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ORIGINAL ARTICLE

Risk Factors of Pulmonary Hemorrhage in Neonate

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ABSTRACT

Introduction: Pulmonary haemorrhage (PH) is a potentially fatal respiratory complication of neonates, particularly those with very low-birth-weight infants (ELBWI), who are predisposed to diseases that need invasive ventilation and critical care after birth. Clinical PH is predicted to affect 1–12 out of every 1000 live babies [1]. Pulmonary haemorrhage is a potentially fatal disease that affects 1-12/1000 live births, with rates reaching 50/1000 births [2].

Objective: To determine the frequency of factors leading to pulmonary hemorrhage in neonates.

Materials And Methods: This study was conducted at Ziauddin University Hospital, Karachi, Pakistan, and the duration of this study was from June 8, 2021 to December 7, 2021. All patients who fulfilled the inclusion criteria and visited to Pediatrics Department of Ziauddin Medical University, Karachi were included in the study. Informed consent was taken from parents / guardians after explaining the procedure, risks and benefits of the study. All of the patient data obtained included demographic information, clinical aspects, and information on mothers and infants. All data obtained were put into the accompanying proforma and utilized electronically for research purposes.

Results: The age of mother was 29.6±7.8 years. In distribution of gender of baby, 63 (45%) were male, 77 (55%) were female. In distribution of factors leading to pulmonary hemorrhage, hypothermia was noted in 25 (17.8%) patients, heart failure in 42 (30.0%), disseminated intravascular coagulation (DIC) 12 (8.5%), oxygen saturation index 124 (88.6%), reduced mean platelet volume 111 (79.3%), polycythemia 20 (14.3%), patent ductus arterioses 22 (15.7%), low birth weight 97 (69.3%), respiratory distress syndrome in 44 (31.4%) while surfactant therapy was noted in 15 (10.7%) patients.

Conclusion: It is to be concluded that oxygen saturation index and diabetes was noted as most common neonatal and mother factors respectively which leads to pulmonary hemorrhage in neonates. More prospective and well-controlled trials are needed to validate the current findings.

Keywords: Factors, IUGR, Neonates, Pulmonary Hemorrhage

INTRODUCTION

Pulmonary haemorrhage (PH) is often an ominous symptom of deteriorating clinical state. It is a life-threatening emergency defined by the ejection of bloody fluid from the upper respiratory tract or the endotracheal tube (ETT). It is a kind of fulminant lung oedema in which red blood cells and capillary filtrate flow into the lungs. PH has been linked to up to 68 percent of newborn fatalities during the first week of life [1]. Pulmonary haemorrhage (PH) is a well-known disease in term and preterm neonates, originally documented in 1855 [2-3]. In extremely low birth weight preterm newborns, pulmonary haemorrhage has the greatest fatality rate [2]. Neonatal pulmonary haemorrhage (NPH) refers to a significant number of pulmonary haemorrhages involving at least two lobes, with a death rate of 50 to 80 percent in severe instances. There is a considerable rise in the risk of bronchopulmonary dysplasia in children who survive [4-5]. It is most prevalent in neonates weighing less than 1500 g, who frequently have a patent ductus arteriosus (PDA) and are ventilated [1]. Prevalence rates in extremely low birth weight neonates have been observed to range between 3% and 32% [6]. In Brazil, two studies were found; one was based on autopsy of babies and found a prevalence of 34.5 percent of PH, while the other was based on blood tests. [1].

Prematurity, intrauterine growth restriction, PDA with a left to right shunt, asphyxia, coagulopathy, respiratory distress syndrome, polycythemia, hypoxemia, disseminated intravascular coagulation, mechanical ventilation, sepsis, hypothermia, male gender, cold injury, multiple births, oxygen toxicity, urea cycle defects, and, more recently, surfactant therapy are all risk factors for PH [6-7]. Concerning prognosis, there is conflicting evidence on neuromotor development; some studies found no influence, while others found an increased incidence of cerebral palsy and cognitive impairments [8-10]. According to certain research, the death rate ranges between 38% and 57% [6,8]. The prevalence of PH in newborns with birth weights less than 1500 g who were treated with a surfactant was observed to be 11.9%[1]. PH is also linked to left-to-right ductal shunting and increased pulmonary blood flow [1]. Surfactant instillation has been shown to enhance Mean Airway Pressure (MAP) and oxygenation indicators in patients with PH [11-12]. Previous research discovered that 23.2 percent of NPH patients had a low 5-minute Apgar score, 17 percent had hypothermia, 20.5 percent had birth weight 2500, 28.6 percent had heart failure, 8 percent had DIC, 90.2 percent had OI 100, 36.6 percent had MPV decreased, and 8 percent had postnatal PS. Diabetes was shown to be a risk factor for mothers during pregnancy in 22.3 percent of cases, pregnancy-induced hypertension in 3.6 percent of cases, and cholestasis in 11.6 percent of cases. There were 27.6 percent with PID, 28.6 percent with placenta previa, 16.1 percent with abruption, 14.3 percent with amniotic fluid, and 62.5 percent with caesarean section. [4].

Infant pulmonary haemorrhage is a dangerous illness with a high neonatal fatality rate. Several risk factors have been linked to the development of pulmonary bleeding, although the precise pathophysiology is unknown. As a result, the goal of this study is to identify the risk factors for pulmonary haemorrhage in newborns in our community so that treatment measures may be developed to decrease neonatal morbidity and death. Furthermore, the number of research conducted in Pakistan on the prevalence, risk factor profile, and prognosis of newborn pulmonary haemorrhage is minimal.

MATERIAL AND METHODS

This study was conducted at Department of Paediatrics, Ziauddin University Hospital, Karachi, Pakistan, and the duration of this study was Six months after the approval of synopsis from June 8, 2021 to December 7, 2021. The sample size was calculated using WHO sample size calculator considering the prevalence of reduced mean platelet volume (MPV) in neonates having pulmonary hemorrhage, P=36.6%[14] with confidence level=95% and margin of error=8%. The total sample size came out to be 140 patients. The sample technique was Non-Probability, Consecutive Sampling.

Sample Selection Inclusion Criteria

- Both genders.

- Either full term or premature.
- All neonates born within 28 days.
- Cases diagnosed with pulmonary hemorrhage (as per operational
- definition).

Exclusion Criteria

- Children with congenital abnormalities.
- Those with inherited metabolic diseases.
- Those who were unable to give informed consent.

Patients developed pulmonary hemorrhage during stay in hospital or at the time of admission in the Department of Pediatrics, Ziauddin University Hospital, Karachi and following inclusion criteria were included in the study. This study was conducted after approval of synopsis from CPSP and from ethical review committee of the institute. After taking informed consent from parents or guardians. All the patient's data collected contained demographic characteristics, clinical features and relevant information of mothers and infants such as maternal age, pregnancy complications and complications (diabetes, pregnancy-induced hypertension, cholestasis, chronic pelvic inflammatory disease), mode of production, the situation placenta (placenta previa and placental abruption), neonatal sex, gestational age, birth weight, Apgar score, whether the application of pulmonary surfactant (pulmonary surfactant, PS) before pulmonary hemorrhage, PaO_2 before pulmonary hemorrhage and FiO_2, Mean platelet volume (mean platelet volume, MPV), neonatal underlying disease (the RDS, low body temperature, heart failure, DIC, etc.). All the demographic and clinical findings including the factors were collected on a predesigned proforma. Confounders and biasness were controlled by strictly following the inclusion criteria.

Patient's data was compiled and analyzed through statistical package for Social Sciences (SPSS) Version 21. Frequency and percentage were computed for qualitative variables like child's gender, mode of delivery, mother's factors during pregnancy (diabetes, hypertension, cholestasis, chronic pelvic inflammation, placenta previa, abruption, and amniotic) and neonatal risk factors (hypothermia, heart failure, disseminated intravascular coagulation (DIC), oxygen saturation index (OI)< 100 and reduced mean platelet volume (MPV)), patent ductus arterioses, low birth weight, respiratory distress syndrome and surfactant therapy. Mean±SD was calculated for quantitative variable i.e. mother's age, gestational age, birth weight, APGAR score at 5 min, oxygen saturation index and mean platelet volume. The stratification was done on age, gender, length of stay, mode of delivery, delivery outcome, booking status and convulsion to see the effect of these modifiers on outcome using Fischer's exact test. P value <0.05 was considered as significant.

RESULTS

In this study 140 patients were included to assess the factors leading to pulmonary hemorrhage in neonates and the results were analyzed as: Mean ± SD of age of mother was 29.6±7.8 with C.I (28.29…….30.90) years as shown in Table 1. Mean ± SD of gestational age was 28.7±1.9 with C.I (28.38…….29.01) weeks as shown in Table 2. Mean ± SD of birth weight was 2.1±0.6 with C.I (1.99…….2.20) kg as shown in Table 3. Mean ± SD of APGAR score at 5 min was 7.3±2.1 with C.I (6.94…….7.65) minutes as shown in Table 4. Mean ± SD of oxygen saturation index was 45.3±8.9 with C.I (43.81…….46.78) mmHG as shown in Table 5.

Table 1: Descriptive Statistics For Age Of Mother n=140

Mean	29.6 (years)
Standard Deviation	7.8
95% Confidence Interval	28.29 30.90
Minimum	18
Maximum	40
Range	22

Table 2: Descriptive Statistics Of Gestational Age n=140

Mean	28.7 (weeks)
Standard Deviation	1.9
95% Confidence Interval	28.38 29.01
Minimum	27
Maximum	32
Range	05

Table 3: Descriptive Statistics Of Birth Weight n=140

Mean	2.1 (kg)
Standard Deviation	0.6
95% Confidence Interval	1.99 2.20
Minimum	1.5
Maximum	3.5
Range	2.0

Table 4: Descriptive Statistics Of Apgar Score At 5 Min n=140

Mean	7.3
Standard Deviation	2.1
95% Confidence Interval	6.94 7.65
Minimum	0
Maximum	10
Range	10

Table 5: Descriptive Statistics Of Oxygen Saturation Index n=140

Mean	45.3 (mmHG)
Standard Deviation	8.9
95% Confidence Interval	43.81 46.78
Minimum	05
Maximum	85
Range	80

DISCUSSION

The majority of pulmonary bleeding occurs in ventilated preterm babies with severe respiratory distress syndrome (RDS) who have received surfactant treatment. A group of very-low-birth-weight (VLBW) newborns had a 0.5-11 percent incidence of pulmonary haemorrhage. Pulmonary haemorrhage is linked with considerable morbidity and death, with fatality rates ranging from 50% to 80%.

Prematurity, intrauterine growth restriction, respiratory issues, patent ductus arteriosus (PDA), bleeding disorders, ventilator use, and surfactant therapy were all risk factors for pulmonary haemorrhage. Surfactant treatment was considered to cause pulmonary bleeding. As a result, doctors may be hesitant to use surfactant again in infants with pulmonary bleeding. The presence of haemoglobin, red cell membrane lipids, and serum proteins, on the other hand, might exacerbate surface tension caused by surfactant malfunction and produce secondary RDS. Until the 1990s, pulmonary haemorrhage (PH) was more commonly identified in premature babies, primarily in situations of asphyxiation or significant illness. It is becoming more commonly described in extremely premature babies.

Depending on the criteria used to identify PH, prevalence rates among extremely low birth weight neonates range from 3% to 32%. Exogenous surfactant is currently widely used to treat respiratory distress syndrome (RDS). It appears to be safe and effective for the treatment of RDS, with a considerable reduction in morbidity and death. However, the risk of pulmonary haemorrhage appears to be enhanced in preterm infants with RDS who are given surfactant. There is limited published data on the clinical outcomes of surfactant-treated infants who develop pulmonary haemorrhage.

Smaller gestational age, lower birth weight, poorer Apgar scores at one and five minutes, severe RDS (grades 3 or 4) and use of surfactant in very low birth weight children are all associated with an increased risk of PH. For the treatment of PH in newborn babies, many treatments have been proposed, including high airway pressures during mechanical ventilation, high frequency oscillation, ECMO, injection of recombinant activated Factor VII, and surfactant replacement therapy.

Surfactant instillation has been shown to effectively cure PH in babies who have previously been treated with surfactant. Pandit et al. found that after six hours of surfactant replacement

treatment, oxygen indices improved in 15 newborns with PH. Amizuka et al. used a surfactant to treat 26 of 27 newborns who had PH 1.5 hours after delivery. The treatment began 3.0 hours after the beginning of PH. In 82 percent of patients, an excellent response to exogenous surfactant was seen. Surfactant was used as a therapy for pulmonary bleeding in the majority of trials.

The findings of our study are discussed below. In recent study, mean gestational age was 28.7±1.9 weeks. Braun KR, et al noted gestational age as 26±2 weeks [3]. In our study, 55 (39.3%) mothers had vaginal delivery while 85 (60.7%) had caesarean. Braun KR, et al noted caesarean deliveries to be 65% [3] while in another study, 62.5% were caesarean cases [4]. In this study, mother factors during pregnancy as diabetes was noted in 63 (45%) patients, hypertension in 29 (20.7%), cholestasis 12 (8.5%), chronic pelvic inflammation 06 (4.3%), placenta previa 43 (30.7%), placental abruption 19 (13.6%) while amniotic fluid index was noted in 32 (22.8%). Braun KR, et al noted abruption in 6% cases [3]. A study of Fan J, et al noted that the risk factor for mother during pregnancy found as the diabetes was 22.3%, pregnancy induced hypertension was 3.6% and cholestasis was 11.6% [4]. The study also reported that there were 27.6% had PID, 28.6% had placenta previa, 16.1% had abruption and 14.3% had amniotic [4].

In present study, neonatal factors were noted as hypothermia were noted in 25 (17.8%) patients, heart failure in 42 (30%), disseminated intravascular coagulation (DIC) 12 (8.5%), oxygen saturation index 124 (88.6%), mean platelet volume 111 (79.3%), polycythemia 20 (14.3%), patent ductus arterioses 22 (15.7%), low birth weight 97 (69.3%), respiratory distress syndrome in 44 (31.4%) while surfactant therapy was noted in 15 (10.7%) patients. The study of Fan J, et al found that in cases of neonatal pulmonary hemorrhage, there were 23.2% had low 5 min Apgar score, 17% had hypothermia, 20.5% had birth weight < 2500, 28.6% had heart failure, 8% had disseminated intravascular coagulation, 90.2% had oxygen saturation index, 36.6% had mean platelet volume reduced and 8% had postnatal PS [5]. In current study, stratification of confounders / effect modifiers with respect to mothers' factors, insignificant difference was noted in age group (P=0.988), gender (P=0.468), mode of delivery (P=0.135) while significant different was found in length of hospital stays (P=0.027), booking status (P=0.001) and delivery outcome (P=0.015).

In our study, stratification of confounders / effect modifiers with respect to neonatal factors, insignificant difference was noted in age group (P=0.496), gender (P=0.760), mode of delivery (P=0.302), length of hospital stays (P=0.305), while significant different was found in booking status (P=0.002) and delivery outcome (P=0.0001).

CONCLUSION

It is to be concluded that oxygen saturation index and diabetes was noted as most common neonatal and mother factors respectively which leads to pulmonary hemorrhage in neonates. More prospective and well-controlled trials are needed to validate the current findings.

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