ORIGINAL ARTICLE

Burden, Predictors And Case Fatality of Neonatal Asphyxia Amongst Neonates At The Limbe Regional Hospital, A Low-Income Setting.

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ABSTRACT

Background: Neonatal asphyxia is a global problem which significantly contributes to both neonatal morbidity and mortality. According to the World Health Organisation,4 million neonates are affected by asphyxia annually. In Cameroon, particularly in the South-West region, useful information concerning this neonatal dilemma is limited. So, we decided to determine the prevalence of neonatal asphyxia, to identify the associated factors and hospital outcome of affected neonates at the Limbe Regional Hospital.

Methods: A 3-year retrospective analytic study from January 2017-December 2019 was carried out from February 2020 to April 2020 including files of term babies unable to breathe by its own effort with Apgar score of less than 7 at 5th mn.

Results: A total of 175 (27.7%) neonates were asphyxiated. We found that the following were independently associated with neonatal asphyxia, antepartum: < 3 obstetric ultrasounds (AOR = 1.92 [1.09-3.38]), negative HIV status (AOR:0.2 [0.09-0.55]), intrapartum: augmented labour (AOR:2.88 [1.03-8.03]) and meconium-stained liquor (AOR: 4.13 [1.7-10.05]). Hospital mortality rate was 4.4% with a case fatality rate of 16% and a threefold chance of dying if the case of asphyxia was referred from another health institution.

Conclusion: The factors associated with neonatal asphyxia are preventable. Thus, efforts should be made to improve the quality of antenatal and intrapartum care services to reduce the burden of neonatal asphyxia.

Keywords: Neonatal Asphyxia, Associated factors, Outcome, Case fatality

INTRODUCTION

Neonatal asphyxia is the inability of a newborn to initiate and sustain adequate respiration after delivery [1]. According to the American College of Obstetricians and Gynaecologists, and the American Academy of Paediatrics, a neonate is labelled to be asphyxiated if umbilical cord arterial pH < 7; Apgar score of 0–3 for more than 5 min; neonatal neurological manifestations [2]. Asphyxia in high-income countries, where adequate obstetric care is available during the peripartum period, have incidences ranging from 4.3 to 8.5% of term live births [3]. This contrasts with an incidence of around 23% in developing countries [4]. In Cameroon, the prevalence is increasing from 1.86% in 2005, 8.5 % in 2009/2013 and 8.69% in 2015 [5–8].

Factors associated with neonatal asphyxia are grouped according to antepartum, intrapartum and neonatal risk factors [9]. Studies revealed that extreme maternal age, lack of attendance of antenatal care, maternal malaria during pregnancy, antepartum haemorrhage,preeclampsia/eclampsia, multiple births, malpresentation, induction of labour using oxytocin, prolonged rupture of membranes, meconium-stained liquor, low birth weight, instrumental delivery, caesarean section are associated with neonatal asphyxia [6,10–11].

The major consequence of neonatal asphyxia is hypoxic-ischaemic encephalopathy (HIE). Diagnosis of HIE requires abnormal findings on neurological examination the day after birth. The clinical spectrum of HIE is described as mild, moderate, or severe according to the Sarnat stages of HIE. [12]. This will lead to detrimental long-term consequences for both child and family. Cognitive and behavioural difficulties are also proven consequences of neonatal asphyxia. This may lead to memory and attention deficit hyperactivity disorder, autism, and schizophrenia [13]., Neonatal asphyxia has significantly contributed to neonatal morbidity and mortality. About one-quarter of all neonatal deaths are caused by neonatal asphyxia worldwide [1]. In the world, 45% of under-five deaths occur during the neonatal period [14]. In developing countries, neonatal death accounted for 52% of under-five deaths [15]. In 2018, the report of the WHO indicated that Sub-Saharan Africa has the highest neonatal mortality rate at 28 deaths per 1000 followed by Central and Southern Asia with 25 deaths per 1000. Thus, a child born in sub-Saharan Africa is 10 times more likely to die in the first month than a child born in a high-income country [16].

The sustainable development goals (SDGs) target an under-five mortality rate of not more than 25 per 1000 live births in every country of the world by 2030 [17]. The lack of knowledge on the causes and consequences of neonatal asphyxia motivated us to scientifically demonstrate the burden. Thus, revealing the prevalence, factors associated, and consequences of neonatal asphyxia is important for creating awareness on the current burden of neonatal asphyxia to tailor control interventions to curb this burden by preventing the disease in the risk group.

MATERIALS AND METHODS

This was a retrospective study at the neonatology unit of Limbe Regional Hospital from February 2020 to April 2020. Ethical Approval was obtained from the Regional Delegate of Public Health and from the hospital authorities. This was to have access to the service, neonatology registers, and the files. Our study population was all term neonates admitted in the neonatology unit of the LRH from 1st January 2017 to 31st December 2019, precisely complete files of term babies unable to breathe after birth by their own effort with Apgar res at 5th min less than 7. We excluded neonates with the presence of major congenital malformations and premature babies because these defects will depress the Apgar score. Patients that met the inclusion criteria were considered eligible for the study. Data was entered into a data extraction form that was used to obtain information on socio-demographic, antenatal history, labour history, and post-natal history. The data extraction form comprised of 06 portions. The 1st portion was identification, 2nd portion sociodemographic data of mothers and neonates, 3rd one antepartum factors, 4th intrapartum elements, 5th neonatal characteristics and the last one hospital outcome. The Independent variables were maternal sociodemographic variables: maternal age, marital status, occupation, religion. Maternal antepartum factors: current pregnancy status, gravida status, place of ANC and gestational age at which antenatal visits started, diseases during pregnancy, number of ultrasounds, HIV status, past medical history. Maternal intrapartum factors: mode of delivery, intrapartum events, type and duration of labour, presentation, colour of the amniotic fluid. Foetal factors: gestational age, sex, quantity of amniotic fluid, birth weight, Apgar score. Hospital outcome: was either death or survival, with or without neurological deficit. All patient information obtained was coded and kept confidential.

DATA MANAGEMENT AND ANALYSIS

Data collected was saved in Laptops and, USB keys for easy retrieval. All data was entered and univariate, bivariate, and multivariate analysis were performed through SPSS version 25.0.

To achieve the very 1st objective, prevalence of neonatal asphyxia was calculated as follows: Number of neonates with neonatal asphyxia/ Total number of examined files all multiplied by 100. To identify the associated factors, factors of neonatal asphyxia were grouped into antepartum, intrapartum, and foetal or neonatal variables. Variables were presented using means, standard deviations, frequency, and percentage for categorical data. Chi square test and fisher's exact test were used where necessary to compare categorical variables. A logistic regression analysis was used to identify the relation of each independent variable to the outcome variable. Variables with p values less than 0.05 in the bivariate analysis were

considered for the multiple logistic regression analysis to control for confounders. Adjusted odds ratio (AOR) with a 95% confidence interval and p-value < 0.05 were used to identify independent variables associated with neonatal asphyxia. Hospital outcome was group into 3 categories: death, discharge with neurological sequelae, discharge without neurological sequelae within the period of hospital stay were recorded.

RESULTS.

A total of 1365 babies were admitted in the neonatology unit of LRH (from the neonatology registry), 1156 neonatal medical records were retrieved for which 524 were excluded for: Incomplete files=206(17.82%), Prematurity=176(15.22%), Congenital malformations=21(1.81%), >7 days of life=121(10.46%). Hence, 632 participants were retained in the study. The number of neonates with a diagnosis of neonatal asphyxia immediately after delivery was 175 giving a prevalence of neonatal asphyxia of 27.7% with an increasing trend in the prevalence of neonatal asphyxia at the LRH from 2017 **(Figure 1)**.

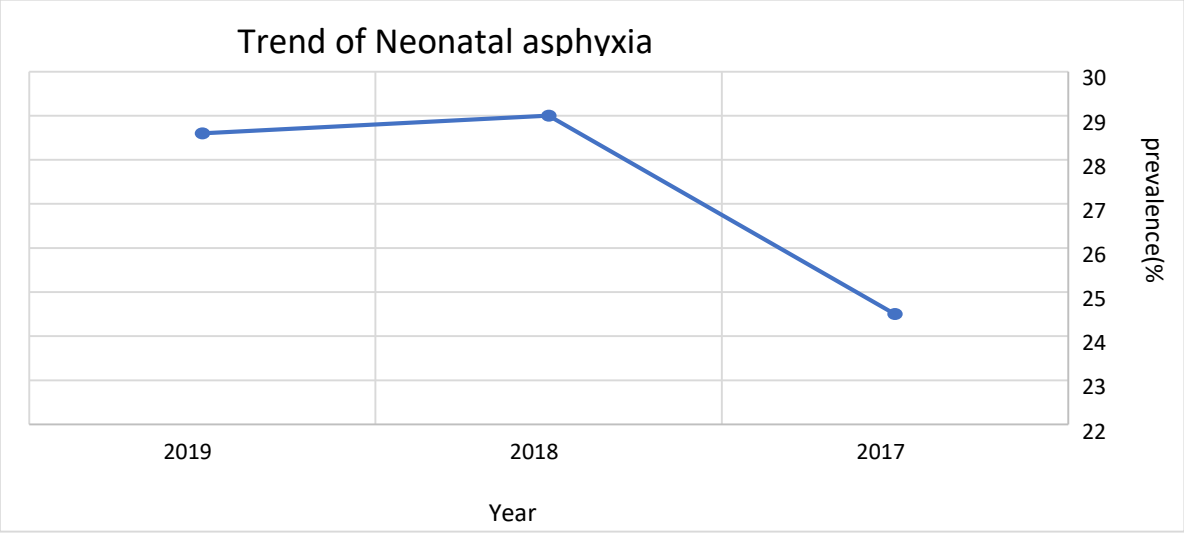

Figure 1 : Trend of Neonatal Asphyxia

On bivariate analysis, attending ANC in district hospitals (OR=2, p< 0.001), starting ANC in the second trimester of pregnancy (OR=1.61, p=0.015), doing less than 3 obstetrical ultrasounds (OR=2.28, p < 0.01) were all predisposing factors of asphyxia**.** Maternal pathologies associated with neonatal asphyxia were mothers with an unknown HIV status (OR=7.67, p<0.01) and a positive HIV status (OR=2.54, p=0.015). Also, a negative HIV status was found to be a protective factor (OR=0.18, p<0.01)**.** Regarding intrapartum variables, the following were significantly associated with neonatal asphyxia: augmented labour (OR=2.7, p=0.023), prolonged labour

(OR=3.74, p<0.001). Neonates born in health centres (OR=4.23, p<0.001) were significantly associated with neonatal asphyxia and giving birth at the regional hospital was a protective factor (OR=0.49, p<0.001). For the intrapartum events, meconium-stained amniotic fluid (OR=7.64, p<0.001) was significantly associated with neonatal asphyxia, and mothers with no intrapartum events (OR=0.52, p=0.002) and with a clear liquor (OR=0.24, p<0.001) were protective factors against neonatal asphyxia. For the associations between neonatal characteristics and neonatal asphyxia, a normal quantity of amniotic fluid was a protective factor against neonatal asphyxia (OR = 0.14, p<0.001). In multivariate analysis, doing less than 3 obstetrical ultrasounds (AOR = 1.92,95%CI:1.09-3.3), augmented labour (AOR = 2.88,95%CI:1.01-13.98), and meconium-stained amniotic fluid (AOR = 4.13,95%CI:1.54-14.05) were independently associated with neonatal asphyxia. Negative HIV status (AOR:0.23,95% CI:0.09-0.55) were independent protective factors against neonatal asphyxia **(Table 1).**

Table 1: Independent factors associated with neonatal asphyxia (multivariate)

Variables	Asphyxia		Adjusted OR (95%)	p-value
	YES (%)	NO (%)		
Number of US done				
< 3	150 (31.2)	331 (68.8)	1.92(1.09-3.30)	0.023
≥3	25 (16.5)	126 (83.5)	1.00	
Total	175 (100)	457 (100)		
HIV status				
Negative	132(23.4)	431(76.6)	0.23 (0.09-0.55)	0.001
Positive	13 (48.1)	14 (51.1)		
Unknown	30 (71.4)	12 (28.6)		
Total	175 (100)	457 (100)		
Type of labour Augmented	10 (50.0)	10(50.0)	2.88 (1.01- 13.98)	0.042
Spontaneous	119 (25.8)	343 (74.2)		
Induction	12 (22.6)	41 (77.4)		
No labour	34 (35.1)	63 (64.9)		
Total	175 (100)	457 (100)		
Colour of amniotic fluid				
Meconium	37 (68.5)	17 (31.5)	4.13 (1.54-14.05)	0.02
Clear	78 (18.3)	349 (81.7)	0.41(0.21-0.99)	0.09
Yellowish	3 (37.5)	5 (62.5)	-	
Reddish	2 (50)	2 (50)	-	
Brownish	4 (57.1)	3 (42.9)	-	
Unknown	26 (27.7)	68 (72.3)	-	
Total	150 (100)	444 (100)		

p < 0.05: threshold of significance, Chi-square test applied, OR: Odds Ratios, CI: Confidence Interval, US ultrasound

The overall neonatal mortality from neonatal asphyxia over the study period was 4.4%. Amongst the 175 cases of asphyxia observed in our study, 75 (42.9%) developed HIE of which 54 (72%) were grade III **(Table 2).**

Table 2 :Distribution of asphyxiated neonates according to outcome

Outcome	Frequency No (%)
STATUS	
Death	28 (16.0)
Survived	136 (77.7)
DAMA*	11(6.3)
Total	175 (100)
HIE	
Yes	75 (42.9)
No	100 (57.1)
Total	175 (100)
SARNAT CLASSIFICATION	
Grade I	2 (2.7)
Grade II	19 (25.3)
Grade III	54 (72.0)
Total	75 (100)

*DAMA: Discharged Against Medical Advice

Mortality was significantly associated with referral cases (p=0.010). **(Table 3).**

Table 3: Association between the mode of admission of asphyxiated neonates and the different outcomes

Outcome	Mode of Admission		p value	OR	95% CI
	Referral (outborn)	Inborn			
Death(n=28)	20 (71.4%)	8 (28.6%)	0.010*	3.06	1.27 - 7.41
Survived(n=136)	55 (40.4%)	81 (59.6%)	<0.001*	0.17	0.07 -0.41
DAMA(n=11)	11 (100.0%)	0 (0.0%)	<0.001*	2.18	1.85 -2.58

p<0.05: threshold of significance, Chi square test , OR: Odds Ratios, CI : Confidence Interval, DAMA: Discharged Against Medical advice ,LRH: Limbe Regional Hospital

DISCUSSION

This study attempted to determine the prevalence, to identify associated factors, and evaluate the hospital outcome of babies with neonatal asphyxia at the LRH to propose early interventions and contribute to existing knowledge which will go a long way to reduce the burden, morbidity, and mortality. Our prevalence of 27.7% was higher than that reported in Cameroon in 2013 and 2015 (8.5% and 8.6% respectively) [6,7], in Gusau in Nigeria in 2018 (21.1%) [18], in Ethiopia, Northeast Amhara in 2019 (22.6%) [19], and in Nepal in 2019 (3.7%) [20]. Our prevalence was also lower than that obtained in Ethiopia (56.9%) in 2017 [21]. This high rate could be explained by the fact that our hospital is one of the referral centres in the Southwest region where complicated cases are referred. On the other hand, the qualification of health personnel and the simple primary health care measures that have been put in place to reduce the burden of neonatal asphyxia in other study areas could be responsible for the differences in prevalence rate, with the prevalence of neonatal asphyxia increasing over the years in our study. This could be explained by the ongoing crisis which resulted in instability hence jeopardizing the quality of antenatal visits. This could have delayed detection and intervention in high-risk pregnancies [22].

There was a significant association between the number of ultrasounds done during pregnancy and neonatal asphyxia. Neonates from mothers who did less than 3 ultrasounds were 2 times more likely to be asphyxiated compared to those who did 3 and above (OR=1.92, 95%CI: 1.09-3.30, p=0.001). A similar finding was reported by Foumane and collaborators in their study in Cameroon who demonstrated the association between neonatal asphyxia and the absence of obstetrical ultrasound [23,24]. This finding can be explained by the fact that screening mothers during pregnancy help to identify high-risk pregnancy or fetuses at risk leading to appropriate and timely action. Ultrasound imaging plays a role in the assessment of fetal growth and wellbeing thus doing at least 3 ultrasounds as recommended has the potential to improve outcome in pregnancy and to afford earlier recognition of pregnancy complications [24]. Babies born from HIV negative mothers were less likely to develop neonatal asphyxia. This finding agreed with the result from a study done in 2010 which found a significant increase of neonatal asphyxia in babies born to HIV infected mothers [25]. The association can be explained by the fact that symptomatic HIV mothers can have opportunistic diseases that may decrease oxygen supply to the foetus. Augmentation of labour was associated with an elevated risk of asphyxia (AOR:2.7, p=0.023). In line with our study, Yadav et al in India had a similar finding [26]. Furthermore, a study done in Scandinavia by Oscarsson et al. found a significant association between oxytocin use and Apgar score < 7 at 5 min [27]. This can be explained by the inappropriate use of oxytocin for augmentation which will lead to hyperstimulation of the uterus. The latter alters the placental blood flow to the fetus and then leads to hypoxia and eventually perinatal asphyxia. Meconium-stained

amniotic fluid was significantly associated with neonatal asphyxia. This finding was in line with other studies done in Ethiopia [10,14]. This is explained by the fact that a foetus under stress passes out meconium in utero. If stress persists, he may eventually aspirate meconium-stained liquor into the lungs, further compromising foetal status [28].The overall neonatal mortality from neonatal asphyxia was 4.4%. It is possible that more asphyxiated babies died at home or were dead on arrival at the LRH but there was no data relating to that information. In Cameroon, Chiabi et al. in 2013 (6.7%), Tchouankeu in 2015(14%), and Douanla et al. in 2018 (21.3%) found a higher rate [6 - 8]. In Nigeria, Ugwu et al had a mortality rate of 27.3% [29]. These results could reflect the quality of care given to our study population. 74 (42.9%) asphyxiated neonates developed hypoxic ischemic encephalopathy. Majority of them were in Sarnat grade III. However, this rate is lower than that observed by Chiabi et al in Cameroon and the features recorded in Nepal [6,20]. These results could be attributed to the fact that the hospitals involved have more specialists and better equipment and as such, receive many high-risk referral cases compared to LRH. In our study, 136 (77.7%) neonates survived though 42 (30.9%) were hypotonic with abnormal reflexes indicating neurological sequelae. Also 94(69.1%) were discharged without clinical sequelae. On the other hand, Chiabi et al in Cameroon found that 12.2% of asphyxiated neonates had neurological sequelae [6]. This difference can be explained by the fact that most of the asphyxiated neonates in the study done by Chiabi et al. were in Sarnat grade I while in our study the majority were in Sarnat grade III. The case fatality rate in our study was 16%. This supports findings done by researchers in India with a case fatality rate of 16.6% [30]. This finding highlights the correct and timely intervention done by the obstetric and neonatology team of the LRH.

CONCLUSION

Neonatal asphyxia is still very common in our setting and some preventable risk factors were meconium-stained liquor, followed by augmentation of labour and number of ultrasounds done (<3). Furthermore, the case fatality rate was 16% and babies who were referred from other hospitals had a threefold chance of dying compared to those who were born at the Regional Hospital Limbe. These results strongly advocate for neonatal hospitalization units in all hospitals were children are born.

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