93/223), in 67.7% of cases it was a dry infection, and in 32.2% a primary infection. The main germs found were *Klebsiella pneumoniae* (11.3%), *Enterobacter cloacae* (11.9%), and Staphylococcus epidermidis (11.3%). In the group of neonates who died with anoxo-ischemic encephalopathy (n=34), 79.4% of cases were convulsions followed by grade 4 intraventricular hemorrhage (11.8%). Deaths due to respiratory failure (n=58/223) were a complication of perinatal asphyxia (41.4%), severe hyaline membrane disease (29.3%), apnea of prematurity (17.2%), and Mendelssohn syndrome (8.6%). Acute anemia (n=6) and DIC (n=4) were the pathologies observed when the cause of death was hematologic disorders (n=10/223). Among the metabolic disorders (n=6), severe hypoglycemia (n=2), hepatocellular insufficiency (n=2), and kernicterus (n=2) were noted.

Risk factors associated with mortality in preterm infants

Table 3 presents the risk factors associated with death. The risk factors associated with mortality in preterm infants are multiparity, maternal diabetes, prenatal check-up not done, gestational age between 22 and 27 SA, Apgar<3, resuscitation at birth, birth weight <1000 g, presence of hypotonia, asphyxia, and thrombocytopenia.

Table 1: Obstetrical and medical characteristics of mothers.

Variables	N=1148	Percentage	95% CI (%)
Gestité= average number 3,43±1.9 (extremes 1 to 14, median 3)			
Primigeste	177	15.4	13.2; 17.6
Paucigeste	573	49.9	46.8; 53.0
Multi-gesture	299	26.1	23.4; 28.8
Large multi-gesture	99	8.6	07.0; 10.2
Parity=mean 2.09±1.3 (extreme 0-9)			
Primipara	458	39.9	37.0; 42.9
Paucipara	541	47.1	44.0; 50.2
Multipara	131	11.4	09.5; 13.4
Large multipara	16	1.4	00.7; 02.1
Unspecified	2	0.2	00.0; 0.45
Hypertension			
Yes	87	7.6	06.1; 09.1
No	1061	92.4	90.8; 94.0
Diabetes			
Yes	43	3.7	02.6; 04.8
No	1105	96.3	95.1; 97.5
HIV			
Negative	1076	93.7	95.6; 97.8
Positive	71	6.2	04.8; 07.6
Not done	1	0.1	00.0; 00.3

Table 2: Characteristics of preterm new-borns.

Variables	Numbers (N=1191)	Percentages	95% CI
Gestational age (GA)			
22-27	92	7.7	6.2-9.2
28-31	315	26.5	23.8-29.2
32-<37	784	65.8	62.9-68.7
Sex			

Variables	Numbers (N=1191)	Percentages	95% CI
Male	606	50.9	47.8-54.0
Female	585	49.1	46.0-52.2
Birth weight (g)			
<1000	113	9.5	7.9-11.5
1001-1499	270	22.7	19.6-24.7
1500-2499	648	54.4	50.1-56.3
>2500-<4000	143	12.0	10.3-14.1
>4000	17	1.4	0.7-2.1
Resuscitation in the birth room			
Yes	249	20.9	18.6-23.2
No	942	79.1	76.8-81.4

Table 3: Risk factors associated with mortality in preterm infants.

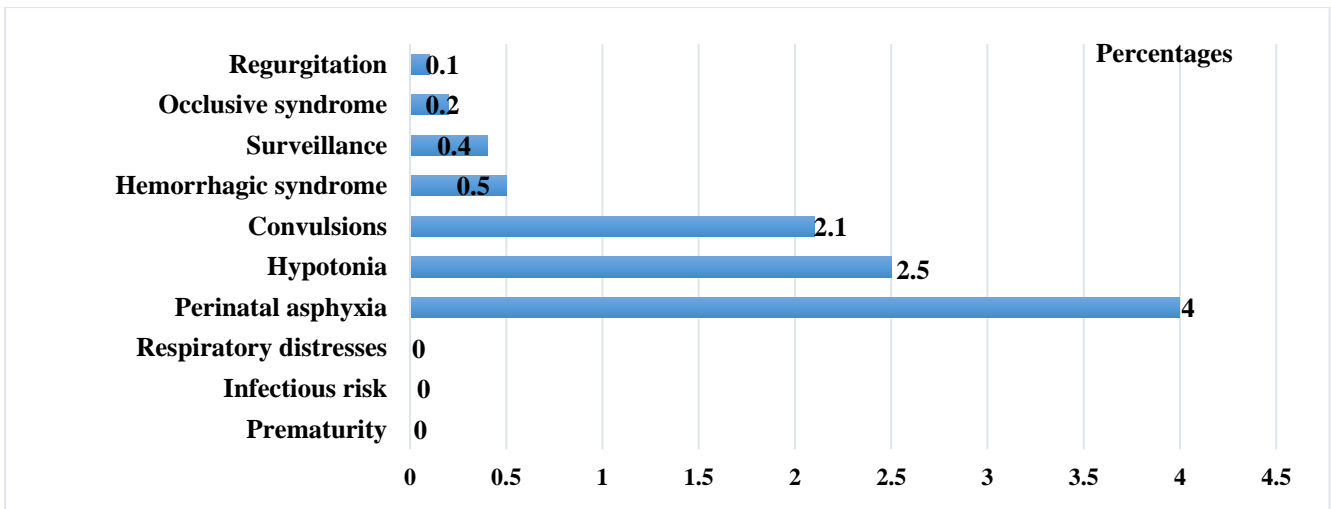| Variables	Becoming		OR	95 CI	P value
	Dead (%)	Alive (%)			
Parity					
Multipara	39 (29.5)	93 (70.5)	2.0	1.3-3.0	0.001
Others	184 (20.3)	875 (79.7)			
Diabetes					
Yes	15 (34.9)	28 (65.1)	2.4	1.3-4.5	0.007
No	208 (18.1)	940 (79.7)			
Prenatal check-up					
Not done	45 (27.0)	141 (73.0)	1.5	1.04-2.05	0.024
Others	178 (20.9)	827 (79.1)			
Gestational age (years)					
22-27	32 (36.0)	86 (64.0)	1.8	1.2-2.7	0.000
Others	191 (20.3)	882 (79.7)			
Apgar at 1 min					
≤3	33 (27.7)	86 (72.3)	1.8	1.2-2.7	0.036
Others	190 (17.7)	802 (82.3)			
Apgar à 5 min					
≤ 3	8 (42.1)	11 (57.9)	3.2	1.35-7.74	0.010
Others	215 (17.7)	957 (82.3)			
Reanimation					
Yes	62 (37.1)	202 (62.9)	1.5	1.04-2.05	0.017
No	161 (20.9)	766 (79.1)			
Birth weight					
≤1000	42 (36.6)	73 (63.4)	2.8	1.92-4.23	<0.001
Others	181 (16.8)	895 (83.2)			
Hypotonia					
Yes	45 (25.4)	132 (74.6)	1.6	1.2-2.3	0.001
No	178 (17.2)	836 (82.8)			
Asphyxia					
Yes	33 (26.6)	91 (69.4)	1.7	1.09-2.5	0.020
No	190 (20.8)	877 (79.2)			
Glycemic dysregulation					
Yes	116 (30.0)	271 (74.4)	2.8	2.09-3.73	0.001
No	107 (13.3)	697 (86.7)			
Hypothermia					
Yes	86 (27.9)	222 (72.1)	2.1	1.56-2.86	< 0.001
No	137 (15.5)	746 (84.5)			
Thrombocytopenia					
Yes	37 (28.9)	91 (71.1)	1.9	1.6-2.9	0.001
No	186 (17.5)	877 (82.55)			

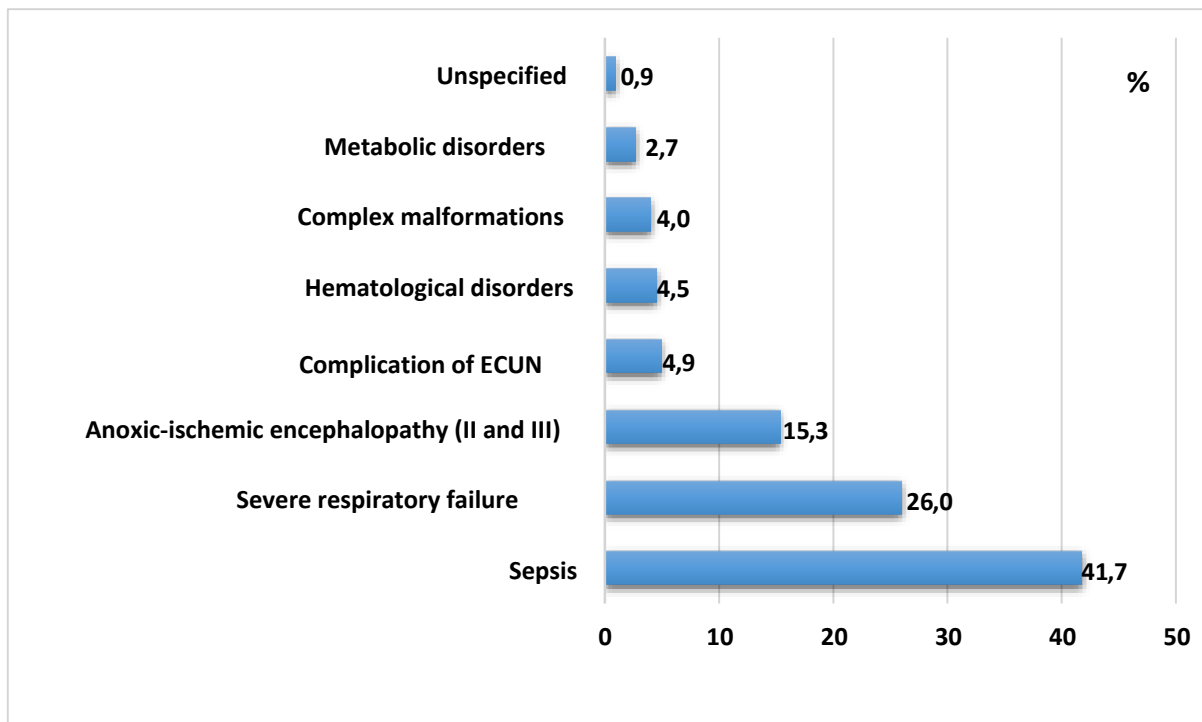**Figure 1: Cause of hospitalization of preterm new-borns.**

Figure 2: Cause of death.

DISCUSSION

Frequency of prematurity at CHUME-FJE

The prevalence of prematurity in the neonatal medicine department of the University Hospital Centre CHUME-FJE (44.6%) is close to those found by Nyenga et al at Sendwe Hospital in Lubumbashi, DRC (43.0%), Kuissi et al at Akanda UHC (44.8%) and Minko et al at Libreville UHC in Gabon (50.3%).[4-6] It is slightly lower than those found by Egesa et al in a community hospital in Uganda (57.0%) and Ouédraogo et al in Ouagadougou (60.8%).

And on the other hand higher than those found by Souam et al at the Mother and Child Hospital in N'Djaména (21.4%), Diouf et al the Albert Royer Children's Hospital in Dakar (16.5%), Chiabi et al.[9,10] 26.5% at the Gynaecology- Obstetrics and Paediatrics Hospital in Yaoundé, Hounkponou et al the Borgou Alibori University Hospital in Benin (17.89%) and Radhanpuri et al at the Dhiraj General Hospital in India (17%).[11-13] These very high hospital prevalence rates can be justified by the fact that most of these hospitals are reference centers for new-born care. In our context, UHCME-JEF is one of the reference structures for pathological pregnancies and new-

borns at risk in our country and has the largest neonatology capacity in the country (45 beds). This justifies the fact that 87.7% of our study population comes from our birth room. Also, the prevalence of prematurity is very high in developing countries. Indeed, approximately 85% of preterm births worldwide occur in Asia and Africa.[1,14] However, these hospital prevalence rates do not truly reflect the prevalence of preterm birth in the general population of our countries. Globally, the prevalence of preterm birth ranges from 5 to 18%.[1] The preterm birth rate at UHCME-JEF was 10.7% during our study period. This result better reflects the situation at the national level and agrees with WHO data on the average prevalence (12%) of prematurity in developing countries.[1,14] However, the high rate of preterm birth is not limited to developing countries, because if in the poorest countries there is an average of 12% of preterm births, we can also note the average of 9% observed in higher-income countries.[1,14] In general, the number of preterm births is increasing every year despite improvements in the management of pregnancies, due to the high number of induced preterm births, medically assisted reproduction (source of increased maternal age and multiple births), and precariousness.[1,14,15]

Mortality rate and causes of death

In our study, the mortality rate of preterm new-borns was 18.7% (n=223/1191). This rate is close to those observed in some East African countries where it ranged from 18.1% to 19.7%.[16] This mortality rate is lower than those found in some African cities, notably by Minko et al in Libreville (50.2%), Diouf et al (50.3%), Nyenga et al in Lubumbashi (44%), Souam et al (42.4%), Chiabi et al in Yaoundé (36.6%), Kuissi et al in Akanda (33.7%), Egesa et al in Uganda (31.6%), Ouedraogo et al in Ouagadougou (30.6%).[4-6,9-11] Aynalem et al (29.78%) in Addis Ababa.[17]

Similarly, our mortality rate is lower than those of some Asian cities such as India (33.5%).[18] On the other hand, the mortality rate at CHUME FJE is significantly higher than that observed by Olack et al in Kenya in a multicentre study in 2021 (5.1%).[19] The majority of deaths occurred between the 1st and 7th day of life in our work. In the study by Chiabi. The three main causes of death of preterm neonates at FJE UHC were sepsis, severe respiratory failure, and anoxic-ischemic encephalopathy. These causes are the most cited in different proportions in most studies in developing countries in Africa and Asia, whereas in developed countries, prematurity and congenital malformations are the most observed causes of neonatal death.[10,11,17-20] These different neonatal mortality rates in Africa and Asia, although disparate, remain very high in these 2 continents. Indeed, WHO estimates that 2.5 million new-borns died in the first month of life, or about 7,000 every day, accounting for 47% of all under-five deaths in 2018.

Of these, approximately 1 million die within the first 4 weeks of life due to complications of prematurity. Thus, prematurity has risen from the 2nd to the 1st cause of mortality in the neonatal period (with a proportion of 35% followed by infection (27%) and asphyxia (23%) and in children under 5 years of age.[4,14,22] According to Lawn et al, in general, this neonatal mortality follows the 'two-thirds rule' two-thirds of infant deaths occur during the first month; among these deaths, more than two-thirds occur during the first week; among the latter, two-thirds occur during the first 24 hours after birth.[22] This high neonatal mortality related to prematurity is not only observed in Africa.

In developed countries, prematurity is the main factor of infant mortality.[15] According to WHO, these three conditions frequently mentioned as causes of neonatal mortality (respiratory distress, infections, and asphyxia) are fortunately preventable with simple but effective, low-cost interventions, even without resorting to intensive care with emphasis on prevention, training of health care personnel and accessibility to care.[1,4,23]

Factors associated with death in preterm new-borns

Risk factors associated with mortality in preterm new-borns in our study are parity, diabetes, prenatal assessment, and gestational age, Apgar at the first and fifth minute, resuscitation at birth, birth weight, hypotonia, asphyxia, hypothermia, glycemic dysregulation, and thrombocytopenia. In the study by Aynalem et al in Ethiopia, the factors found were maternal diabetes mellitus (OR= 2.29 (95% CI=1.43, 3.65), neonatal sepsis (OR= 1.62 (95% CI=1.11, 2.37), respiratory distress (OR= 1.54 (95% CI=1.03, 2.31), extreme prematurity (OR= 2.87 (95% CI=1.61, 5.11) and low Apgar score (AHR= 3.11 (95% CI=1.79, 5.05).[17] For Ouédraogo Yugbaré et al in Burkina Faso, Apgar score lower than 7 at one min, vaginal delivery, low birth weight, singleton pregnancy, length of hospitalization less than or equal to seven days, and the Saint-Camille health facility were the risk factors significantly associated with mortality.[8]

In the East African meta-analysis, respiratory distress syndrome (OR=3.2; 95% CI=22, 4.6) and birth asphyxia (OR=2.6; 95% CI= 1.9, 3.4) were the risk factors found.[16] In Uganda, mothers>35 years (OR=4.5; 95% CI=1.35-15.31), lack of pregnancy follow-up (OR=4.7; 95% CI=1.05-21.21), preterm 'out-born' (OR=2.3; 95% CI=1.20-4.50), single-fetal pregnancy (OR=3.7; 95% CI=1.74-7.89), extremely preterm new-borns (OR=12; 95% CI=2.24-64.27), male neonates (OR=2.0; 95% CI=1.04-3.74), resuscitated at birth (OR=3.4; 95% CI=1.66-6.82), presence of respiratory distress syndrome (OR=2.6; 95% CI=1.22-5.70, apnea (OR=6.2; 95% CI=1.09-35.38), or hypothermia (OR=2.3; 95% CI=1.09-4.92) at admission were at greater risk of death.[7] The risk factors associated with the mortality of preterm new-borns are numerous and those found in our study are the most frequently observed in most studies. This high number of risk factors can be explained by the physiological fragility that characterizes this class of the population. Souam et al demonstrated in their study that the good prognostic

factors are gestational age close to term (p=0.000), normal Apgar score (p=0.002), delivery by cesarean section (p=0.000), birth at the referral hospital (p=0.004), early admission (p=0.039) and absence of respiratory distress (p=0.000).[9]

In consideration of these data, we can say that reducing the mortality of preterm new-borns is ultimately related to the prevention of preterm births, which is linked to a rigorous screening of pregnant women for the risk of preterm delivery. Chiabi et al show in their study that attending prenatal consultations reduces the possibility of preterm delivery (OR 6.19; 95% CI=1.15 to 33.22, p=0.033).[11]

CONCLUSION

Prematurity remains one of the main causes of hospitalization and mortality in the neonatal medicine department at FJE UHC with a prevalence of 44.6% in hospitals and a mortality rate of 18.7%. The risk factors associated with the mortality of preterm new-borns are multiparity, maternal diabetes,non-follow-upp of pregnancy, birth in apparent death, very premature birth, very low birth weight, glycemic dysregulation, hypotonia, hypothermia,a and thrombocytopenia. To effectively reduce the mortality rate in our hospital, we must act in the direction of prevention with good monitoring of the pregnancy and better management of the delivery. Then will come better care of premature new-borns in the delivery room, an effective strategy in the fight against secondary infections, and the availability of the necessary equipment for the management of respiratory distress of the new-born.

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