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Review Article

Epidemiology of respiratory distress in pregnancy and the newborn in Delta state Nigeria

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ABSTRACT

Epidemiology can be said to be the branch of medicine that deals with the incidence, distribution, and also possible control of diseases and other factors relating to health. Thus, epidemiology includes controlled clinical evaluations of different treatment methods; comparative assessment of lifestyle factors, such as smoking, drugs, and drinking habits; estimations of the risks of occupational factors; and cross-sectional and time-series analyses of factors that may affect health. To identify epidemiology of respiratory distress in pregnancy and new born. 34 international publications on respiratory distress disease in pregnancy and new born were reviewed for the presentation of this article. Respiratory distress syndrome (RDS) is a frequent newborn morbidity worldwide with reported prevalence of 18.5% in France, 4.24% in Pakistan and 20.5% in China. 20% of all global maternal deaths happen in Nigeria. Total number of maternal deaths in 2015 in the 46 most developed countries was 1700, resulting in a maternal mortality ratio of 12 maternal deaths per 100,000 live births. Given the state of the economy in the low and middle-income countries, Nigeria, like most of the other countries lack the resources (material, manpower and financial) require for optimal newborn care services. Newborn respiratory distress affects almost half of newborns. It is a major cause of neonatal admissions and has a high mortality rate. Many of its significant risk factors and etiologies are preventable. Adequate follow-up of pregnant women and during labor are of great necessity for early detection of risk factors and timely intervention in order to prevent the occurrence of neonatal respiratory distress.

Keywords: Neonatal respiratory distress, Epidemiology, Maternal mortality ratio, RDS

INTRODUCTION

Epidemiology can be said to be the branch of medicine that deals with the incidence, distribution, and also possible control of diseases and other factors relating to health. Thus, epidemiology includes controlled clinical evaluations of different treatment methods; comparative assessment of lifestyle factors, such as smoking, drugs, and drinking habits; estimations of the risks of occupational factors; and cross-sectional and time-series analyses of factors that may affect health. It all involves evaluating the statistical and biologic importance of variations in the frequency of occurrence of illnesses and related phenomena of health and health care. Epidemiologic study involves examination of the extent to which observed rates of a given phenomenon differ significantly from those that would be expected under specified conditions. With epidemiologic studies, one can validate the models used in predicting hazards and can characterize the actual and potential health effects of such exposures. In the same vain epidemiology can be said to be the study of the distribution and determinants of health related states or disease in human population and it is the

method for disease surveillance, outbreak investigation, and observational studies that identify risk factors of zoonotic disease in both human and animal population's thereby directing further research investigation and implementing disease control measures.[1]

Environmental epidemiology is all about determining how environmental exposures impact human health.[1] It seeks to understand how various external risk factors may predispose to or protect against disease, illness, injury, developmental abnormalities, or death. Environmental epidemiology studies the relationship between environmental exposures (including exposure to chemicals, radiation, microbiological agents, etc.) and human health. Observational studies, which simply observe exposures that people have already experienced, are common in environmental epidemiology because humans cannot ethically be exposed to agents that are known or suspected to cause disease. The inability to use experimental study design is a limitation of environmental epidemiology. This discipline directly observes effects on human health rather than estimating effects from animal studies. Being one of the most important tools used in environmental management decision making, environmental epidemiology owns its capacity to assess and monitor environmental hazards in different settings and quantify their health impact on the population at risk.[1] Environmental epidemiology seeks to clarify the relation between physical, biologic, and chemical factors and human health.

HEALTH EFFECT OF POLLUTION

A growing body of epidemiological research in recent years has focused on the potential impact of prenatal exposure to air pollution on birth outcomes. Although the bronchopulmonary tract has multiple protective mechanisms, such as mucosal cilia and air-blood barrier, air pollutants are able to accumulate in or pass through lung tissues dependent on the size and chemical nature of pollutants.[3] The vapor of air pollutants is prone to be absorbed by human tissues or dissolved in body fluids, mainly relying on their hydrophilicity and hydrophobicity. Particulate matter 10 micrometers or less in diameter (PM_{10}) particles with larger size (~10 μm) are able to reach the proximal airways and be mostly eliminated by mucociliary clearance. Particulate matter 2.5 micrometers or less in diameter (PM 2.5), as a notable risk factor for health, can invade more deeply into the lungs.[3,4] The ultrafine particles are capable of translocation through blood circulation to distal organs and tissues, such as liver tissue for detoxification and placental tissues during pregnancy.[4] The outcomes of those researches have been related to exposure to air pollution during pregnancy, which including low birth weight, reduced birth size, and intrauterine growth retardation.[5] A cohort study is the design of choice for evaluating the impact of air pollution on fetal growth as pregnancy is a process in which the relationship between a given type of exposure and an associated effect may be observed in a limited period of time.[6] Many researchers have investigated large populations using birth data from health care registries[7] whereas other cohort studies had smaller samples, but more detailed, primary data.[8] However, it is agreed the severity of air pollution is more on pregnant women, children, babies, those with respiratory problems, and the elderly.[9]

Table 1: Overview of main health effects on humans from some common types of pollution.[2]

Type	Air pollution	Water pollution	Soil contamination
Components	Lead, CO, Particulate matter, Ozone, volatile organic compound, SO_2, NO_X	Bacteria, Parasite, Chemical	Pesticides
Health Effect	Nerve damage, headache, fatigue, respiratory illness, cardiovascular illness, cancer risk, nausea, skin irritation	headache, fatigue, cardiovascular illness	headache, fatigue, cardiovascular illness, nausea, gastroenteritis

Burden of disease in pregnancy related to air pollution

Exposure to ambient air pollution during the pregnancy is considered having a long-term impact on human health. The prenatal stage is characterized with an exquisite inflammatory homeostasis in mother and mysterious organogenesis in developing fetus, together presenting a highly susceptible window in human lives for adverse effects of environmental pollutants.[10] Maternal exposure to air pollution can directly influence the fetus through the transfer of pollutant chemicals through amniotic fluid and placenta.[11]

In America one out of every twelve babies born are underweight with variety of reasons though exposure to air pollution while pregnant is speculated to cause this complication. An ideal pregnancy delivers six to nine-pound babies at 38-40 weeks. Babies less than five pounds eight ounces are considered low birth weight. Beate Ritz, an epidemiologist at the university of

California, Los Angeles school of public health, find it hard to breathe because of the smog when she first moved to Los Angeles in 1989. She had two pregnancies in the early 1990s and became concerned about how the air pollution may have had an effect on her children, which led her into the study on pregnant women and in one of her first studies, she found that babies born in Los Angeles between 1994 and 1996 and whose mothers were exposed to high levels of pollutants during pregnancy had lower birth weights and were more likely to be born preterm than babies whose moms breathed cleaner air.[12]

Children's burden of disease related to air pollution

Globally in 2016, one in every eight deaths was attributable to the joint effects of ambient air pollution (AAP) and household air pollution (HAP) with a total of 7 million deaths. About 543,000 deaths in children fewer than 5 years and 52,000 deaths in children aged 5-15 years were attributed to the joint effects of AAP and HAP in 2016, where HAP from cooking and AAP cause more than 50% of acute lower respiratory infections (ALRI) in children fewer than 5 years of age in LMICs and of the total deaths attributable to the joint effects of HAP and AAP worldwide in 2016, 9% were in children.[13]

Table 2: Death rate per 100,000 children attributable to effects of HAP and AAP in 2016.

WHO region	Income level	Children < 5 year	Children 5-14 year
African	LMIC	184.1	12.9
	HIC	4.3	1.4
Americas	LMIC	14.2	0.7
	HIC	0.3	0
South-East Asia	LMIC	75	2.5
European	LMIC	8.8	0.6
	HIC	0.3	0
Eastern Mediterranean	LMIC	98.6	3.6
	HIC	5.3	0.4
Western Pacific	LMIC	20.5	1
	HIC	0.3	0
All	LMIC	88.7	4.5
	HIC	0.6	0.1
World		80.5	4.1

LMIC- Low and middle-income country; HIC- High-income country; HAP- Household air pollution; AAP- Ambient air pollution.

An experiment was conducted recently with rats, where pregnant females were exposed to ultrafine ammonium sulfate particles by a geoscientist by name Renyi Zhang of Texas A and M University and his collaborators. Ammonium sulfate is a common air pollutant from industry and vehicle emissions, says Zhang, and the concentrations which were used by them are comparable to what can be found in cities in Asia. At the end of their study, they found that the offspring of pollutant exposed rats had lower birth weights, were born sooner, and were also more likely to be stillborn. Zhang and his team went further to use ultrafine particles in their study because those may be the most dangerous to fetuses. 'The small particles can actually get deeper into your body than the big particles,' says Zhang. Particulate matter that is smaller than 2.5 μm in diameter, and especially ultrafine particles that are 0.1 μm or smaller, can actually move through tissue.[7,12] Ritz says they are well known to be able to actually go through cell membranes, and be found in lung lining cells and the smallest particles can also cross the blood brain barrier or can eventually reach the placenta. The ability of very small particles to travel through the mother's body and potentially into the fetus could be how air pollutants cause health and developmental problems in children, according to Ritz.[12]

RDS in new born

This is also known as hyaline membrane disease, neonatal RDS, infant RDS, and surfactant deficiency. RDS is a common breathing disorder that usually affects newborns. RDS do occurs most often in babies born preterm, affecting almost all newborns that are born before 28 weeks of pregnancy. Less often, RDS can affect full term newborns. Premature newborns suffer from RDS because their lungs are not able to make enough surfactant. Surfactant is a foamy substance that keeps the lungs fully expanded so that newborns are able to breathe in air once they are born. Insufficient surfactant makes the lungs collapse and the newborn end up working hard to breathe. Due to their size they might not be able to breathe in enough oxygen to support the body's organs and lack of oxygen can damage the baby's brain and other organs if not treated promptly.

Newborn respiratory distress does present a diagnostic and management challenge. Newborns with respiratory distress commonly exhibit tachypnea with a respiratory rate of more than 60 respirations per minute. They may present with grunting, retractions, nasal flaring, and cyanosis. Common causes include transient tachypnea of the newborn, RDS, meconium aspiration syndrome, pneumonia, sepsis, pneumothorax, persistent pulmonary hypertension of the newborn, and delayed transition. Congenital heart defects, airway malformations, and inborn errors of metabolism are fewer common etiologies. Surfactant is increasingly used for RDS. The best technique to be used is for the newborn to be intubated, then given surfactant, and quickly extubated to nasal continuous positive airway pressure. Newborns should be screened for critical congenital heart defects via pulse oximetry after 24 hours but before hospital discharge.[14]

Infant RDS (IRDS) is the leading respiratory disorder among preterm infants (birth <37 gestational weeks). The disorder is caused by immaturity of the lungs, and if left untreated severe IRDS can lead to death. However, over the last three to four decades, pre- and perinatal treatment

has improved, leading to increased survival both of children born preterm and of preterm children with IRDS.[15,16]

RDS affects about 1 percent of newborn infants and is the leading cause of death in babies who are born prematurely.[17] About 12 percent of babies born in the United States are preterm, which is higher than in other developed countries.[15] Each year about 10 percent of premature babies in the United States develop RDS. With increasing prematurity, the risk of RDS rises. Babies born before 29 weeks of gestation have a 60 percent chance of developing RDS, but babies born at full term rarely develop this condition.[18]

EPIDEMIOLOGY OF RESPIRATORY DISEASES RELATED TO AIR POLLUTION

Maternal risk factors for preterm birth include previous preterm birth, periodontal disease, low maternal body mass, poor prenatal care, poverty, being uninsured, and being a member of a minority group.[19] RDS is the commonest cause of newborns' hospital admissions with reported estimate of 33%. Hence it is suggested that swift diagnosis and intervention are important to improve outcomes, which connote importance of primary healthcare.[20] As may be expected; however, epidemiological factors and prevalence differ with geographical locations vis-à-vis the environment determinants.

Epidemiology- global

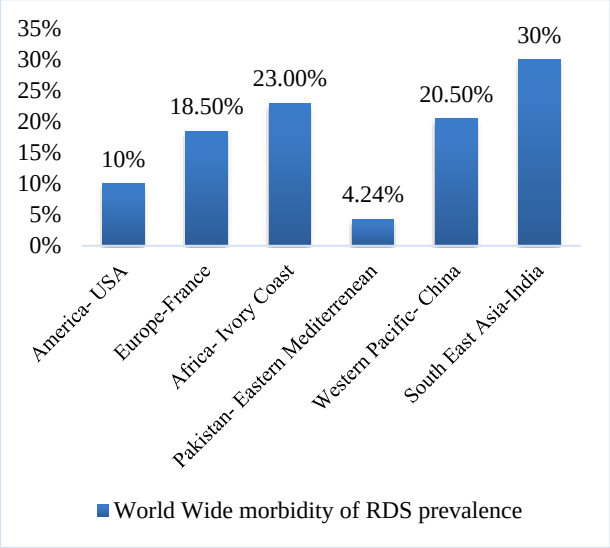

Figure 1: Worldwide morbidity of RDS prevalence.

RDS global prevalence is shown in figure 1.[21,22] Although RDS is not uncommon in term infants, it was found that 6.8% of RDS cases are in term or near-term infants.[23] In another study, 48/1986 (2.42%) newborn developed RDS, of which 7 (14.6%) were more than 2500 grams.[24] The reported incidence of RDS in a center in Pakistan was 1.72%, of which 6.38% were term infants.[25] Another study indicated a prevalence of 0.15% (13/8634) in infants born at more than 37 weeks' gestation. The reported risk factors that are associated with RDS include male gender, caesarian section delivery, maternal medical conditions including metabolic diseases, and multiple pregnancies.[26,27]

The world health organization (WHO) says the high number of maternal deaths in some parts of the world reflects inequities in access to health services, and highlights the gap between rich and poor. Nearly 100% of global maternal deaths occur in developing countries with more than half of these deaths occurring in sub-Saharan Africa and almost one third happening in South Asia. More than half of maternal deaths occur in fragile and humanitarian settings. WHO adds that poor women in remote areas are the least likely to receive adequate health care. This is especially true for regions with low numbers of skilled health workers, such as sub-Saharan Africa and South Asia. Globally in 2015, births in the richest 20% of households were more than twice as likely to be attended by skilled health personnel as those in the poorest 20 per cent of households (89 versus 43%). This means that millions of births are not assisted by a midwife, a doctor or a trained nurse.

On the other hand, acute RDS (ARDS) is a severe lung condition. It occurs when fluid fills up the air sacs in your lungs. It is a state of diffuse inflammatory lung injury characterized by acute-onset, non-cardiac pulmonary edema with hypoxemia as defined by an arterial partial pressure of oxygen-to-inspired oxygen ratio of under 300,[28] and causes refractory hypoxemia, increases lung 'stiffness' and impairs the ability of the lung to eliminate carbon dioxide. ARDS is a rare occurrence in the pregnant patient with an estimated incidence of 16-70 per 100,000 pregnancies.[29,30] Ranieri also said ARDS is an acute inflammatory lung injury, associated with increased pulmonary vascular permeability, increased lung weight, and loss of aerated lung tissue. Having too much fluid in your lungs can lower the amount of oxygen or increase the amount of carbon dioxide in your bloodstream. ARDS can prevent your organs from getting the oxygen they need to function, and it can eventually cause organ failure. It is a medical emergency and a potentially life-threatening condition. Those that are hospitalized are those that are commonly affected by ARDS which are caused by trauma. ARDS is a rare occurrence in the pregnant patient with an estimated incidence of 16-70 per 100,000 pregnancies.[29,30]

Epidemiology - sub-Sahara Africa

The etiologies and risk factors associated with newborn respiratory distress have not been well cited in low-income countries and particularly sub-Saharan Africa.[21,22,31] The risk factors found in high-income countries include prematurity, male gender, asphyxia, caesarean delivery, maternal diabetes mellitus, and

hypertensive disorders of pregnancy, antepartum hemorrhage, multiple pregnancies, and rapid labor. Newborn respiratory distress can be caused by a benign etiology, such as transient tachypnea of the newborn, or could be the first manifestation of serious infection, encephalopathy or congenital malformations. Early detection of its risk factors and anticipation of the management of its etiologies are imperative.[21,22] A tremendous decrease in the newborn respiratory distress specific mortality rate has occurred over the past six decades in high-income countries due to several innovations in neonatology that are insufficient or non-existent in low-income countries.[21,22,31] However, there have been gradual improvements in health infrastructures and level of care in sub-Saharan Africa over time.

According to UNICEF report in 2013, global under-five mortality rate has been reduced by 47% since 1990. Yet, this still means that 216 million children under-five years of age died in the subsequent 23 years. Sub-Saharan Africa has the highest child mortality rate in the world but also has the fastest population growth; and up to 50 % of infant deaths in their first day of life. Among the top five culprit countries is Nigeria.[32] Between 2009 and 2011, a study of the leading causes of death in the taboo health and demographic surveillance system (HDSS) in south-central Côte d'Ivoire (a rural region of West Africa) revealed that of the 712 deaths analyzed, maternal and neonatal conditions accounted for 8.3% of deaths, primarily due to pneumonia and birth asphyxia in newborns.[33] Interventions in spite of challenges in this region of the world have led to mortality reductions. Greater reductions in child mortality as well as gains in coverage for interventions in child survival has been achieved by Niger Republic than neighboring countries in West Africa. The mortality rate in children younger than 5 years declined significantly from 226 deaths per 1000 live births in 1998 to 128 deaths in 2009, an annual rate of decline of approximately 5%. It was estimated that about 59,000 lives were saved in children younger than 5 years using a lives saved tool (LiST). This decrease in child mortality was attributed to the introduction of insecticide-treated bed nets; improvements in nutritional status; vitamin A supplementation; treatment of diarrhea with oral rehydration salts and zinc, and care-seeking for fever, malaria, or childhood pneumonia; and vaccinations as shown in figure 2.

A developing country with a well-established medical infrastructure like South Africa, the neonatal and childhood mortality is surprisingly high. The top five leading causes of death in 1266 children under 5 years of age treated at the Pietersburg/Mankweng hospital complex in the north of South Africa were prematurity/low birth weight, pneumonia, diarrheal diseases, birth asphyxia, and severe malnutrition. The ten most common conditions represented 73.9 % of mortality causes at this facility (which are prematurity/low birth weight, pneumonia, diarrheal diseases, birth asphyxia, and severe malnutrition, HIV/AIDS, hydrocephalus, unintentional injuries, meningitis and other infections).[34]

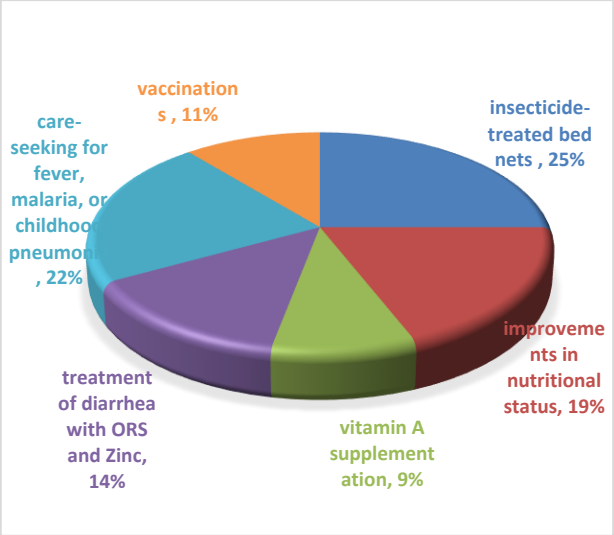

Figure 2: Factors attributed to decrease in child mortality.[33-35]

Epidemiology-Nigeria

Given the state of the economy in the low and middle-income countries, Nigeria, like most of the other countries lack the resources (material, manpower and financial) require for optimal newborn care services. Therefore, the newborn care physicians in Nigeria need to be innovative, learn to apply the basic principles of child health and adopt a holistic approach in their practices. This group of practitioners cannot rely too much on the availability of equipment and other facilities, as it obtains in the high-income parts of the world, to impact on newborn care in their setting. According to the 'world health organization on maternal health in Nigeria, almost 20% of all global maternal deaths happen in Nigeria. Between the year 2005 and 2015, there was an estimate that over 600,000 maternal deaths and no less than 900,000 maternal near-miss cases occurred in the country. Figure 3 shows the estimates of maternal mortality in Nigeria compared with 46 most developed countries in 2015.

In fact, a Nigerian woman has a 1 in 22 lifetime risk of dying during pregnancy, childbirth or postpartum/post-abortion; whereas in the most developed countries, the lifetime risk is 1 in 4900.[35] About 15% of term infants and 29% of late preterm infants admitted to the neonatal intensive care unit develop have significant respiratory symptoms; this is even higher for infants born before 34 weeks' gestation.[26,36] The clinical presentations of respiratory distress the newborn include difficulty with breathing (nasal flaring, recessions or retractions in the intercostal, subcostal, or supracostal spaces, grunting, head nodding); too fast breathing (tachypnoea-respiratory rate more than 60 breaths per minute); too slow or shallow breathing (bradypnoea-respiratory rate less than 30 per minute, apnea); noisy breathing (stertor, expiratory

wheezes, inspiratory stridor, grunting) or hypoxemia (cyanosis); with or without associated disorders like poor feeding, poor colour, poor activities, vomiting. Regardless of the cause, if not recognized and managed quickly, respiratory distress can escalate to apnea, respiratory failure, cardiopulmonary arrest and death.[26]

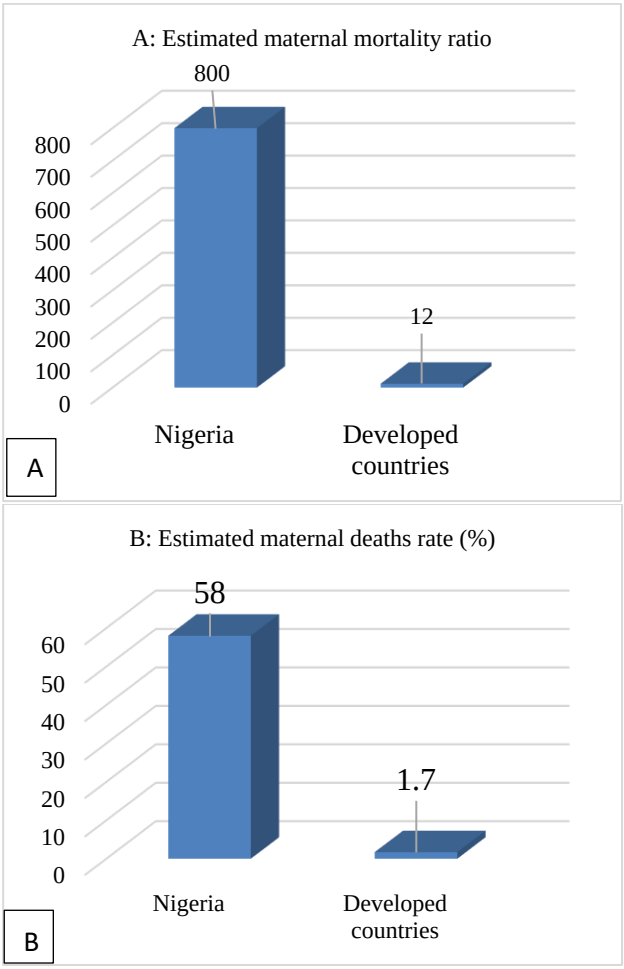

Figure 3: Comparison of maternal mortality and death in Nigeria relative to developed countries.

Even though respiratory distress in newborn is not limited to any part of the world, predominant causes differ from region to region. Racial and gender predilection to neonatal respiratory distress are unknown.[14] Causes may differ based on factors like sepsis rate, preterm rate, small for gestational age rate. However, in many developing countries where there are no facilities for mechanical ventilatory support, management of respiratory distress can be a herculean task.

Though, RDS is common among the newborn in developing countries, there is dearth of data on the subject from Nigeria, especially Delta State. Although, it is known that the major causes of newborn morbidities and mortality include birth asphyxia as common (Figure 4).[37]

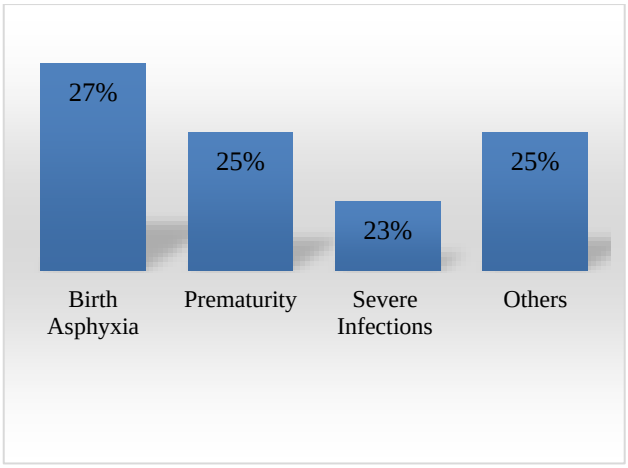

Figure 4: Major causes of newborn morbidities and mortality in Nigeria.

Efforts to address some of these underlying causes of mortality among infants and young children through the child survival strategies (CSS) gave less attention to neonatal health.[38] Other contributory factors like the poor health-seeking behaviour of women, low hospital delivery rate with a low skilled attendance at birth (ranging from 35% to 40%), were not directly addressed by the CSS.[37] Neonatal care services including routine care of well newborn infants were provided by only major teaching hospitals in Nigeria in the past. Sophisticated and highly specialized neonatal care facilities were not available even though sick babies were cared for in the neonatal ward, also delivery room resuscitation of the newborn was not routinely done making birth asphyxia, prematurity, sepsis, respiratory disorders and jaundice the major killers of newborn babies.[39] By 1990, it was realized that further reductions in neonatal mortality could not be achieved unless attention was shifted to the care of the extremely low birth weight infants using intensive care unit (ICU) facilities, particularly, respiratory support.[31] This management strategy was instituted in 2013 and small babies are now ventilated in the context of neonatal ICU.

DISCUSSION

RDS is a common breathing disorder that usually affects newborn. They occur mostly in babies born preterm, affecting almost all newborn that are born 28 weeks of pregnancy and in few cases, it affects full term newborns. Preterm newborns suffer RDS because their lungs are not able to make enough surfactant which is a foamy substance that keeps the lungs fully expanded so that newborns are able to breathe in air once they are born. Newborn with respiratory distress so exhibit tachypnea with a respiratory rate of more than 60 respirations per minute and my present with grunting, retraction, nasal flaring and cyanosis. Newborn respiratory distresses usually occur in about 7% of deliveries and affect 1% of newborn, resulting in about 860 deaths per year and is a

leading cause of death in babies who are born prematurely.[14]

In the United State about 12 percent of babies born are preterm and is higher than in other developed countries.[15] With increasing prematurity, the risk of RDS rises. Babies born before 29 weeks of gestation have a 60 percent chance of developing RDS but babies born at full term rarely develop this condition. The total number of life birth in the United State for all races was 4,089,950 in 2003; and about 0.6 percent of newborn had RDs (about 24,000 or 6 per 1,000 live births).[20] Then in the year 2005, there were 4,138,000 live births in the United States, and a slightly larger number of babies were affected with RDS because the rate of premature births had increased from 11.6 percent to 12.7 percent, mainly due to a rise in late preterm births (34 to 36 weeks of gestation). Even though the number of RDS cases in the United States is growing, the infant mortality rate from RDS has dramatically declined from about 25,000 deaths per year in the 1960s to 860 deaths in 2005 because of surfactant replacement therapy. Infant deaths from RDS were 2.6 times greater in African American babies than in Caucasian babies, although Caucasian babies are at a higher risk to develop the condition. RDS is a frequent newborn morbidity worldwide with reported prevalence as shown in figure 1 above. Nigerian woman has a greater risk of dying during pregnancy, childbirth or postpartum/post-abortion when compared with most developed countries.[35]

CONCLUSION

Newborn respiratory distress affects almost half of newborns. It is a major cause of neonatal admissions and has a high mortality rate. Many of its significant risk factors and etiologies are preventable. Adequate follow-up of pregnancy and labor for early detection of risk factors and timely intervention may improve the outcome of neonatal respiratory distress. RDS stays one of the major problems among newborns and it is considered to be the major reason for increased morbidity and mortality among infants, newborn respiratory distress affects almost half of newborns. It is a major cause of neonatal admissions and has a high mortality rate. Prematurity is a predictor of newborn respiratory distress. Prematurity goes along with structural and functional immaturity of the lungs (a deficiency in pulmonary surfactant).[40] Many of its significant risk factors and etiologies are preventable. Adequate follow-up of pregnancy and labor for early detection of risk factors and timely intervention may improve the outcome of newborn respiratory distress. A minimum of four antenatal visits during pregnancy is recommended by WHO. The good follow-up of pregnancy allows early detection and management of potential threats to the mother and newborn. Respiratory distress in term infants is still a significant cause of admission to newborn intensive care unit and a predisposing factor for mortality and morbidity. Preterm babies are the main risk factor for development of RDS. Mother's illnesses, especially hypertension and diabetes are very strong risk factors for the disease in preterm babies. There is little or no data from Delta State.

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