Research Article

Determinants of Mortality among Preterm Neonates Admitted with Respiratory Distress in Addis Ababa Public Hospitals Neonatal Intensive Care Units, 2021, Multi-Center Prospective Follow-Up Study

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Abstract

Background: Respiratory distress is a breathing problem that affects newborns, mostly those who are born preterm, the earlier a baby is born, the more likely the baby will develop respiratory distress. Some studies were conducted about incidence and associated factors of respiratory distress in preterm neonates but there are constraints of studies regarding on determinants of preterm mortality admitted with respiratory distress. Thus, this study will provide an important input to improve treatment practice and increase neonatal survival rate especially those neonates are highly vulnerable to death due to the most frequent preterm complications (respiratory distress).

Objective: To identify determinants of mortality among preterm neonates admitted with respiratory distress in Addis Ababa public hospitals neonatal intensive care units, 2021.

Methods: This institutional based prospective follow up study was conducted in Addis Ababa public hospitals neonatal intensive care units among all preterm neonates admitted with respiratory distress from February 12-May 12, 2021. Collected data was entered in to Epi data version 4.6 and it was exported to SPSS version 26 software for further analysis. After computing bi-variable logistic regression, variables with p-value ≤ 0.25 were taken into multi-variable model to minimize confounders. The cut point to declare the presence of statistical significance between the variables were p-value < 0.05 or AOR, 95% CI.

Results: This study concluded that, mortality of preterm neonates admitted with respiratory distress was 43.7 % (CI: 0.38-0.50). Pre-eclampsia/eclampsia (AOR=2.9, 95% CI: 1.32-6.39), feeding initiation time > 24 hours of admission (AOR=5.4, 95% CI: 2.24-12.86), NEC (AOR=4.4, 95% CI: 1.67-11.59), thrombocytopenia (AOR= 3.7, 95% CI: 1.45-10.27) and hyperbilirubinemia (AOR=0.19, 95% CI: 0.08-0.46) were the identified determinants for preterm mortality admitted with respiratory distress.

Conclusion and Recommendation: In this study, mortality among preterm neonates admitted with respiratory distress was high. Therefore, major interventions on the identified determinants have to be implemented and further studies shall be conducted on preterm neonates with neonatal hyperbilirubinemia.

Keywords: Preterm • Respiratory Distress • Determinants • Mortality • Addis Ababa • Babies

Introduction

Respiratory distress is a breathing problem that affects newborns, mostly those who are born preterm, the earlier a baby is born, the more likely the baby will develop respiratory distress. The most common causes of respiratory distress in neonates are transient tachypnea of the newborn, surfactant deficiency and underdeveloped lung anatomy, meconium aspiration syndrome pneumonia, sepsis, pneumothorax, persistent pulmonary hypertension, and congenital malformations. Risk factors which can increases the likely hood of respiratory distress

are prematurity, being born with meconium-stained amniotic fluid, caesarian section delivery, gestational diabetes, maternal chorioamnionitis, or prenatal ultra-sonographic congenital malformation findings, such as oligohydramnios or structural lung abnormalities. Pre-natal administration of corticosteroids between 24 and 34 weeks gestation reduces the risk of respiratory distress of the newborn when the risk of preterm delivery is high. Treatment options are resuscitation, oxygenation, surfactant replacement, ventilation and antibiotics initiation based on the cases is helpful [1].

The most common symptoms of respiratory distress are breathing problems at birth that get worse, blue skin color (cyanosis),flaring nostrils, rapid breathing, grunting and chest retractions in which the symptoms of respiratory distress usually get worse by the third day. Respiratory distress in preterm babies diagnosed by a combination of physical examination and diagnostic tests such as chest X-rays of the lungs, blood gas tests, echocardiography.

Preterm birth, intrapartum-related complications (birth asphyxia or inability to breathe at birth), infections and birth defects are the leading causes of most neonatal deaths. Preterm related complications are the single largest direct cause of neonatal deaths throughout the world, responsible for 35% of the world's neonatal death (1.1 million deaths per year).

In Africa half of the neonatal deaths are from preterm babies caused by only preterm complications and sub-Saharan African countries loss approximately 290,000 neonates in each year due to preterm complication. Ethiopian neonatal deaths are due to preterm birth complications (37%), intra partum related complication (28%) and infection (24%). Even though respiratory distress alone is not a cause for mortality, different studies identify that it is a significant predictor for preterm morbidity and mortality.

Respiratory distress is one of the most common reasons an infant is admitted to the neonatal intensive care unit in which 15% of term infants and 29% of late preterm infants admitted to the neonatal intensive care unit develop significant respiratory morbidity; this is even higher for infants born before 34 weeks' gestation. Newborn respiratory distress occurs in about 7% of deliveries. The incidence of respiratory distress in different parts of the world is high especially in Ethiopia it ranges up to 42.9%.

A quality improvement project conducted in Wales identified that for the good management included levels of positive end expiratory pressures and timing of introduction of enteral feeds, delayed cord clamping, stabilization with intubation, early enteral feeding and caffeine administration. Another study conducted in Kenya, revealed that hypothermia, hyperglycemia and neonatal sepsis were common co-morbidities associated with poor treatment outcome of preterm neonates with respiratory distress. This study also said that there was a high mortality mainly occurring in the first 10 days of life [2].

Different studies were conducted about incidence and associated factors of respiratory distress in preterm neonates, however there are constraints of data or studies about determinants of mortality in preterm neonates admitted with respiratory distress. Conducting such kinds of studies will provide an important input to improve treatment practice and increase neonatal survival rate especially those neonates are highly vulnerable to death due to preterm complication like respiratory distress. Therefore, this study was designed to determine determinants of mortality among preterm neonates admitted with respiratory distress in Addis Ababa public hospitals neonatal intensive care units, 2021.

Materials and Methods

Study area, design and study period

The study was conducted in Addis Ababa, the capital and largest city of Ethiopia. The city has twelve public hospitals. From these hospitals, the study was conducted in five randomly selected public hospitals of Addis Ababa. These are Tikur Anbessa Specialized Hospital (TASH), Gandhi Memorial Hospital (GMH), Ras-Desta Damtew Memorial Hospital (RDDMH), Yekatit-12 Hospital Medical College (Y12-HMC) and St. Peter Specialized Hospital (SPSH). An institutional based prospective cohort follow up study was conducted from February 12-May 12, 2021.

Population

All preterm neonates admitted with respiratory distress at admission at Neonatal Intensive Care Unit (NICU) in selected public hospitals of Addis Ababa were sources of population and all preterm neonates admitted with respiratory distress to NICU of selected public hospitals in Addis Ababa during the study period (from Feb 12 to May 12, 2021) were study population.

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Inclusion and Exclusion Criteria

All alive neonates admitted to NICU by the diagnosis of preterm respiratory distress in selected public hospital with in the study period were included whereas preterm neonates diagnosed with major congenital anomaly were excluded from the study.

Sample size determination and Sampling procedure technique

All preterm neonates diagnosed with respiratory distress were included without sample size determination. For this study sampling was not performed simply, all preterm neonates diagnosed with respiratory distress during the sated study period were sampled.

Study Variables

Dependent variable

Determinants of preterm mortality admitted with respiratory distress

Independent variables

Maternal socio demographic related predictors; (residence, maternal age, educational status, marital status and occupation), maternal obstetrical and medical predictors; multiple pregnancies, Preterm Prolonged Rupture Of Membrane (PPROM), mode of delivery, preeclampsia, Ante Natal Care (ANC) follow up, steroid administration, hypertension, DM, Human Immuno Deficiency Virus / Acquired Immuno Deficiency Syndrome (HIV/AIDS) and sepsis), Preterm demography related predictors (age at admission, sex, weight, gestational age and weight for gestational age), preterm admission diagnosis characteristics (APGAR score, diagnosis at admission, new medical between the follow up) and treatment related factors (antibiotics, feeding, aminophylline, calcium gluconate CPAP, CPAP type, Kangaroo Mother Care (KMC), nurse to patient ratio and feeding) [3].

Operational Definitions/ Definition of Terms

Preterm: neonates born before 37weeks of gestation

Poor treatment outcome: Neonates who died during the study period

Good treatment outcome: Neonates who have been discharged

Respiratory distress: Respiratory problem combined with tachypnea, cyanosis chest retraction

Data collection tool and procedure

Data were collected using a structured and pretested questionnaire adapted after reviewing different literatures. The questionnaire was first developed in English and translated into Amharic versions and re-translated back into English by language experts to assure its consistency. Training was given for data collectors and supervisors by a principal investigator. The questionnaire was pre-tested on 5% of study participants in Zewditu Memorial Hospital. Some modifications on the questioner were added after pre-test. During data collection, trained supervisors strictly supervised the correctness of the questionnaire. A principal investigator also checked the completeness and correctness of the questioner.

Data analysis procedure

Data was cleaned manually, coded and entered into Epi data version 4.6 and exported to SPSS version 26 software for analysis. After coding, and entering the data to the software descriptive statistics were used to calculate the result in proportion, frequencies and cross tabulation. Tables, figures and graphs were used to present the result. Bi-variable and multi-variable logistic regression analyses were carried out. Variables with p-value ≤ 0.25 were taken into multi-variable model to control for possible confounders. The cut point to declare the presence of statistical associations between dependent and independent variable were p-value < 0.05 or AOR, 95% CI.

Result

Indexed mothers socio-demographic related factors

At the end of this cohort, there were a total of 277 preterm neonatal admissions with respiratory distress. Most of the preterm neonates (82.3%) were born to mothers at the age of 20-35 years old. Significant majorities (90.6%) of the indexed mothers were married and only 19.5% of them had higher educational status. Mother with urban residency covers 87% and 34.1% of the total were house wives Mothers with urban residency cover 87% and 34.1% of the total were housewives.

Indexed mothers pregnancy, obstetrics and health related determinants

In this study, more than half of the indexed mothers had four ANC visits and 72.9% of

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them had a singleton type of pregnancy. From the total indexed, only 44.4% steroids and 1.8% of the mothers delivered gave instrumentally. In regard to known risk factors for preterm delivery, 37.8% had pre-eclampsia or / and eclampsia and 40.1% of them had PROM [4].

Demographical related determinants of preterm neonates

In this study, more than half (54.9%) of the neonate were male and 41.5% of them were born at 34 and above weeks of gestation. Low birth weight neonates were high in proportion to other birth weight classifications which cover 51.6% from the total and percentile comparison of the birth weight with that of gestational age, 88.1% were appropriate for their gestation age and also, only 49.8% of the preterm neonate had normal range first minute APGAR score.

Comorbidity at admission and subsequent medical problem related determinants

In this study, respiratory distress was the outcome variable in which it was encountered at admission. However, there were much comorbidity diagnosed at the same time during admission and later developed medical problems. Based on that, from the total study subjects, 90.6% of them had early onset neonatal sepsis at admission and 79.1% were hypothermic at admission. Neonatal hyperbilirubinemia (70.9%), thrombocytopenia (53.0%) and apnea (50%) were the leading three medical disorders developed by preterm neonates admitted with respiratory distress [5].

Treatment and health service related determinants of the study participants

In the treatment of respiratory distress and related problems, combinations of supportive and medical treatments were given for the study subjects. Accordingly, 54.2% of the neonates were kept on homemade CPAP type, only 22.2% of them had got KMC and 69.0% of the preterm neonates were cared for by nurses with ≥ 1:2 nurse to patient ratio.

Over all outcome of the study participants

At the end of this cohort high proportion of preterm death admitted with respiratory distress were recorded. From the total study participants, only 56.3% of the neonates survived. Male neonates cover 24.9% and 25.6% of the deaths were from 28-32 weeks of gestation age. In regard to length of hospital stay, 70.4% of the study participants stayed in hospitals < 8 days,

13.6% 8-16days and the rest of 16% stayed in hospital for more than 16days. Death may not be from a single cause but also from a combination of medical problems. As it was recorded on the death summery chart, the immediate causes of 23.1% of the deaths were respiratory failure secondary to respiratory distress, 17.3% of the deaths were multi-organ failure secondary to sepsis, DIC and pulmonary hemorrhage were cover 1.4 each with 0.4% of unexpected death. In this study there were not any preterm neonates admitted with respiratory distress born at less than 28 weeks of gestation and from the total preterm neonates born with extreme low birth weight only 1 neonate was survived.

Determinants of preterm mortality admitted with respiratory distress

After bi-variable logistic regression, variables having a p-value less than 0.25 were transported to multi-variable logistic regression which yields. Based on this, pre/eclampsia (AOR: 2.9 (1.32, 6.39)), feeding initiation time > 24 hours of admission (AOR: 5.4 (2.24, 12.86)), NEC (AOR: 4.4 (1.67, 11.59)), thrombocytopenia (AOR: 3.7 (1.45, 10.27)) and hyperbilirubinemia (AOR: 0.19 (0.08, 0.46)) were statistically significant determinants with p-value < 0.05 for preterm death admitted with respiratory distress. This means that preterm neonates being born from pre/eclampsia mother increased the risk of mortality by three times compared with those counterparts. Preterm neonates with respiratory distress who resume feeding after 24 hours of admission had 5.4 times more risk of death compared with those neonates whom feeding initiation had been initiated less than 12 hours of admission. Similarly, preterm neonates who had developed necrotizing enterocolitis increased the risk of death by 4.4 folds compared to those neonates without necrotizing enterocolitis. Thrombocytopenia increases the risk of preterm death by 3.7 folds in comparison with non-thrombocytopenic preterm neonates admitted with respiratory distress. Preterm neonates admitted with respiratory distress developing neonatal hyperbilirubinemia were 81% less likely to die compared to those who didn't develop the case. Variables like hypothermia, EONS, APH, First minute APGAR score, time of antibiotic initiation and HAI were statistically insignificant with p-value > 0.05 [6, 7].

Discussion

Preterm related complications remain the first

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leading cause of neonatal death. According to the 2019 Ethiopia Demographic and Health Survey, neonatal mortality was 33 per 1,000 live births. Respiratory distress is one of the most respiratory system complications which are common in preterm neonates. In fact, respiratory distress by itself is not fatal if it is managed appropriately and timely. However, especially in developing countries like Ethiopia, respiratory distress is a common problem in preterm neonates which can cause morbidity and mortality. But there is no any study which indicate that how many preterm neonates die after they have been admitted with respiratory distress, as far as our research shows. Therefore, this study aimed to assess the determinants of mortality among preterm neonates admitted with respiratory distress in Addis Ababa public hospitals intensive care units, 2021.

In this study, the proportion of mortality among preterm neonates admitted with respiratory distress was 43.7% (CI: 0.38-0.50). This finding shows the highest result compared with the reports from America which said that between 2003 and 2013, the number of deaths due to respiratory distress dropped from 20.5 per 100,000 live births to 13.4 and another report in the same country concluded from 941 enrolled infants with respiratory distress, 108(11%) died. The possible discrepancy in these findings might be due to the management difference between America and Ethiopia in which America uses sophisticated mechanical technologies, such as ventilators, surfactants and even sometimes ECMO according to the status of the neonates, unlike Ethiopia.

Respiratory distress alone may not cause death if the management is applied timely and efficiently, but for preterm neonates admitted with respiratory distress, this study identified determinants of mortality. Accordingly, among preterm neonates admitted with respiratory distress being born from pre-eclampsia / eclampsia, mothers increased the risk of preterm death by almost three folds (1.32, 6.39) than those of neonates born from mothers without pre-eclampsia/eclampsia. This finding is supported by the fact that the anti-angiogenic intrauterine environment of pre/eclampsia affects fetal lung development. This may predispose premature infants to severe respiratory failure shortly after birth and later, to abnormal development of the lung vascular and alveolar structures. As a result, cardiopulmonary failure may end with death in preterm neonates, which will be expected.

Delay in feeding initiation time was one of the significant determinants of mortality among preterm neonates admitted with respiratory distress, which increases the risk of death by 4.4 folds compared with neonates having initiation of feeding less than 12 hours before admission. This finding is supported by scientific evidence which says that early initiation of feeding can stimulate gut maturation, generalized organ development and breast milk has its own immunoglobulin which can increase the immunity level of preterm neonates. In addition, the finding of this study was supported by the fact that postnatal nutrition and metabolic capacity impact postnatal growth and development and have long-term consequences on the lung, brain, and other organ development and cognitive function. Adequate volume of fluids, the protein content, and energy balance in the newborn, and especially preterm nutrition should cover metabolic expenditure and growth requirements, thus setting the ground for optimal outcomes. Therefore, preterm neonates, those who didn't start feeding early lack the above, mentioned advantages of feeding which may increase the risk of death [8].

Likewise, necrotizing enterocolitis was one of the significant determinants of preterm mortality. Preterm neonates admitted with respiratory distress and those who developed necrotizing enterocolitis had were more than fourfold increased risk of mortality compared with preterm neonates without necrotizing enterocolitis. This finding is supported by the fact that the patient may experience systemic signs related to respiratory failure and circulatory collapse, such as cyanosis and unresponsiveness, since necrotizing enterocolitis affects multi organ systems and it leads to mortality. Additionally, this study was conducted on all preterm neonates in which necrotizing enterocolitis are highly dominated, which might increase the incidence of necrotizing enterocolitis which can be another possible explanation [9].

Preterm neonates developing thrombocytopenia after they have been admitted with respiratory distress have three point seven times more risk of dying than those neonates without thrombocytopenia. This finding is supported by the fact that platelets for lung injury in respiratory distress are largely predicated, there is substantial evidence which links platelets to the development of lung injury. Inhibition of platelet-neutrophil aggregation resulted in reduced neutrophil recruitment, increased animal survival time, and

less hypoxia. In practical aspects, neonates with respiratory distress are not well nourished, which is one cause of neonatal thrombocytopenia. If preterm neonates become thrombocytopenic, blood coagulation problems become a critical issue and lung bleeding tendency is high. Lung bleeding leads to pulmonary hemorrhage and, finally will end up with cardiopulmonary arrest [10].

Preterm neonates with hyperbilirubinemia were 81% (AOR: 0.19, CI: 0.08, 0.46) less likely to die compared with their counterparts. This finding seems against the truth; hence neonatal hyperbilirubinemia is a risk for morbidity and mortality of neonates. However, in this study, it was found to be a protective factor. This could be explained as neonatal jaundice causes alarm in preterm neonates which may increase the follow-up. This will help to prevent the possible complications either by early diagnosis or timely treatment which ends up with a positive outcome. Or, it means that in this study participants with hyperbilirubinemia did not die. It doesn't mean hyperbilirubinemia is good for preterm neonates with respiratory distress.

Conclusion

Generally, the mortality of preterm neonates admitted with respiratory distress was found to be high relative to other complications. Being born from pre-eclampsia/ eclampsia mothers, feeding initiation after 24hours of admission, necrotizing enterocolitis and thrombocytopenia were the identified determinants of death whereas hyperbilirubinemia was the factors identified as a protective variable. The authors of this study recommend that responsible bodies better to invest on the identified factors and, further studies on preterm neonates admitted with respiratory distress and developed neonatal hyperbilirubinemia shall be conducted.

Declaration

Ethical Consideration

Ethical clearance was obtained from St. Peter specialized hospital Institutional Review Board (IRB) with version number V231/12/02/2021. Informed written consent was obtained from each index mother after explaining the purpose and procedure of the study. No name or other identifying information was included in the instrument. Formal letter was submitted to GMH, Y12HMC, TASH, SPSH and RDMH NICU department in order to get permission to carry out the study. The eligible study participants were enrolled in the study only after written informed consent has been taken.

Considering the sensitivity of this research, all the basic principles of human research ethics (respect of persons, beneficence, voluntary participation, confidentiality and justice) were respected. The information regarding the study participants was kept confidential by using specific identification for each of them and was not used apart from this study. Other medical information which is not necessary for the study purpose was not accessed.

Consent for Publication

All authors approved that this manuscript is eligible for publication and the indexed mothers were well informed as the paper can be published while informed consent was signed.

Availability of Data and Materials

The data and other documents used in this study are available from the corresponding author.

Competing Interests

All authors confirmed that they have no conflict of interest.

Conflict of Interest

None

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