DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

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RESPIRATORY DISTRESS, ASSOCIATED RISK FACTORS AND EARLY OUTCOME AMONG NEONATES ADMITTED AT MUHIMBILI MEDICAL CENTRE, DAR ES SALAAM.

by

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ABSTRACT

Respiratory distress is the most frequent life threatening morbidity to occur in the neonate. A prospective unmatched case control study on respiratory distress, associated risk factors and early outcome among neonates admitted at MMC was carried out for 8 months from March to November 1995. 648 neonates were studied, 328 of these were cases and 320 were controls.

Respiratory distress contributed to 7.6% of all the neonatal admissions. Overall, respiratory distress contributed to 18.7% of all the neonatal deaths during the study period. The mortality rate among neonates with respiratory distress was 45.4%.

6% of all the neonatal admissions were due to Respiratory distress syndrome (RDS). Neonates with RDS had significantly lower birth weights and gestational age compared with the controls. Birth asphyxia increased significantly the proportion of neonates with RDS. EPH gestosis significantly lowered the proportion of neonates with RDS.

The frequency of RDS in males was significantly higher than in females. There was no significant association between RDS and mode of delivery, antepartum haemorrhage or premature rupture of membranes of more than 24 hours. Expiratory grunting was significantly associated with increased mortality among RDS cases.

Pneumonia in the first week of life contributed to 1.5% of all the neonatal admissions during the study. Meconium stained liquor was significantly associated with increased frequency of pneumonia in the first week of life. However, there was no significant association between pneumonia occuring in the first week of life and premature rupture of membranes, prolonged labour or birth asphyxia.

Since RDS which is more or less confined to the preterm infant was the commonest disorder causing respiratory distress in the newborn, it should be possible to reduce its incidence by measures aimed at preventing premature delivery.

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DECLARATION

I declare that this dissertation is my own original work, and that it has not been submitted for a similar degree in any other University.

..... 7-11-96

G.S. MLAY Date

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ABBREVIATIONS

ABD	Assisted Breech Delivery
AMP	Adenosine Monophosphate
APH	Antepartum Haemorrhage
BOH	Bad Obstetric History
CCM	Chama Cha Mapinduzi
CDH	Congenital Diaphragmatic Hernia
CHD	Congenital Heart Disease
CPD	Cephalopelvic Disproportion
EPH Gestosis	Edema, Proteinuria and Hypertension during Gestation.
GA	Gestation Age
IVH	Intraventricular Haemorrhage
LSCS	Lower Segment Caesarean Section
LCVE	Low Cavity Vacuum Extraction
MAS	Meconium Aspiration Syndrome
MMC	Muhimbili Medical Centre
NEC	Necrotizing Enterocolitis
OFC	Occipital Frontal Circumference
$Pa0_2$	Arterial partial Pressure of Oxygen
PDA	Patent Ductus Arteriosus
PROM	Premature Rupture of Membranes
RDS	Respiratory Distress Syndrome
SVD	Spontaneous Vaginal Delivery
TBA	Traditional Birth Attendant

TGA	Transposition of Great Arteries
TOF	Tetralogy of Fallot
TTNB	Transient Tachypnoea of the Newborn
USA	United States of America
VSD	Ventricular Septal Defect

1.0 INTRODUCTION AND LITERATURE REVIEW

Respiratory distress is the most frequent life threatening morbidity to occur in the newborn. Respiratory distress is defined as respiratory rate of 60 per minute or greater and is accompanied by other physical signs which include cyanosis, intercostal, subcostal, suprasternal and substernal retraction, flaring of alae nasae and expiratory grunting.[1] Various conditions can cause respiratory distress in the newborn and these include both pulmonary and extrapulmonary causes.[2] Among the pulmonary disorders the most common conditions are Respiratory distress syndrome, Transient tachypnoea of the newborn, meconium aspiration syndrome, pneumonia and pneumothorax; less common causes of respiratory distress are pulmonary hypoplasia, upper airway obstruction, rib cage abnormalities, space occupying lesions such as diaphragmatic hernia and pulmonary haemorrhage. The extrapulmonary disorders causing respiratory distress in the newborn are vascular abnormalities like persistent foetal circulation, congenital heart diseases, hypovolemia, anaemia and polycythemia; and the neuromuscular disorders such as cerebral oedema, cerebral haemorrhage, drugs, muscular disorders, spinal cord problems and phrenic nerve damage.

1.1 PULMONARY CAUSES

1.1.1 Respiratory distress syndrome. (RDS)

Respiratory distress syndrome is a physiological manifestation of neonatal pulmonary immaturity and is still the major cause of neonatal morbidity and mortality.[3] It is the most common pulmonary disorder in the newborn and is also a leading cause of deaths, accounting for 25,000 neonatal deaths annually in USA; and it is estimated that 50% of all neonatal deaths are the result of RDS and its complications.[1] RDS occur due to failure to develop functional residual capacity and the tendency for the affected lungs to become atelectatic. This correlates with high surface tension and absence of surfactant. Surfactant is a lipid

compound with dipalmitoly-phosphotidylcholine (lecithin) as its major constituent, other constituents are phosphotidylgycerol, two apoproteins and cholesterol.[4] RDS is rare in term infants and occurs with increasing frequency and severity at decreasing gestation age. Other factors which probably predispose to RDS are intrauterine hypoxia or birth asphyxia, antepartum haemorrhage (APH), maternal diabetes, caesarean section and sepsis.[5]

RDS is diagnosed by clinical manifestation of tachypnoea, expiratory grunting, retractions and increasing oxygen requirements, and the radiological findings of groundglass appearance, reticulogranular densities and air bronchogram.[6] The incidence of RDS is difficult to determine because of differing diagnostic criteria. However, in USA it occurs in about 60% of those between 32-36 week's gestation and in about 5% before 37 weeks gestation and rare at term.[4] In the same country, Annibale et al[7] in their study involving 522 newborns with birth weights between 600grams and 1750grams, the incidence of Hyaline membrane disease or RDS was 47.3% while Hales et al[8] in a case control study consisting of 692 term neonates reported an overall frequency of respiratory morbidity of 5.1%. Luerti et al[9] in a large survey conducted between 1980 and 1985 in selected periods in 11 neonatal units placed in 5 Italian regions involving 1624 liveborn infants of 26-37 week's gestation showed that a total of 131 (7.8%) newborns developed RDS and the frequency was higher in males than in females. However, it has been argued that in developing countries there is greater maturity for birth weight and low incidence of RDS when compared with developed countries.[10] Singh et al[11] in a 4 year study of neonatal morbidity in a New- Delhi Hospital involving 7,015 neonates diagnosed RDS in 5.7% of all neonates studied.

In another study conducted in Cape Town (South Africa) in 1960, the incidence of RDS was 12.6% for infants born before 38 week's gestation and 8 years later, Malan et al[12] found that the overall incidence of RDS in gestation up to and including 38 weeks was 5%. In a study of morbidity and mortality pattern of 327 admissions at Special Care Baby Unit at the

University College Hospital in Nigeria in a 1 year period, Dawodu et al[10] found that the incidence of respiratory distress in infants weighing more than or equal to 2000 grams was 16.8% while for those weighing more than or equal to 2000 grams was 23.1%. The overall frequency of respiratory distress was 19.9%. In the study of morbidity and mortality of admissions to the Special Care Baby Unit at New Mulago Hospital Kampala Uganda involving 1598 infants during the 12 months period of 1989, the overall neonatal mortality rate was 18% and the major causes of deaths in descending order of frequency were; birth asphyxia, RDS, aspiration syndromes, very low birth weights, infections, and congenital malformations. Birth asphyxia was the most common cause of death in infants weighing over 2500grams while RDS predominated among deaths below 2500grams.[13] In Tanzania the exact incidence of RDS is unknown and the little information available as part of other studies indicate a marked difference due to different methodology. Mbise et al[14] in the study of morbidity and mortality among 335 low birth weight infants at Muhimbili Medical Centre (MMC) Dar es Salaam revealed an incidence of RDS of 14.3% In another study of neonatal outcome among low birth weight infants and factors related to outcome done at the same hospital Manji[15] found the incidence of RDS of 2.8%. However, the later study had more stringent criteria.

Factors influencing incidence of RDS

Caesarean Section

Caesarean section performed before onset of labour is an important factor in the aetiology of surfactant deficiency and hence RDS. In USA, a case-control study by Hales et al[8] involving 692 term neonates delivered by either elective caesarean section or caesarean section in labour or vaginally, 9.1% of neonates delivered by caesarean section developed respiratory morbidity compared to 0.6% of neonates delivered vaginally. In the same study, when compared, the neonates delivered by caesarean section after onset of labour and those delivered by caesarean section before onset of labour, a high frequency of respiratory morbidity was found among those delivered by elective caesarean section; 23 out of 186 (12.4%) and 10 out of 177 (5.6%) respectively. In the Cape Town study by Malan et al[12] there was a significant increase in the incidence of RDS after caesarean section compared with vaginal delivery; 48 out of 624 (7.7%) compared with 163 out of 3551 (4.6%) respectively.

Maternal Diabetes Mellitus

Maternal diabetes mellitus has been established as a factor in increasing the risk of RDS. In the comparison between the incidence of RDS in 805 infants of diabetic mothers and 10,152 controls from Joslin clinic, Boston; when standardized for risk factors such as gestational age and route of delivery, the incidence of RDS was 5.6 times greater in the diabetic group.[16] In Madison, USA, Curet et al[17] in the study of amniotic fluid phospholipid content and RDS in diabetic and non diabetic pregnancies found that three of the 69 (4.5%) diabetic patients and 26 of the 514(5.3%) non diabetic patients had infants who developed RDS. In this study the incidence of RDS was highest at less than 32 week's gestation (42%) and lowest after 37 week's gestation (0.6%). In the Cape Town study[12], of 178 infants born to mothers with diabetes only one developed RDS, while the 1966 figures though small suggested a correlation between maternal diabetes and the incidence of RDS.

Role of Steroids and Premature Rupture of Membranes in Reducing the Incidence of RDS.

Premature rupture of membranes (PROM) of more than 24 hours, high risk pregnancies involving placental insufficiency, amnionitis or endometritis may result into acceleration of lung maturation and hence low incidence of RDS, probably on the basis of increased endogenous production of corticosteroid secondary to stress.[16] Controlled double blinded studies have demonstrated that administration of glucocorticoids to the mother before premature delivery decreases the incidence of RDS.[18] Besides glucocorticoids, thyroid releasing hormone, catecholamines, drugs that elevate cyclic AMP, prolactin and oestrogen may enhance maturation whereas others such as insulin and testosterone may delay maturation. However, Hallak et al[19] in Detroit in a retrospective analysis of 1935 patients who were delivered between 24 and 35 week's gestation and for whom data was available; when they controlled for gestational age or birth weight, they would find no difference in the frequency of RDS related to PROM (P=0.08), but there was a suggestion that RDS was actually more frequent after PROM. In Ireland, Crowly et al[20] in a systematic review of data from 12 controlled trials involving over 3,000 participants, showed that corticosteroids reduce the occurrence of RDS overall and in all subgroups of trial participants that were examined. The reduction in the respiratory morbidity was associated with a reduction in the risk of intraventricular haemorrhage (IVH), necrotizing enterocolitis (NEC) and death. In USA, Garite et al[21] in a double blind placebo controlled clinical trial of betamethasone given to mothers with intact membranes and threatened premature delivery between 24 and 28 weeks of pregnancy where 36 patients were randomized to receive betamethasone (2 doses) and 41 received placebo, found no difference in the overall incidence of RDS between the two groups. In Lebanon, Suidan et al[22] found that babies born after premature rupture of membranes at 28-32 week's gestation had a significantly lower incidence of RDS than in

babies without premature rupture of membranes. In the same study, the incidence of RDS among babies exposed prenatally to a complete course of steroids between 28-32 week's gestation was about half the incidence of RDS observed in the untreated babies of the same gestational age. In Nigeria, Aerede[23] in the study of neonatal outcome in 109 pregnancies complicated by premature rupture of membranes found no protective effect or benefit from premature rupture of membranes in relation to development of RDS.

Effect of Hypertension in Pregnancy

There is a controversy over the effects of hypertension in pregnancy on the incidence of neonatal respiratory distress syndrome. Tubman et al[24] in Northern Ireland investigated the association between maternal hypertension and the incidence of RDS in 268 very low birth weight babies of less than 34 week's gestation and found that maternal hypertension was associated with an increased incidence of RDS. Malan et al[12] in their study on the incidence of RDS in Cape Town found that toxaemia defined as maternal hypertension (Blood pressure exceeding 140/90mmHg at rest with patient lying down) with or without albuminuria significantly lowered the incidence of RDS.

Role of surfactant in the treatment and prevention of RDS

Exogenous surfactant preparations have been tested in both the prevention and treatment of RDS. Preparations have varied from synthetic surfactant to modified or unmodified extracts of natural surfactant. In USA, Soll et al[25] in a trial of single dose of modified bovine surfactant extract for prevention of RDS where 79 infants were treated with surfactant and 81 with air placebo, infants receiving the surfactant had less severe radiographic changes at 24 hours of age and a decreased average fraction of inspired oxygen, (31% versus 42%, P = 0.002) compared with the control group. A beneficial effect was noted on the incidence of pneumothorax and an increase was noted on the incidence of NEC. No difference on the incidence of patent ductus arteriosus (PDA), intraventricular haemorrhage and sepsis or bronchopulmonary dysplasia were seen. Long et al[26] in a multicenter double-blind placebo controlled rescure trial conducted at 21 American hospitals where two doses of synthetic surfactant or air was administered to 419 infants weighing 700-1350 grams who had RDS and arterial/alveolar oxygen pressure ratio < 0.22, reported that among infants receiving synthetic surfactant, improvement in alveolar-arterial oxygen pressure ratio and oxygen and ventilator needs through seven days of age were apparent. Deaths from RDS were reduced by two thirds. The incidences of pulmonary interstitial emphysema and pneumothorax were reduced by half and one third respectively. The incidence of other complications of RDS and prematurity including NEC, PDA and IVH did not differ in the two groups. There was no significant reduction in the incidence of bronchopulmonary dysplasia. Henrik et al[27] in a multicenter study in Sweden and Denmark where 35 infants with moderate to severe RDS were assigned to surfactant therapy plus a nasal continuous airway pressure and 33 infants to nasal continuous airways pressure alone, reported that there was a significant increase in the mean arterial oxygen tension in the surfactant treated babies and the need for subsequent mechanical ventilation was significantly reduced with surfactant therapy.

1.1.2 Meconium Aspiration Syndrome (MAS)

Meconium is present in the amniotic fluid in 10% of all births, and its presence suggests that the infant may have suffered some asphyxial episode in utero.[2] Meconium inhaled by the foetus may become lodged in the trachea or bronchi causing mechanical obstruction leading to impaired aeration of the lungs, and chemical inflammation leading to atelectasis and pulmonary shunting, all causing a severe form of respiratory insufficiency. The infants are often meconium stained and usually have tachypnoea frequently up to 100 breaths per minute.[28] The finding of meconium stained gastric aspirate, finger nails and skin may be confirmatory. Cyanosis is obvious in the most severely affected infants while chest retractions are not a prominent sign.

Chest X-ray shows coarse non- uniform irregular shadows, the lungs are overinflated and pneumothorax, emphysema and pneumomediastinum may be present.[28] Factors that apparently place meconium stained neonate at highest risk of meconium aspiration syndrome includes postmaturity, maternal toxaemia, prolonged labour and moderate to severe foetal heart deceleration.[16] In a six months clinical investigation, Gregory et al[16] examined the mouth and trachea immediately after birth of all babies with meconium stained amniotic fluid and found that 8.8% of 1000 babies had meconium in the amniotic fluid and 4.6% had it in the trachea. In 8 infants (0.8%) meconium was present in the trachea but not the mouth. Of the cases with meconium in the trachea half (23 babies) developed severe respiratory symptoms and abnormal chest X-rays, and 7 of these babies developed pneumothorax or pneumomediastinum.

Wissel et al[29] studied a population consisting of all neonates in several USA army medical centres in a period of 15 years (1973-1987). Total number of deliveries were 176,790 liveborn neonates and of these 21,472 (12.5%) were complicated by meconium stained amniotic fluid. Of the meconium stained neonates 1162 (5.41%) had a diagnosis of MAS and

69 of them died; half succumbed on the first day. In the same country Nathan et al[30] compared prospectively the outcome in 8,136 term singleton cephalic pregnancies with meconium and 34,573 similar pregnancies with clear amniotic fluids and found that perinatal mortality increased from 0.3 per 1000 births with clear amniotic fluid to 1.5 per 1000 births with meconium ($P < 0.001$) and most of these deaths resulted from meconium aspiration. Again in USA, Yoder[31] in a prospective study of 4,938 liveborns more than 36 week's between January 1990 and December 1992, found that 799 (16%) had meconium stained amniotic fluid and MAS was significantly more common in suctioned infants compared with those selectively not suctioned. In India, Narang et al[32] found meconium stained amniotic fluid amongst 7.4% of all deliveries and among these 238 (10.5%) babies developed MAS; passage of thick meconium was significantly associated with severe asphyxia and carried a bad prognosis with an increased risk of development of MAS, hypoxic ischaemic encephalopathy, seizures and pulmonary air leak syndrome. In the same country a prospective study involving 150 infants with wheezy attacks by Gupta et al[33] revealed that 40% of the cases had previously had MAS compared with 2.6% of the controls. Sunoo et al[34] in Hawaii in their study on the incidence of meconium aspiration found meconium in amniotic fluid in 2,633 obstetric patients and MAS occurred in 77 cases out of 14,527 deliveries.

All deaths associated with meconium as well as 84% of the cases of severe MAS occurred in infants born of patients with oligohydramnios and a gestational age of 41 weeks or greater. In Malaysia, Malik et al[35] studied the outcome in 148 inborn meconium stained neonates prospectively over a 5 months period and found that 53 infants (38.5%) developed MAS. There was a significantly higher rate of meconium aspiration syndrome, mechanical ventilation and hospital stay in neonates with meconium in the trachea than in neonates with no meconium in the oropharynx. In Tanzania, Mbise et al[14] found that 5.9% of 335 low birth weight infants had aspiration syndromes.

1.1.3 Transient Tachypnoea of the Newborn (TTNB).

This is a mild transient form of respiratory distress which has been attributed to delayed clearance of foetal lung liquid in the first few hours after birth.[16] The criteria for diagnosing TTNB consists of early evidence of tachypnoea, transient cyanosis at room air, nasal flaring, grunting and retraction. However, significant improvement is observed by 24-48 hours of life.[8] For this diagnosis, supplemental oxygen is often but not always required, chest X-ray may demonstrate diffuse haziness in both lung fields with some clearing towards the periphery and occasional interlobar fissure fluid. The condition is more common in children delivered by caesarean section; more liquid is probably present in the lungs at birth after caesarean section than after normal delivery, indeed the delayed rise in arterial partial pressure of oxygen (PaO2) as compared with normal births suggest a slower than normal clearance of liquid from the lungs.[16] In Tanzania, Manji[15] in his study on neonatal outcome among low birth weight babies and factors related to outcome reported that 1.5% of the neonates had TTNB.

1.1.4 Pneumonia in the Newborn

Pneumonia is an important cause of morbidity and mortality in the newborn infant and is the most common inflammatory lesion found at autopsy in the neonatal period.[4] Congenital pneumonia is caused by inhalation of infected amniotic fluid and is frequently associated with premature rupture of membranes, chorioamnionits, prolonged labour, premature labour or foetal distress.[16] It is most commonly associated with group B streptococcus, gram negative enteric bacilli, Chlamydia and Herpes simplex virus.[4] Accurate diagnosis of congenital pneumonia may be difficult because the affected neonate is often apnoeic at birth and later shows the same type of grunting respiration with subcostal and sternal retraction and cyanosis which is seen in RDS. Besides, pneumonia is equally common in premature and mature

infants.[36] Pneumonia may also be acquired postnatally with symptoms usually not evident until after several days of life and is caused by Staphylococcus aureus, Pseudomonas aeurogenosa, Klebsiella, Serratia spp. and respiratory viruses.[4] The infant with pneumonia will present with signs of respiratory distress consisting of tachypnoea, grunting and mild to moderate retraction. Dullness, decreased breath sounds and rales may be elicited but signs of pneumonia are often absent.[28] Chest X-ray signs vary from bilateral homogenous consolidation seen in inutero pneumonia to patchy bronchopneumonia which occurs in postnatal infections. In USA, Schaffer et al[37] in a review published in 1955, reported pneumonia in 35% of all autopsies and believed it to be the cause of death in 8% of those infants. Aerede[23] in the study of neonatal outcome in 109 pregnancies complicated by prolonged rupture of foetal membranes over a 3 year period, reported an overall mortality of 29 (26.6%) and 19 of these deaths were from infections of which 12 were pneumonia. In Dar es Salaam Tanzania, Mbise et al[14] found pneumonia in 3% of 335 low birth weight infants.

1.1.5 Pneumothorax

Pneumothorax develops when extra-alveolar air ruptures into the pleural space with partial or complete collapse of the affected lung and it usually appears as a complication of some other respiratory problem.[38] Conditions predisposing to the development of pneumothorax include foetal distress or difficult delivery, aspiration of meconium, amniotic fluid, blood or mucus, vigorous resuscitation at birth, and intermittent positive or negative pressure mechanical ventilation.[39] With a small pneumothorax there may be mild apnoeic spells, irritability or restlessness, while more severe cases demonstrate respiratory distress with tachypnoea, grunting, retractions and cyanosis. A tension pneumothorax may be noted clinically by finding of a unilateral bulge of the chest wall with decreased breath sounds and

shift of the cardiac apex beat away from the side of the pneumothorax. Pneumothorax is usually evident radiologically as a radiolucency between the parietal and visceral pleura. Depending on the degree of tension, there is shift of the heart and mediastinum away from the involved side while the underlying ipsilateral lung collapses to a variable degree.[39] In Indonesia, Boedjang[38] reported that out of 7,445 neonates born at Ciptomangunkusumu General Hospital in 1987 and 1988, 2,368 neonates suffered from respiratory difficulties and among these 10 babies had pneumothorax. Pneumothorax occurred as a complication of severe asphyxia (due to over vigorous initial resuscitation) and its incidence was 0.09%, that of RDS 2.13%, bronchopneumonia 6.25% and aspiration pneumonia 2.8%. The overall incidence of pneumothorax in the newborns with respiratory difficulties was 0.42% and the mortality was 20%. Mandal et al[40] studied 54 infants presenting with pneumothorax in the first 24 hours of life, and found that 46 infants required intubation and ventilation support; 18 (39%) survived and 28 (61%) died.

1.1.6 Congenital Diaphragmatic Hernia (CDH).

Congenital diaphragmatic hernia is the result of failure of the pleuroperitoneal folds to fuse completely. Consequently displacement of abdominal viscera into the chest may occur with subsequent impairment of respiration.[28,39] The left hemidiaphragm is involved more frequently than the right (80 to 90% of patients). Tachypnoea is often the initial sign, the respirations are deep and laboured, or gasping and irregular with associated sternal and costal retractions.[39] The diagnosis is confirmed by a chest X-ray in which loops of bowel are visible on the side of the hernia, the mediastinal structures are displaced to the opposite side, the lung on the affected side is compressed while the lung on the opposite side is emphysematous.[28] Congenital diaphragmatic hernia account for 8% of all major congenital anomalies.[41] In Haifa Israel, Nitecki et al[42] over a period of 18 years diagnosed 81 patients

as having CDH at the Department of Paediatric Surgery Ramban Medical Centre, 11 (13.5%) of whom presented after the first 24 hours of life. In Ireland, Rasheed et al[43] in a 10 year review (1980-1989), there were 59 neonates with CDH admitted to Our Lady's Hospital for sick children. The hernia was present in the left side in 47 cases and 11 cases were right sided. The overall mortality was 35.6%, with increased mortality for right-sided hernia of 54.6%. In the same country Sweed et al[44] in a retrospective review of live births at 3 maternity hospitals in Dublin found 116 cases of CDH among 368,772 live births. In USA, Torfs et al[45] in a population based study of CDH in 1983-1987, in California population of 718,208 births diagnosed CDH in 237 infants, a birth prevalence of 3.30 per 10,000 total births (live and still births) while Steinhorm et al[46] in a retrospective review of all Minnesota birth and death records between 1988 and 1990 found that 48 patients had diagnosis of CDH, among these 29 (60%) survived.

1.1.7 Choanal Atresia

Choanal atresia is a rare malformation characterized by complete or incomplete block of the nasal passages by a membrane or bonny septum.[28] When only one side is affected the infant usually does not have severe symptoms but when both sides are affected, the infant may suffer from severe asphyxia immediately after birth and may succumb from suffocation.

The most important clue in the newborn that aid in detection of choanal atresia are persistent breathing through the mouth, cyanosis when the mouth is closed and return to normal colour when the infant cries.[28] The diagnosis is confirmed by the inability to advance a nasogastric tube past the posterior nasal passages. In South Africa, Singh[47] diagnosed choanal atresia in 30 neonates over a five year period. The incidence was 1:8,300 livebirths. In this study there was a female predominance of 5:1. Morgan et al [48] at the Hospital for Sick children, Great Ormond street, London treated 50 cases of choanal atresia over a six year period (1982-

88). In USA, Bryan[49] reviewed the infant medical records of the University of California San Francisco genetic files from 1968-1978 and identified a total of 17 infants with choanal atresia. In 65% of them the atresia was bilateral and left sided choanal atresia predominated.

1.2 EXTRAPULMONARY CAUSES

1.2.1 Cardiovascular Disorders

Several cardiovascular conditions may present with symptoms suggesting surfactant deficiency. However, clinical and radiological evidence of cardiac or hepatic enlargement, cyanosis out of proportion to the degree of respiratory difficulty, a loud murmur (by no means always present) and abnormalities of electrical axis in electrocardiogram are all signs suggesting congenital heart disease. Richard and Co-workers (1955) found that if still births were included, the incidence of congenital heart malformation in the newborn period was 0.83%; if still births were excluded it was 0.7%.[50] The study on the incidence of congenital heart malformations in the neonatal period in three centres, Toronto, Boston and Baltmore revealed that transposition of the great vessels was the leading anomaly in this age group followed closely by ventricular septal defect (VSD), coarctation of aorta and hypoplastic left heart syndrome.[50] Data from the children's hospital, New York showed the distribution of causes of severe cardiac distress in 98 newborn infants in 1968-1970 as follows;[51] hypoplastic left heart 16%, transposition of great arteries

(TGA) 15%, tetralogy of fallot (TOF) 4%, pulmonary stenosis and atresia 15%, trancus arteriosus 6%, ventricular-septal defect (VSD) 6%, coarctation of aorta isolated 5% and others 24%.

2.0 RATIONALE AND OBJECTIVES

2.1 Rationale of the Study

There are many studies on the various conditions causing respiratory distress in the newborn worldwide, most of them in developed countries. It is known that most of the associated risk factors are preventable and treatable in the antenatal, intrapartum and early neonatal period and this has lead to a significant reduction in neonatal mortality. However, in Tanzania the problem of respiratory distress in the newborn, the associated risk factors and outcome has not been comprehensively studied. It is this lack of information which has prompted the study. It is envisaged that the study will provide some of the epidemiological data which will be the basis for appropriate case management and prevention of respiratory distress in the newborn.

2.2 Objectives of the Study

2.2.1 Broad Objective

To identify the associated risk factors and early outcome among neonates with respiratory distress admitted at MMC.

2.2.2 Specific Objectives

1. To determine the proportion of neonates with respiratory distress admitted at MMC.
2. To find the various disorders of importance causing respiratory distress in the newborn.
3. To determine the association between respiratory distress and

    i) Maternal factors:

        a) antepartum haemorrhage

        b) maternal diabetes

        c) EPH Gestosis

d) duration of labour

e) premature rupture of membranes

f) mode of delivery

g) meconium stained amniotic fluid.

ii) infant factors:

a) birth weight

b) gestational age

c) sex of the infant

d) birth asphyxia

e) expiratory grunting.

4. To assess the average duration of stay in the unit and the age at death among neonates with respiratory distress.

5. To compare the outcome in terms of mortality among neonates with respiratory distress and those without respiratory distress.

3.0 PATIENTS AND METHODS

3.1 Study Design

The study design is a prospective unmatched case control study which was carried out for 8 months, between March and November 1995, at the neonatal unit at Muhimbili Medical Centre (MMC). MMC is the only referral and teaching hospital in Dar es Salaam. Most of patients treated at MMC are referred from smaller peripheral hospitals within the city, private and government owned. A few number of patients are referred from other regions. The hospital has a 70 bed neonatal unit which admits neonates from within the hospital and those who have problems requiring special care from outside the hospital.

3.2 Sample size estimation

Using Epi Info version 5[52,53] for calculating minimum sample size in unmatched case control study (comparing ill and not ill), with an assumed 15% exposure risk factor in cases with confidence interval of 95%, power of 90% and odds ratio of 2, the sample size required was 295 cases and 295 controls.

Assumption: Only one risk factor (prematurity) was considered in the sample size determination this being the greatest risk factor. Sample size for other factors did not exceed this.

3.3 Selection of cases

a) **Inclusion criteria**

All neonates less than 8 days old with respiratory distress defined as a respiratory rate of 60 or more breaths per minute accompanied by any of the following signs; grunting, cyanosis, intercostal and subcostal recession or alae nasal flaring were consecutively recruited in the study.[1] This included neonates delivered at the maternity unit, those referred from other centres and those delivered at home.

b) **Exclusion criteria.**

i) Neonates readmitted in the unit who were already included in the study.

ii) Neonates with severe congenital malformations e.g. anencephally, bilateral cleft lip and palate.

3.4 Selection of controls

Neonates less than 8 days old without signs of respiratory distress, but matched by gestational with the cases were randomly recruited in the study as controls. This included those delivered at the maternity unit, those referred from other centres and those delivered at home.

3.5 Data collection and analysis

Informed consent was obtained from the mother before her infant was included in the study. On admission, details of antenatal, intrapartum care, and any other relevant information was obtained from the mother, the antenatal clinic card, partograms and concerned medical personnel. All the neonates in the study were seen by the investigator under two supervisors who are neonatologists working in the unit. The respiratory rate was counted in one full minute twice and the second count was taken. Thorough clinical examination was done to every neonate in the study. Weight of the undressed neonate using a standard beam balance (seca) to the nearest 10 gram, occipital-frontal circumference using a graduated non-elastic measuring tape and length using a graduated length board were taken. Gestational age assessment was done in all neonates in the study using the Dubowitz method[54] at 4 to 6 hours and within 24 hours after birth to the nearest two weeks, but in very sick babies only the external criteria by Parkins[55] was used (appendix I,II). The information obtained together with the clinical findings and anthropometric measurements were entered in the questionnaire. For

the cases, a postero-anterior chest X-ray and any other relevant investigations were done. All chest X-rays were read by a radiologist based at MMC. For controls only relevant investigations to the clinical diagnosis were carried out.

Data collected in the questionnaire as well as total number of admissions at the neonatal unit, total number of deliveries and sex distribution obtained from the midwifery book of the maternity unit were entered and analysed in the computer using SPSS/PC+ (Statistical Package for social sciences/Personal Computer). The chi-square test, odd's ratio and the unpaired t-test were used to analyse the data. In those tests in which the expected number of incidents of a particular complication in a given period was too small 2 tailed Fisher's exact test was applied.

3.6 Patient management

Infants in the study were managed according to the management protocol in the ward and daily clinical progress was noted and management was reviewed accordingly. The neonates in the study were followed up until discharged or death. The cause of death was established on clinical judgement, relevant laboratory investigations and circumstances of death. Causes of death were classified according to WHO mannual on international statistics classification of diseases.[56]

4.0 RESULTS

Total number of livebirths during the study period at MMC maternity unit were 9,493. Total number of admissions at the neonatal unit during the same period were 4,298, of which 3,243 (75 %) were from the maternity unit and 1,055 (25%) from peripheral hospitals and health centres. 648 neonates aged less than 8 days were included in the study and among these 331 (51%) were males and 317 (49%) were females with a male to female ratio of 1.04:1. Out of the 4,298 admissions at the neonatal unit, 328 had respiratory distress. Therefore, respiratory distress contributed to 7.6% of all the admissions at the neonatal unit during the study period. The control group consisted of 320 neonates who were randomly selected, but matched by gestational age with the cases. Of the 328 neonates with respiratory distress, 256 (78%) had RDS, 64 (19.5%) had pneumonia, 5 (1.5%) had TTNB while 3(1%) had MAS. One neonate had both pneumonia and cyanotic congenital heart disease.

The 256 preterm neonates with RDS were compared with an equal number of preterm neonates who had no signs of respiratory distress. Likewise the 64 term neonates with pneumonia were compared with an equal number of term neonates who had no signs of respiratory distress.

The characteristics of mothers of neonates under the study with respect to age are shown in Table 1. Out of the 648 mothers, 151 (23%) were teenagers while 451(70%) were aged between 20 and 34 years and 46 (7%) between 35 and 44 years. The mean maternal age among the cases was 24 years with a standard deviation of 6 years. The youngest mother was 15 and the eldest was 44 years. The mean maternal age in the control group was 23 years with a standard deviation of 5 years. The youngest mother was 14 and the eldest was 39 years. There was a significant difference between the mothers of cases and controls with respect to age (unpaired t-test; $P < 0.05$).

Table 1: Characteristics of mothers by age.

Age (Years)	Cases (%)	Controls (%)	Total (%)
14 - 19	77 (23.4)	74 (23.0)	151 (23.3)
20 - 34	217 (66.2)	234 (73.0)	451 (69.6)
35 - 44	34 (10.4)	12 (4.0)	46 (7.1)
Total	328 (100)	320 (100)	648 (100)

Table 2 shows the characteristics of mothers by parity. It was the first delivery in 298 (46%) mothers. It was the second to fourth delivery in 278 (43%) mothers. 72 (11%) mothers had delivered five times or more. There was no significant difference between the mothers of cases and controls with respect to parity.

Table 2: Characteristics of mothers by parity

Parity	Cases (%)	Controls (%)	Total (%)
1	143 (43.6)	155 (48.4)	298 (46.0)
2 - 4	142 (43.3)	136 (42.5)	278 (42.9)
> = 5	43 (13.1)	29 (9.1)	72 (11.1)
Total	328 (100)	320 (100)	648 (100)

$X^2 = 3.24$ $P > 0.05$

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4.1 Respiratory distress syndrome (RDS)

Out of the 4,298 admissions at the neonatal unit, 256 had RDS. Therefore, the proportion of neonates with RDS seen during the study was 6% of all the admissions at the neonatal unit. Out of 256 neonates with clinical diagnosis of RDS, 149 (58.2%) had chest X-rays done, of which only 30 (20.1%) showed the typical groundglass appearance with air bronchogram. The rest of the films showed non-specific pulmonary appearance. It was not possible to do chest X-rays in 107 (41.8%) neonates because they were too sick to be transported to the X-ray unit. Transporting a sick neonate is a hazard in itself. Because of the reasons given above, diagnosis of RDS in this study was based on the following clinical criteria; evidence of prematurity and presence of any two of the following beginning within the first 3 hours of life and lasting for at least 24 hours or until death; respiratory rate of 60 or more in one minute, expiratory grunting, sternal or intercostal recession and the need for supplemental oxygen. [1,59,60]

The distribution of RDS cases and controls according to gestational age is shown in table 3. Among the 55 neonates with gestational age of 28 to 29 weeks, 45(82%) had RDS while only 10(18%) had no RDS. Of the 216 neonates with gestational age of 34 to 36 weeks, only 63 (29%) had RDS while 153(71%) had no RDS. The mean gestational age among the cases was 32 weeks and the range was from 28 to 36 weeks. The mean gestational age among the controls was 34 weeks and the range was from 28 to 36 weeks. Neonates with RDS were of significantly lower gestational age than the controls (unpaired t-test; $P<0.01$). Table 4 shows the distribution of cases and controls according to birth weight. Out of 512 preterm neonates studied, 39 had birth weights below 1000 grams, and of these 29(74.4%) had RDS while 10 (25.6%) had no RDS.

Table 3: Distribution of cases and controls according to gestation age.

Gestation (weeks)	Cases (%)	Controls (%)	Total (%)
28 - 29	45 (81.8)	10 (18.2)	55 (100)
30 - 33	148 (61.4)	93 (38.6)	241 (100)
34 - 36	63 (29.2)	153 (70.8)	216 (100)
Total	256	256	512

Of the 183 neonates among the cases and controls with birth weight of 1000 to 1499 grams, 119(65%) had RDS while 64(35%) had no RDS. Out of the 227 neonates among cases and controls weighing 1500 to 1999 grams, 85(37.4) had RDS while 142(62.6%) had no RDS. The mean birth weight among the cases was 1413 grams with a standard deviation of 362 grams and the range was from 750 grams to 2400 grams. The mean birth weight among the controls was 1612 grams with a standard deviation of 344 grams and the range was from 730 grams to 2400 grams. Neonates with RDS were of significantly lower birth weight than the controls (unpaired t-test; $P < 0.001$).

Table 4: Distribution of cases and controls according to birth weight

Weight (grams)	Cases (%)	Controls (%)	Total (%)
< 1000	29 (74.4)	10 (25.6)	39 (100)
1000 - 1499	119 (65.0)	64 (35.0)	183 (100)
1500 - 1999	85 (37.4)	142 (62.6)	227 (100)
2000 - 24000	23 (36.5)	40 (63.5)	63 (100)
Total	256	256	512

Table 5 shows relationship between RDS and EPH gestosis. 17 (6.6%) mothers among the RDS cases had EPH gestosis compared with 33 (12.9%) among the controls. 239 (93.4%) mothers among the RDS cases had no EPH gestosis compared with 223 (87.1%) among the controls. EPH gestosis significantly lowered the proportion of neonates with RDS ($P < 0.05$). EPH gestosis in this study was defined as maternal hypertension (blood pressure exceeding 140/90 mmHg at rest with patient lying down) with or without albuminuria.

Table 5: Relationship between RDS and EPH gestosis.

EPH gestosis	Cases (%)	Controls (%)	Total (%)
Present	17 (6.6)	33 (12.9)	50 (9.8)
Absent	239 (93.4)	223 (87.1)	462 (90.2)
Total	256(100)	256 (100)	512 (100)

Odds ratio = 0.48 , (CI 0.25, 0.92), $X^2 = 4.99$, $P < 0.05$.

Table 6 shows the relationship between RDS and premature rupture of membranes of more than 24 hours. 28(10.9%) mothers among the neonates with RDS had premature rupture of membranes of more than 24 hours based on maternal history of watery vaginal discharge compared with 16(6.4%) mothers among the controls. 228(89.1%) mothers among the neonates with RDS had no premature rupture of membranes compared with 240 (93.6%) mothers among the controls. There was no significant association between RDS and premature rupture of membranes found in this study.

Table 6: Relationship between RDS and PROM

PROM	Cases (%)	Controls (%)	Total (%)
Present	28 (10.9)	16 (6.4)	44 (8.6)
Absent	228 (89.1)	240 (93.6)	468 (91.4)
Total	256(100)	256 (100)	512 (100)

Odds ratio = 1.84, (CI 0.93, 3.67), $X^2 = 3.01$, $(P>0.05)$.

Table 7 shows the relationship between RDS and mode of delivery. 22 (8.6%) neonates among the RDS cases were delivered by caesarean section compared with 29 (11.3%) among the controls. 234 (91.4%) neonates among the RDS cases were delivered vaginally compared with 227 (88.7%) among the controls. Caesarean section delivery was not significantly associated with increased proportion of neonates with RDS ($P>0.05$).

Table 7: Relationship between RDS and Mode of delivery.

Delivery mode	Cases (%)	Controls (%)	Total (%)
LSCS	22 (8.6)	29 (11.3)	51 (10.0)
Vaginal	234 (91.4)	227 (88.7)	461 (90.0)
Total	256(100)	256 (100)	512 (100)

Odds ratio = 0.74, (CI 0.39, 1.37), $X^2 = 0.78$, $(P > 0.05)$.

Table 8 shows the relationship between RDS and sex. Out of the 512 preterm neonates under the study, 261 were males, and of these 150 (57.5%) had RDS while 111(42.5%) had no RDS. Of the 512 preterm neonates studied, 251 were females, and of these, 106(42.2%) had RDS while 145(57.8%) had no RDS. The male to female ratio was 1.4:1. RDS was significantly more common in males than in females ($P < 0.001$).

Table 8: Relationship between RDS and Sex.

Sex	Cases (%)	Controls (%)	Total (%)
Males	150 (57.5)	111 (42.5)	261 (100)
Females	106 (42.2)	145 (57.8)	251 (100)
Total	256	256	512

$X^2 = 11.9$, $(P < 0.001)$.

Table 9 shows the relationship between RDS and birth asphyxia defined as an Apgar Score at one minute less than 6 [6] . 84 (32.8%) neonates among the RDS cases had birth asphyxia compared with 38 (14.8%) among the controls. 172 (67.2%) neonates among the cases had no birth asphyxia compared with 218 (85.2%) among the controls. Birth asphyxia was significantly associated with increased proportion of neonates with RDS. ($P< 0.001$).

Table 9: Relationship between RDS and birth asphyxia.

Asphyxia	Cases (%)	Controls (%)	Total (%)
Present	84 (32.8)	38 (14.8)	122 (23.8)
Absent	172 (67.2)	218 (85.2)	390 (76.2)
Total	256 (100)	256 (100)	512 (100)

Odds ratio = 2.80, (CI 1.78, 4.42), $X^2 = 21.79$, ($P < 0.001$).

Table 10 shows the relationship between RDS and antepartum haemorrhage. 6 (3.2%) mothers among the RDS cases had antepartum haemorrhage compared with 7 (2.7%) mothers among the controls. 250 (97.7%) mothers among the cases had no antepartum haemorrhage compared with 249 (97.3%) mothers among the controls. There was no significant association between RDS and antepartum haemorrhage ($P > 0.05$).

Table 10: Relationship between RDS and antepartum haemorrhage.

APH	Cases (%)	Controls (%)	Total (%)
Present	6 (2.3)	7 (2.7)	13 (2.5)
Absent	250 (97.7)	249 (97.3)	499 (97.5)
Total	256 (100)	256 (100)	512 (100)

Odds ratio =0.85, (CI 0.25, 2.87), ($P > 0.05$).

4.1.1 MORTALITY:

Out of 256 neonates with RDS, 134 (52.3%) died compared with 32 (12.5%) deaths among the controls as shown in table 11. 122 (47.7%) neonates among RDS cases survived compared with 224 (87.5%) among controls. RDS was significantly associated with increased mortality ($P < 0.001$). Among the 134 neonates with RDS who died, 88% of them died during the first week of life. Out of the 797 neonates who died at the unit during the study, 16.8% of them had RDS.

Table 11: Outcome among RDS cases and controls.

Outcome	Cases (%)	Controls (%)	Total (%)
Died	134 (52.3)	32 (12.5)	166 (32.4)
Survived	122 (47.7)	224 (87.5)	346 (67.6)
Total	256 (100)	256 (100)	512 (100)

$X^2 = 90.93$, $(P<0.001)$.

4.1.2 EXPIRATORY GRUNTING:

Grunting is produced when the infant expirates against a closed glottis. It is a compensatory mechanism on the part of the infant to raise end-expiratory alveolar pressure during expiration. [57] Grunting often accompany chest retractions and must always be regarded as indicative of a serious disease. [58] As seen in table 12, out of the 129 neonates with grunting, 76(59.0%) died while 53(41%) survived. Out of the 127 neonates with no grunting,

58(47.5%) died while 69(54.3%) survived. Grunting was significantly associated with increased mortality ($P<0.05$).

Table 12: Expiratory grunting in relation to mortality.

Grunting	Died (%)	Survived (%)	Total (%)
Present	76 (59.0)	53 (41.0)	129 (100)
Absent	58 (45.7)	69 (54.3)	127 (100)
Total	134	122	256

$X^2 = 3.99$, $(P<0.05)$.

4.1.3 DURATION OF STAY:

Table 13 shows the duration of stay among RDS cases and controls. 149 (58.2%) neonates among the cases and 157 (61.3%) neonates among the controls stayed at the neonatal unit for less than 8 days. The mean duration of stay among the cases was 9 days with a standard deviation of 9 and the range was from one to 49 days. The mean duration of stay among the controls was 7 days with a standard deviaton 6 and the range was from one to 37 days. Neonates with RDS stayed significantly longer at the neonatal unit compared with the controls (unpaired t-test; $P<0.05$).

Table 13: Duration of stay among cases and controls.

Duration (Days)	Cases (%)	Controls (%)	Total (%)
< = 7	149 (58.2)	157 (61.3)	306 (59.7)
8 - 28	98 (38.3)	98 (38.3)	196 (38.3)
> = 28	9 (3.5)	1 (0.4)	10 (2.0)
Total	256 (100)	256 (100)	512 (100)

4.2 PNEUMONIA

Out of the 328 neonates with respiratory distress, 64 (19.5%) had pneumonia in the first week of life. The proportion of neonates with pneumonia in the first week of life was 1.5% of all the neonatal admissions during the study period. Pneumonia was diagnosed on the basis of clinical and radiological findings with the exception of 8 neonates who died before chest X-rays were taken and in this case diagnosis was based on clinical findings of dyspnoea, chest retractions and crepitations. Prolonged labour defined as labour lasting for 24 hours or more was observed in 7 (10.9%) mothers among the pneumonia cases compared with 2 (3.1%) mothers among the controls as shown in table 14. Prolonged labour was not significantly associated with occurrence of pneumonia in the first week of life ($P > 0.05$).

Table 14: Relationship between pneumonia and prolonged labour.

Labour duration (HRS)	Pneumonia cases(%)	Controls (%)	Total (%)
> = 24	7 (10.9)	2 (3.1)	9 (7.0)
< 24	57 (89.1)	62 (96.9)	119 (93.0)
Total	64 (100)	64 (100)	128 (100)

Odds ratio = 3.81, (CI 0.68, 27.76), X^2 =1.91, 2 tailed Fishers exact test, P>0.05).

Table 15 shows the relationship between pneumonia and premature rupture of membranes of more than 24 hours. 5 (7.8%) mothers among the 64 pneumonia cases had premature rupture of membranes compared with 1 (1.6%) among the 64 controls. However, premature rupture of membranes was not significantly associated with occurrence of pneumonia in the first week of life.

Table 15: Relationship between pneumonia and premature rupture of membranes.

PROM	Pneumonia cases(%)	Controls (%)	Total (%)
Present	5 (7.8)	1 (1.6)	6 (4.7)
Absent	59 (92.2)	63 (98.4)	122 (95.3)
Total	64 (100)	64 (100)	128 (100)

Odds ratio = 5.34, (CI 0.58, 12.4), X^2=1.57, 2 tailed Fishers exact test; P>0.05.

Out of 64 mothers among the cases of pneumonia,18 (28.1%) had meconium stained liquor compared with 8 (12.5%) mothers among the controls as shown in table 16. Meconium stained liquor was significantly associated with occurrence of pneumonia in the first week of life ($P<0.05$).

Table 16: Relationship between pneumonia and meconium stained liquor.

Meconium	Pneumonia cases(%)	Controls (%)	Total (%)
Present	18 (28.1)	8 (12.5)	26 (20.3)
Absent	46 (71.9)	56 (87.5)	102 (79.7)
Total	64 (100)	64 (100)	128 (100)

Odds ratio = 2.74, (CI 1.01, 7.62) $X^2=3.91$, $P< 0.05$.

Table 17 shows the relationship between pneumonia in the first week of life and birth asphyxia. Of the 64 neonates with pneumonia, 21 (31.8%) had birth asphyxia compared with 11 (17.2%) neonates among the controls. There was no significant association between pneumonia and birth asphyxia ($P>0.05$).

Table 17: Relationship between pneumonia and birth asphyxia.

Asphyxia	Pneumonia cases(%)	Controls (%)	Total (%)
Present	21 (32.8)	11 (17.2)	32 (25.0)
Absent	43 (67.2)	53 (82.8)	96 (75.0)
Total	64 (100)	64 (100)	128 (100)

Odds ratio = 2.35, (CI 0.9, 5.89); X^2 = 3.38; P> 0.05.

4.2.1 MORTALITY

Out of the 64 neonates with pneumonia in the first week of life 13 (20.3%) died. One neonate among the controls died. Pneumonia contributed to 1.6% of all the neonatal deaths at the unit during the study period.

4.2.2 DURATION OF STAY

Out of the 64 neonates with pneumonia, 45 (70.0%) stayed in the unit for less than 8 days while 16 (25%) stayed for 8 to 27 days. 3 (5%) neonates among the cases stayed at the unit for 28 days or more.

All neonates in the control group stayed at the unit for less than 8 days.

4.3 TRANSIENT TACHYPNOEA OF THE NEWBORN (TTNB).

Out of the 4,298 neonates admitted at the unit during the study, 5(0.12%) had TTNB. The criteria for diagnosing TTNB in this study was based on the presence of any two of the following; respiratory rate of 60 or more in one minute, expiratory grunting, sternal or intercostal recession and increased oxygen requirements but all resolving in less than 24 hours coupled with a negative X-ray findings.[59]

4.4 MECONIUM ASPIRATION SYNDROME (MAS)

Meconium stained liquor was noted in 26(19.1%) of the 136 term neonates under the study. Of the 26 neonates with meconium stained liquor, 3(2%) had MAS.

The criteria for diagnosing MAS in this study was based on presence of meconium stained liquor, respiratory rate of 60 or more in one minute and chest X-ray film showing non-uniform irregular shadows, hyper-inflated lungs or presence of emphysema. [28] Two of the neonates with MAS died.

4.5 CONGENITAL HEART DISEASE (CHD).

One neonate under the study had cyanotic congenital heart disease and pneumonia. However, the neonate died before the nature of the cardiac lesion was determined by echocardiogram. 0.02% of all the admissions at the neonatal unit during the study were due to CHD.

5.0 DISCUSSION

The proportion of neonates with respiratory distress seen during the study was 7.6% of all admissions at the neonatal unit. However, this is lower than the frequency of 19.9% for the admissions at the Special Care Baby Unit in Nigeria in a one year period which was reported by Dawodu et al.[10] Mortality rate among neonates with respiratory distress was 45.4%. Respiratory distress alone contributed to 18.7% of all the neonatal deaths during the study period.

5.1 Respiratory Distress Syndrome (RDS).

The overall frequency of RDS in this study was 6% of all neonatal admissions at the unit. Out of the 256 neonates with clinical diagnosis of RDS 149 (58.2%) were X-rayed and among these only 30 films showed the typical groundglass appearance with air bronchogram. The rest of the films showed non-specific pulmonary appearance. It has been argued that, the radiological findings in RDS are not entirely specific. Bronchopneumonia for example may be entirely indistinguishable from surfactant deficiency on purely radiological criteria.[16] It has also been doubted whether the radiological signs of RDS are important enough to make an important positive contribution to the diagnosis. It has also been claimed that larger infants may present with a typical clinical picture of RDS without a diagnostic chest X-ray. However, the definitive diagnosis of RDS is possible only at autopsy[57].

The proportion of neonates with RDS found in this study is comparable with those reported by other authors.[4,9,11,12] However, the proportion of neonates with RDS in the present study is lower than the 14.3% reported before by Mbise et al[14] while on the other hand, it is higher than the 2.8% reported by Manji.[15] However, both these studies were dealing with low birth weight neonates.

Association between preterm delivery and RDS has been reported several times. The proportion of neonates with RDS declines very rapidly with advancing gestation age as was found in this study where 82% of all neonates with gestational age of 28 to 29 weeks had RDS compared with 29.2% of neonates with gestational age of 34 to 36 weeks. Similarly, Jones et al[60] found a decrease of RDS defined clinically from 38% at 26 to 29 weeks of gestation to 1.8% at 34 to 37 weeks. Neonates with RDS in this study had a significantly lower gestational age and birth weight compared with the controls ($P<0.001$). Tubman et al[24] also found that babies who developed RDS were of significantly lower birth weight and gestational age.

Another factor which is related to RDS is maternal hypertension which is considered to protect a premature neonate against development of RDS. However, the evidence for this is conflicting.[24] Maternal hypertension in the present study significantly lowered the proportion of neonates with RDS compared with the controls ($P<0.05$). Malan et al[12] in South Africa reported similar findings while Tubman et al [24] in Northern Ireland found that maternal hypertension significantly increased the proportion of neonates with RDS.

Premature rupture of membranes of more than 24 hours has been cited as protective from RDS. A decrease in RDS incidence after premature rupture of membranes of more than 24 hours has been attributed to a rise, due to stress, in cortisol secretion by the foetus which may accelerate lung maturation. [16] In the present study, there was no significant difference in the frequency of RDS related to premature rupture of membranes of more than 24 hours. Hallack et al[19] in Detroit similarly found no difference in the frequency of RDS related to premature rupture of membranes. However, Tubman et al[24] in their study, found a significantly lower incidence of RDS related to premature rupture of membranes of more than 24 hours.

The influence of caesarean section delivery on the frequency of RDS has been disputed.[16] The risk of RDS is increased when caesarean section is performed before onset of labour. The proportion of neonates with RDS delivered by caesarean section was not significantly higher than those delivered vaginally in this study. Other investigators also report a smaller influence of caesarean section delivery. For example Jones et al[60] found no effect of caesarean section at gestations below 32 weeks and that, at 34 to 37 weeks, the incidence of RDS was 5% after caesarean section compared with 2% after normal delivery. However, Malan et al[12] in South Africa found a significant increase in incidence of RDS after caesarean section delivery.

The frequency of RDS in this study was significantly higher in males than in females ($P<0.001$). The male to female ratio was 1.4:1. Similarly, the male to females ratio was 1.4:1 for RDS in the British Perinatal mortality survey in 1968 and it was 1.7:1 in USA mortality statistics in the same year.[16] Luerti et al[19] in Italy also found a higher frequency of RDS in males than in females. No explanation has been offered for the higher incidence of RDS in male than in female babies.

Prenatal asphyxia which is known to cause pulmonary vasoconstriction in the foetus seems to predispose the newborn infant to RDS.[16] In the present study, birth asphyxia was significantly associated with a higher frequency of RDS ($P<0.001$). Similarly, Jones et al[60] found that, the incidence of RDS in neonates with Apgar score of 5 or less was twice as high as in those with a score above 5. However, none of these findings completely excludes the possibility of the increased frequency of RDS being apparent only, due to inability to distinguish between clinical signs of RDS and those caused by asphyxia on the lungs and circulation.

There are several reports of APH which causes foetal asphyxia, being associated with increased incidence of RDS. Malan et al[12] in their study found that APH increased the incidence of RDS significantly. However, in this study, APH was not significantly associated with increased frequency of RDS.

Maternal diabetes has been established as a factor in increasing the risk of RDS. It is postulated that increased foetal levels of insulin interfere with incorporation of choline into lecithin, producing deficiency in phosphotidylglycerol in the lungs and amniotic fluid.[57] In the present study none of the mothers of neonates under the study was diabetic.

5.1.1 Mortality

RDS contributed to 16.8% of all neonatal deaths at the unit during the study. Mortality among RDS cases was 52% and it was four times higher than in the controls. The mortality among neonates with RDS in this study is almost twice the 28% for USA in 1968.[16] Specialized intensive care units have reduced the mortality from RDS in developed countries.

5.1.2 Expiratory grunting

Expiratory grunting which is a compensatory mechanism on the part of the infant to raise end-expiratory alveolar pressure must always be regarded as indicative of a serious disease.[58] In the present study, expiratory grunting was significantly associated with increased mortality ($P < 0.05$).

5.2 Pneumonia

The proportion of neonates with pneumonia in the first week of life was 1.5% of all the neonatal admissions during the study. However, this is lower than the 3% reported before by Mbise et al[14] probably because the present study included only neonates aged less than 8 days.

Premature rupture of membranes of more than 24 hours, foetal hypoxia, prolonged and difficult delivery are important risk factors.[1] Fredrick and Butler[61] in their analysis of 578 deaths established a correlation between congenital pneumonia and prolonged labour as well as premature rupture of membranes of more than 24 hours. However, in the present study, prolonged labour as well as premature rupture of membranes were not significantly associated with increased frequency of pneumonia probaby because the number of neonates with pneumonia was small.

Asphyxia by stimulating large gasps would favour penetration of infected liquor to the lung periphery.[57] In the present study, birth asphyxia was not significantly associated with increased frequency of pneumonia in the first week of life.

Aspiration of meconium stained liquor leads to birth asphyxia and severe respiratory distress at or soon after birth and the meconium being a good culture media for microorganisms, super-added infections often supervenes.[57] In this study, meconium stained liquor was significantly associated with increased frequency of pneumonia in the first week of life ($P < 0.05$).

6.0 DIFFICULTIES ENCOUNTERED DURING THE STUDY

1. It was not possible to do chest X-rays to all neonates with respiratory distress because they were too sick to be transported to the X-ray unit.
2. Majority of X-rays of neonates with clinical diagnosis of RDS showed non-specific pulmonary appearance.
3. Because of the two difficulties mentioned above, diagnosis of RDS in this study was based on clinical criteria alone.
4. Metabolic disorders causing respiratory distress like hypoglycaemia, hypocalcaemia and hypothermia were not studied. This is one of the limitations of this study.

7.0 SUMMARIES

1. Respiratory distress contributed to 7.6% of all the neonatal admissions and 18.7% of all the neonatal deaths during the study period.
2. Respiratory distress syndrome was the commonest disorder causing respiratory distress in the newborn, accounting for 6% of all the admissions at the neonatal unit. It carried a mortality rate of 52%.
3. Neonates with RDS had significantly lower birth weights and gestational age compared with the controls.
4. RDS was significantly more common in males than in females and it was significantly associated with birth asphyxia.
5. EPH gestosis significantly lowered the proportion of neonates with RDS. However, there was no significant association between RDS and PROM, mode of delivery or APH.
6. Expiratory grunting was significantly associated with increased mortality, thus its presence indicates a serious disease.
7. Pneumonia in the first week of life was the second commonest disorder causing respiratory distress, contributing to 1.5% of all the admissions at the neonatal unit. MAS, TTNB, and CHD were less common disorders causing respiratory distress.
8. Meconium stained liquor was significantly associated with increased proportion of neonates with pneumonia in the first week of life. However, there was no significant association between pneumonia and factors such as birth asphyxia, PROM or prolonged labour.
9. Neonates with respiratory distress stayed at the neonatal unit significantly longer than the controls. Mortality among neonates with respiratory distress was highest in the first week of life, being 132(88.6%) out of 149 deaths among the cases.
10. Mortality among neonates with respiratory distress was 149(45.4%) compared with 33(10%) deaths among the controls.

8.0 RECOMMENDATIONS

1. Since RDS is more or less confined to the preterm infant, there is a need to reduce its incidence by measures aimed at preventing premature delivery.
2. Birth asphyxia was among the factors associated with increased proportion of neonates with RDS, hence there is a need to improve the quality of antenatal and intrapartum care.
3. Neonates with RDS who presents with expiratory grunting need intensive care and probably mechanical ventilation since mortality among these neonates is very high. Therefore, there is a need to establish a well equipped neonatal intensive care unit.
4. It is known that antenatal steroids given to mothers before premature delivery can decrease the incidence of RDS, likewise, surfactant and continous positive airways pressure (CPAP) reduces morbidity in RDS, there is therefore a need to do intervention studies on the same.

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