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Prevalence and Risk Factors of Apnea in Preterm Neonates Admitted to the French Medical Institute for Mothers and Children Hospital in Kabul City: An Analytic Cross-Sectional Study

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Abstract

Introduction: Prematurity is one of the leading causes of neonatal death in Afghanistan and complicates a lot of serious problems including apnea. Although recurrent and prolong apnea of prematurity (AOP) may be directly or indirectly associated with significant adverse outcomes, there isn't enough scientific information regarding the prevalence and risk factors of this problem in Afghanistan, therefore, this study was performed to obtain such information.

Objective: To determine the prevalence rate and risk factors for apnea of prematurity in neonates admitted to the Neonatal Intensive Care Unit of the French Medical Institute for Mothers and Children Hospital, Kabul City.

Patients and Methods: This analytic cross-sectional study was conducted at the Neonatal Intensive Care Unit of the French Medical Institute for Mothers and Children Hospital in Kabul City, Afghanistan. The study participants were preterm neonates. Statistical analysis was performed by SPSS 24.

Results: A total of 75 preterm newborns were enrolled in this study and the apnea of prematurity were developed in 48% of them. The prevalence of such apnea was 71.4% in extremely low birth weight preterm neonates, 47.4% in very low birth weight neonates, and 36.4% in low birth weight neonates. Based on gestational age, the prevalence rates of apnea in the early and moderate preterm neonates were 55.6% and 52.8% respectively, whilst also in late preterm neonates it was 42.8%. The apnea of prematurity appeared more prevalent in boys (54.3%) than girls (45.7%). The preterm neonates in the apnea group versus the non-apnea group had the mean birth weight of (1233.33±235.25g vs 1333.46 ±274.44g, 90%CI= -198 _ -1.4), mean maternal age of (24.78±3.68y vs 26.62 ±4.58y, 90%CI= -3.44_-0.23) and RR of anemia (2.2, P=0.05).

Conclusion: The overall prevalence rate of AOP in preterm neonates was 48% and the highest rates were seen within extremely low birth weight and early preterm neonates. Lower neonatal birth weight, neonatal anemia and younger maternal age were found to be the risk factors for apnea of prematurity.

Keywords: Cessation of Respiration, Newborn, Prematurity

Introduction

Globally, about 2.4-2.8 million neonates died in 2017 and during this period,

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south Asia and Africa had the highest neonatal mortality rate [1,2].The neonatal mortality rate in Afghanistan is one of the highest in the world and it was reported by UNICEF in 2019, 37 deaths per 1000 live births [3,4]. Prematurity, defined as neonate delivered before 37 weeks of gestation, is one of the major causes (35%) of early neonatal mortality in Afghanistan [5,6]. Apart from high mortality, Prematurity is also an important cause of neuromotor disability. It has been estimated that 15 million preterm babies are born worldwide every year [2,6]. Birth weight less than 1500g is classified as low birth weight [6].

Apnea is defined as a cessation of breathing for 20 seconds or longer or a shorter pause accompanied by bradycardia (<100 beats per minute), cyanosis, or pallor. In practice, many apneic events in preterm infants are shorter than 20 seconds. Approximately, all infants born at ≤28 weeks of gestation have apnea; beyond 28 weeks of gestation, the proportion of apnea decreases, from 85% at 30 weeks of gestation to 20% at 34 weeks of gestation [7, 8].

Apnea or cessation of respiration is an important cause of mortality and brain damage in immature babies especially those with a gestation of fewer than 34 weeks or weight less than 1500g [9]. It is due to the immaturity of the central nervous system (apnea of prematurity) or secondary to other causes such as metabolic disturbances [10,11]. The prevalence of apnea in neonates with very low birth weight who were admitted to NICU of the Aditya Hospital of India was 44% [12]. In the NICU of Enugu State University Teaching Hospital, South-East Nigeria, the prevalence of apnea was reported 84%, 47%, and 15% in ELBW, VLBW, and LBW neonates respectively [13]. The prevalence of apnea in preterm infants increase with low gestational age and birth weight of the newborn infants [14, 15].

Despite high neonatal mortality due to prematurity and its complications, there is not enough scientific information regarding the epidemiology of AOP in preterm newborns of Afghanistan.

The present study was carried out to find the prevalence rate and risk factors of AOP in preterm neonates who were admitted to the Neonatal Intensive Care Unit (NICU), French Medical Institute for Mothers and Children (FMIC) Hospital, Kabul City. Such information is highly required for better neonatal care, generation of hypotheses, further researches, and health policymaking.

Patients and Methods

Study Design, Setting, and Population

We conducted an analytic cross-sectional study in the Neonatal Intensive Care Unit (NICU), French Medical Institute for Mothers and Children (FMIC) Hospital, Kabul City during July-December 2019. The study population was comprised of in-born and out-born preterm neonates (infants up to 28day old) with weights less than 2500g.

Inclusion and Exclusion criteria

Neonates with a gestational age of fewer than 37 weeks and a birth weight of less than 2500g were enrolled in this study. No cases were excluded from the study.

Sample size and sampling strategy

The sample size calculation was performed by Stata 14. A hypothesized difference of two years with standard deviation of 3.5 between mean maternal age of study and control group was took into consideration. With an alpha error of 10% and power of 80%, the two-sample means test estimated a sample size of 74 neonates. During the study period, thirty-six premature neonates who had apnea of prematurity (Apnea group) and the other thirty-nine premature neonates without apnea of prematurity (Control group) were recruited by census sampling method.

Variables:

The main variables are:

- The birth weight of neonates in gram was determined by accurate balance during the first 24hr of life. According to the birth weight the neonates were classified as low birth weight (1500-2500g), very low birth weight (1000-1500g), and extremely low birth weight (less than 1000g)
- The gestational age of neonates in weeks was determined by Last Menstrual Period (LMP) or antenatal maternal ultrasound or New Ballard Score. Prematurity was defined as birth occurring at less than 37 weeks of gestational age and was classified as early (less than 32 weeks of gestation), moderate (32-33 weeks of gestation) and late (34-36 weeks of gestation).
- The Apgar score in the 1st minute of birth was recorded. The neonates with Apgar score of less than 7 at 1st minute were accepted as perinatal asphyxia.
- The apnea was defined as a cessation of breathing for 20 seconds or longer or a shorter pause accompanied by bradycardia (<100 beats per minute), cyanosis, or pallor. Persistent of apnea attacks in preterm neonates with no other obvious causes or despite the correction of secondary causes was accepted as apnea of prematurity. The attacks of apnea were detected by continuous cardio-respiratory monitor and clinical examination.
- Neonatal sepsis was diagnosed by the presence of three of the five criteria: elevated C-Reactive Protein, leukocytosis or leucopenia, elevated count of premature granulocytes, temperature instability and symptoms of infection.
- Neonatal anemia was defined as hemoglobin level of less than 13gr/dl.

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- Respiratory distress syndrome (RDS) was diagnosed by the presence of at least two of the following clinical signs, as well as characteristic radiographic finding of the chest: tachypnea (>60/min), dyspnea with inspiratory subcostal or intercostal retractions, nasal flaring, expiratory grunting and cyanosis in room air. On chest radiography, homogenous lung disease, classically described as having a ground-glass reticulo-granular appearance with air bronchograms, was a pathognomonic sign of RDS.
- The diagnosis of NEC was based on a combination of clinical symptoms and signs, including feeding intolerance, abdominal distention and bloody stools, as well as radiological features, such as pneumatosis intestinalis, portal venous gas and pneumoperitoneum.
- PDA was diagnosed by echocardiography and intraventricular hemorrhage was detected by the cranial ultrasound.
- The maternal age in year, type of delivery (vaginal or cesarean), and parity was defined as the number of births with the gestational age of more than 20 weeks.
- In-born newborns were those delivered at the Obstetric Unit of FMIC hospital, whereas out-born babies were those delivered at other hospitals.

Ethical consideration:

This study was approved by the Department of Neonatology (Protocol no 5 dates 3/2/2021), Kabul University Medical Science, and the Ethical Board of FMIC hospital. Although, this was an observational study and the data were obtained from the patient documents, verbal consents were taken from patients' guardians for participating in this study. The Helsinki Declaration was taken into consideration and all the personal information remained anonymous.

Data collection tools & Statistical analysis:

Initially, raw data were collected in data collection sheets and then entered in SPSS 24 software for statistical analysis. We detected the significance level by using independent t-test, Chi-square test, and Binary Logistic Regression. A power of 80% and an alpha error of 0.1 were accepted so the p-value less than 0.1 were significant.

Results

Seventy-five preterm newborn babies were evaluated for the prevalence and pattern of AOP at the Neonatal Intensive Care Unit (NICU) of French Medical Institute for Mothers and Children (FMIC) Hospital, Kabul City. The demographic characteristics of the mentioned preterm neonates are described in Table-1. As shown in Table-2 the overall prevalence rate of AOP in newborn babies was 48% and the highest prevalence rates were seen within groups of ELBW and early preterm infants.

After the comparison of data between apnea and non-apnea groups, as shown in [Table-3], the lower mean neonatal birth weight and anemia, as well as mean maternal age had a significant association with the development of AOP. The neonatal age, sex, gestational age, number of deliveries, and mode of delivery, as well as sepsis, perinatal asphyxia, RDS, NEC, PDA, IVH, hypocalcemia, hyponatremia, hypomagnesemia and hypokalemia had no statistically significant relationship with the risk of apnea in such infants. However, the risk of mortality was higher in the non-apnea group but such a finding wasn't statistically significant.

Discussion

The current analytic cross-sectional study revealed the prevalence and figures of AOP in preterm neonates admitted to the NICU of the French Medical Institute for Mothers and Children Hospital, Kabul City. Based on the results, the overall prevalence rate of AOP was 48% and the highest rates were demonstrated within groups of ELBW and early preterm neonates, 71.4% and 55.6% respectively. The apnea of prematurity was more prevalent in boys than girls [Table-2]. The current study also found a relationship of low neonatal birth weight and anemia as well as low maternal age with the development of AOP in neonates [Table-3]. It means a lower

Table 1: Demographic Characteristics of the Participants.

Variables	Mean (SD)	Number (%)
Age in days	7.9 (2.6)	-
Birth weight in grams	1285.4 (259.6)	-
Gestational age in weeks	31.7 (2.4)	-
Apgar Scores of 1st minute	7 (3)	
Maternal Age in years	25.7 (4.2)	-
Number of Deliveries	2.4 (1.4)	-
Class of Birth Weight LBW (1500-2000 g) VLBW (1000-1499) ELBW (less than 1000g)	 - - -	 11 (14.7) 57 (76) 7 (9.3)
Class of GA Late Preterm (34-36 W) Moderate Preterm (32-33 W) Early Preterm (<32W)	 - - -	 14 (18.7) 25 (33.3) 36 (48)
Sex Boys Girls	 - -	 35 (46.7) 40 (53.3)
Mode of Delivery Vaginal Cesarean	 - -	 37 (49.3) 38 (50.7)
Place of Delivery In-born Out-born		 62(82.7) 13(17.3)

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neonatal birth weight and hemoglobin, as well as a younger maternal age increase the risk of AOP in newborn babies.

Shinde R et al. conducted a retrospective observational study on VLBW neonates admitted to NICU of Aditya Hospital, Hyderabad of India. According to the result of this study, the prevalence of AOP in very low birth weight was 44% [12]. Chidiebere et al. were carried out a prospective study at the Neonatal Intensive Care Unit (NICU) of Enugu State University Teaching Hospital, South-East Nigeria. The prevalence of AOP was demonstrated 20% and 14% in VLBW and LBW neonates respectively [13]. Henderson-Smart reported an incidence of 85% in premature infants born at 30 weeks, with a subsequent decrease to 20% in those born at 34 weeks [15]. Compared to the studies of Shinde R et al., Chidiebere et al. and Henderson-Smart et al., the current study found higher prevalence rates of AOP within groups of LBW and VLBW premature infants [Table-2]. This difference may be attributed to the higher prevalence rate of prematurity and associated factors of apnea in preterm neonates of our country.

Table-2: Prevalence Rate of AOP in Different Categories of Preterm Neonates.

Categories of Neonates	Neonates with AOP, n	Neonates Without AOP, n	Prevalence Rate, %
All Neonates, n=75	36	39	48
Classes of Birth Weight, No LBW (1500-2000 g) VLBW (1000-1499) ELBW (less than 1000g)	 4 27 5	 7 30 2	 36.4 47.4 71.4
Classes of Gestational Age, No Late Preterm (35-36 W) Moderate Preterm (32-34 W) Early Preterm (<32W)	 5 11 20	 9 14 16	 35.7 44 55.6
Sex, No Boys Girls	 19 17	 16 23	 54.3 42.5

Ogunlesi et al. conducted a retrospective study at the Olabisi Onabanjo University Teaching Hospital of Nigeria. This research found a significant relationship between neonatal birth weight and prevalence of AOP in newborn infants [16]. The association of fewer birth weight with AOP was also detected in our study. Therefore, the findings of both studies are similar. The current study also uncovered an association of young maternal age with AOP [Table-3]. Fuchs et al. performed a large cohort study and revealed that younger women (20–24 years) had an increased risk of premature deliveries (aOR=1.08, 95% CI 1.01–1.15) [17]. As the younger maternal age is a risk factor of preterm birth, it may also explain the increased risk of apnea in such an infant group.

The association of neonatal anemia with AOP was the other important finding of the current study. Anemia causes a decrease in oxygen carrying capacity, which can lead to decreased oxygen delivery to the central nervous system and a decrease in the efferent output of respiratory neuronal network, all of which raise the risk of apnea [18].

Conclusion

The current study demonstrated an overall prevalence rate of 48% for AOP in neonates and the highest rates appeared within groups of extremely low birth weight and early preterm newborns babies. The lower mean neonatal birth weight and neonatal anemia, as well as the younger maternal age were

Table 3: Comparison of Factors Associated with AOP in Preterm Neonates.

Variables	Neonates with AOP (n=36)	Neonates Without AOP (n=39)	P-value (90%CI)
Birth Weight in grams, Mean (SD)	1233.33 (235.25)	1333.46 (274.44)	0.09 (-198 _ -1.4)
Gestational age in weeks, Mean (SD)	31.81 (2.01)	31.62 (2.73)	0.7 (-0.74_0.15)
Maternal Age in years, Mean (SD)	24.78 (3.68)	26.62 (4.58)	0.06 (-3.44_-0.23)
Number of Delivery, Mean (SD)	2.44 (1.3)	2.69 (1.5)	0.4 (-0.78_0.28)
Class of Birth Weight, No (%) LBW (1500-2000 g) VLBW (1000-1499) ELBW (less than 1000g)	 4 (36.4) 27 (47.4) 5 (71.4)	 7 (63.6) 30 (52.6) 2(28.6)	 0.34 0.14 0.22
Class of GA, No (%) Late Preterm (35-36 W) Moderate Preterm (32-34 W) Early Preterm (<32W)	 5 (35.7) 11 (44) 20 (55.6)	 9 (64.3) 14 (56) 16 (44.4)	 0.56 0.83 0.29
Sex, No (%) Boys Girls Odds Ratio (OR)	 19 (54.3) 17 (56.7) 1.6	 16 (45.7) 23 (43.3) 0.6	 0.3

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Mode of Delivery, No (%)			
Vaginal	18 (48.6)	19 (51.4)	
Cesarean	18 (47.4)	20 (52.6)	
Odds Ratio (OR)	1.05	0.95	0.45
Associate Illnesses No (%)			
Sepsis	12 (33.3)	12 (30.8)	0.5
Perinatal Asphyxia	10 (27.8)	11(28.2)	0.64
RDS	16 (44.4)	18 (46.1)	0.53
Anemia	8 (22.2)	4 (10.2)	0.05
NEC	4 (11.1)	5 (12.8)	0.55
PDA	4 (11.1)	9 (25)	1.14
IVH	3(8.3)	3 (7.8)	0.62
Hypocalcemia	9 (25)	14 (35.9)	0.22
Hyponatremia	4 (11.1)	6 (15.4)	0.42
Hypomagnesemia	4 (11.1)	5 (12.8)	0.55
Hypokalemia	11 (50.6)	7 (17.9)	0.12
Mortality, No (%)	12 (33.3)	9 (23.1)	
Risk Ratio (RR)	1.4	0.6	0.3

SD= Standard deviation, GA= Gestational age, g=gram, W=Week, CI= Confidence Interval, LBW=Low Birth Weight, VLBW= Very Low Birth Weight, ELBW= Extremely Low Birth Weight, RDS=Respiratory Distress syndrome, NEC= Necrotizing enterocolitis, PDA= Patent Ductus Arteriosus, IVH= Intraventricular Hemorrhage.

the risk factors of AOP in neonates. However, the incidence of mortality was higher in the non-apnea group, such a finding wasn't statistically significant. These findings are most useful for better neonatal care, the generation of hypotheses, further researches, and health policymaking.

Conflict of Interests Statement

The authors declare they have no interest of conflict.

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Authors' contribution: Conceptualization, design, data analysis, manuscript drafting and editing was performed by the first author. The second and third authors designed the data collection instruments, collected the data and reviewed the manuscript. The fourth author coordinated and supervised data collection. The final report was approved by all authors.

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