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Pattern and risk factors of early neonatal morbidity and outcome in Omdurman Maternity Hospital Nursery Unit

By

Dr. Hind Mohammed Mirghani Ahmed

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Supervisor

Prof. Salah Ahmed Ibrahim
FRCPCH, MD
Department of Paediatric & Child Health,
Faculty of Medicine, U of K

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قال الله تعالى :

(يا أيها الناس إن كُنتم في ريب من البعث فإنا خلقنـاكم من تراب ثم من نطفة ثم من علقةٍ ثم من مضغة مخلقة وغيـر مخلقة لنبين لكم ونقر فى الأرحام ما نشاء إلى أجل مسمى ثـم نخرجكم طفلاً ثم لتبلغوا أشدكم ومنكم من يتوفى ومنكم من يرد إلى أرذل العمر لكيلا يعلم من بعـد عِلـم شـيئاً وتـرى الأرض هامدة فإذا أنزلنا عليها الماء اهتزت وربت وأنبتـت من كل زوج بهيج)

صدق الله العظيم

سورة الحج/ الآية (5)

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Dedication

To:

my family for their great help and support,

my lovely kids "Ahmed & Mohammed"

&

To all newborns in Sudan wishing them nice future.

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I would like to express my gratitude to my supervisor Prof. Salah Ahmed Ibrahim, Department of Paediatrics and Child Health, Faculty of Medicine, University of Khartoum for his generous support, criticism, encouragement and guidance.

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
ANC	Antenatal Care
CPAP	Continuous positive airway pressure
E. coli	*Echirichia coli*
ENMR	Early Neonatal Mortality Rate
GBS	Gram Positive Group B Streptococci
IVH	Intra-ventricular Haemorrhage
LBW	Low Birth Weight
LNMR	Late Neonatal Mortality Rate
MAS	Meconium Aspiration Syndrome
NICU	Neonatal Intensive Care Unit
NMR	Neonatal Mortality Rate
PMR	Perinatal Mortality Rate
RDS	Respiratory Distress Syndrome
VLBW	Very Low Birth Weight

ABSTRACT

Neonatal mortality and morbidity remains a major problem in many developing countries, most of its predisposing factors are preventable.

The objectives of this study were to determine the incidence of early neonatal outcome in Omdurman Maternity Hospital Nursery Unit, to describe the pattern of early neonatal morbidity and to evaluate the risk factors associated with early neonatal mortality.

The study was prospective, case control, hospital-based study, conducted in Omdurman Maternity Hospital in the period from August 2004 till January 2005, where 202 newborns admitted to Omdurman Maternity Hospital Nursery Unit were followed till their 7^{th} day of life and 202 newborns delivered at the nearest time in the hospital was taken as a control. The outcome of the study was 174 newborns were alive (72.8%), while 55 newborns were early neonatal deaths (27.2%) and the incidence of early neonatal mortality in this study was estimated to be 6.6/1000 live births.

Causes of early neonatal morbidity were found to be prematurity (39.1%), followed by birth asphyxia (19.3%), neonatal

jaundice (12.4%), congenital malformations (11.4%) and neonatal sepsis (6.4%).

Prematurity accounted for about half early neonatal mortality (56.4%), other causes of early neonatal mortality were congenital malformations (20.0%), birth asphyxia (4.5%) and neonatal sepsis (3.6%).

Risk factors associated with early neonatal mortality in this study were found to be gestational age of less than 37 weeks (RR: 2.8).

Another risk factor associated with early neonatal mortality was the birth weight of less than 1.50 kg, which carried five times risk of early neonatal mortality (RR 5.18).

Maternal factors such as age, education and number of antenatal care visits and positive history of neonatal deaths carried no relative risk for early neonatal mortality in this study (RR = 0.806, 0.218, 0.74 respectively).

ملخص الأطروحة

ظلت وفاة الأطفال فى الشهر الأول من الولادة مشكلة كبيرة فى عدد مـن الـدول النامية ومعظم هذه العوامل يمكن تفاديها.

الهدف من هذه الدراسة تحديد حدوث وفاة حديثي الولادة فى الأسـبوع الأول فـى وحدة حديثي الولادة بمستشفى الولادة بأمدرمان واصفاً نماذج لأمراض حديثى الولادة وتقيـيم عوامل الخطورة الناجمه عنها.

أجريت هذه الدراسة بمستشفى أم درمان للولادة فى الفترة مـن أغـسطس 2004م وحتى يناير 2005م والتى استقبل فيها عدد (202) مولود فى وحدة حديثى الـولادة وتمـت متابعتهم لمدة (7) أيام منذ تاريخ ولادتهم وكانت نتيجة هذه الدراسة أن 174 (72.8%) مـن هؤلاء المواليد ظلوا أحياء بينما 55 من هؤلاء المواليد توفوا فى الأسبوع الأول مـن الـولادة بنسبة 27.2% وحدوث هذه الوفاة فى الأسبوع الأول قدرت بنسبة (6.6/1000) من المواليـد الأحياء فقط.

وجد أن انواع الأمراض التى تصيب حديثى الولادة: الأطفال الخدج بنسبة 39.1% تبعتها حالات اختناق الأطفال أثناء الولادة (19.3%)، الإصابة بمرض اليرقان (12.4%)، التشوه الخلقى (11.4%)، و تخثر الدم (6.4%). وقد وجد أن حالات الأطفال الخدج تعـادل

نصف عدد وفيات حديثى الولادة فى الأسبوع الأول (56.4%)، كما أن الأسباب الآخر المسببة للوفاة كانت التشوه الخلقى (20.0%)، الإختناق أثناء الولادة (4.5%) وتخثر الدم (3.6%).

وجد أن عوامل الخطورة التى تصاحب وفاة حديثي الولادة الذين كان وزنهم 1.5 كليو جرام تمثل خمس أضعاف الخطورة لوفاة حديثى الولادة فى الأسبوع الأول.

عوامل الأمومة مثل العمر والمستوى التعليمى وعدم متابعة الحمل ووفاة طفل حديث الولادة فى السابق لا تحمل أى نوع من الخطورة لوفاة حديثي الولادة فى الأسبوع الأول.

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INTRODUCTION & LITERATURE REVIEW

1.2. Definitions and incidence:

1.1.1. Definitions:

Perinatal period is the period from 24 weeks gestation or time of the live birth if less than 24 weeks gestation to the seventh day of postnatal period.

Neonatal period is the first 28 days of life of a live born infant of any gestation which consist of early neonatal period which is the first seven days of life of live born infant of any gestation and the late

neonatal period which is the period after seventh day till 28 days of birth[1].

Perinatal mortality rate (PMR) is the number of stillbirths in addition to the early neonatal deaths per 1000 total live births[1].

Neonatal mortality rate (NMR) is defined as number of deaths in the first 28 days per 1000 live births[2] and it accounts for about 65% of infant mortality which is defined as deaths occurring from birth till 12 month of life per 1,000 live birth[2,3].

1.1.2. Incidence of perinatal and neonatal mortality:

1.1.2.1. Globally:

The perinatal mortality rate (PMR) is 53/1000 (7.5 million annual perinatal deaths) and the neonatal mortality rate (NMR) is 36/1000 (5.1 million annual neonatal deaths). Of the 141 million annual livebirths, 127 million (90%) are born in developing countries which compared to developed countries have a higher PMR (57/1000 vs 11/1000 live births) and NMR (39/1000 vs 7/1000 live births). Five million annual neonatal deaths (98%) of the world's total occur in developing countries[4]. Asia-Oceania region has a PMR of 53/1000 and a NMR of 41/1000 live births. It

has half of the world's livebirths and two-thirds of the world neonatal deaths.

1.1.2.2. Early neonatal mortality in Northern Brazil:

Early neonatal mortality in Brazil was found to be 25.5/1000 live births, 75% of early neonatal deaths were due to prematurity, other main risk factors associated with early neonatal deaths were maternal smoking, complications during pregnancy and inadequate antenatal care[5].

Perinatal mortality in Turkey was 34.9/1000 with early neonatal deaths was 17.2/1000 live births in a study done in 29 districts throughout Turkey and the most important causes of deaths were prematurity (stillbirths 2.7%) and lethal congenital malformation (13.2%)[6].

1.1.2.3. Early neonatal mortality in Asia:

Level and risk factors of perinatal mortality was investigated in Ahmed Abad, India, through combined institutional surveillance in three governmental teaching hospitals. The perinatal mortality in the studied hospitals was 7.9/1000 live births and 34/1000 live births for early neonatal mortality and the risk of both stillbirths and early neonatal mortality were significantly

increased by a history of previous stillbirths, prematurity in the last pregnancy, low maternal weight and absence antenatal care[7].

In Pakistan, a retrospective study was carried out in Neonatal Care Unit, Rawalpindi General Hospital from January 1995 to December 1996, there were 3005 admissions and 268 deaths, resulting in 9% neonatal mortality. Eighty-eight percent of twins mortality was due to early neonatal deaths. Neonatal infections and birth asphyxia were the two major causes of neonatal mortality 37% and 31% respectively, followed by respiratory distress syndrome, meconium aspiration syndrome and congenital malformations. Maternal risk factors like maternal age, parity, socioeconomic status had no effect on neonatal mortality compared to pregnancy related factors such as toxaemia, antepartum haemorrhage (APH) which had substantial effect on early neonatal mortality[8].

1.1.2.4. Neonatal Mortality in Africa:

Early neonatal mortality is responsible for almost 75% of overall neonatal mortality in west Africa[4].

In a study done in a rural community in Ethiopia, data were collected from 1987 to 1996 in which the overall neonatal mortality rate was 27/1000 live births. The mortality rates in the

early and late neonatal periods were 20/1000 and 8/1000 live births respectively. The mortality incidence rates showed that, every day, three of every 1000 newborns die in their first week of life. Neonatal mortality accounted for 43% of infant mortality. Increased risk of neonatal mortality was found to be associated with living in a rural lowland area, twin births and male gender[9].

A population-based, matched case-control study was conducted in a rural area in Gambia. NMR was 39/1000 live births (95% CI 36.8-41.2) ENMR was 21/1000 and LNMR was 18/1000 live births. Neonatal infection accounted for 57% of all deaths. In the early neonatal period, 30% of deaths were due to prematurity. Risk factors for neonatal death were primiparity odd ratio (OR 2.18), previous stillbirth (OR 3.19), prolonged labour (OR = 2.80)[10].

A retrospective, descriptive hospital based study was conducted in neonatal intensive care unit in Harare, Zimbabwe to determine neonatal outcome and factors associated with mortality. A total of 234 neonates were admitted to the NICU in 1998 the commonest reason for admission was respiratory distress, case fatality was 46.4% of which 85.9% died during their first week of life, median age of death was 3 days. Birth weight, age at

admission to NICU, sex and duration of stay in the NICU had no significant influence on mortality[11].

A retrospective analysis of neonatal morbidity and mortality was conducted over a ten years period (1980-1990) at a tertiary hospital in Nigeria, 7,225 babies were admitted into the neonatal unit. Overall neonatal mortality was 13.0%, major causes of death were low birth weight, neonatal jaundice, neonatal infections and birth asphyxia and causes of admission were neonatal jaundice (45.6%), prematurity (18.0%), birth asphyxia (14.2%) and neonatal infections (9.3%)[12].

In Egypt a study done by Oona Campbell and others, the data were collected from a representative sample of women who gave birth from 17, 521 households, which were included in the Egypt demographic and health survey 2000. The results of the study stated that NMR was 25/1000 live births, 17 were early neonatal deaths and only 8/1000 live births were late neonatal deaths and the neonatal causes of death were prematurity 39%, asphyxia 18%, infection 7%, congenital, malformations 6% and unclassified 29%. 55% of infant mortality was due to deaths in the neonatal period[13].

1.1.2.5. Neonatal mortality in Sudan:

Omer studied 1144 neonates who were delivered in Khartoum Teaching Hospital and admitted to Newborn Unit in the period from January 1972 until December 1973, he found that 280 cases (24.5%) of the studied newborns were of low birth weight and the mortality among them was 36.1%, while it was 4.3% for the rest of the group[14].

Regarding pattern of diseases among the studied newborns, 49 cases were clinically diagnosed as hyaline membrane disease (RDS) of then 30 newborns were died accounted for 61.2% of whole newborns with RDS.

Regarding congenital malformations, 60 cases were seen with different congenital malformations, Central nervous system malformations accounted for 11 cases, which is the third predominant group following musculoskeletal malformations and gastrointestinal malformations. The overall case fatality rate for cases with congenital abnormalities was 35%[14].

In a community based study done in East Nile Province in Sudan, in the period from 1989 -1994 which was based on developing a surveillance system that monitor pregnancies and assessing the effects of intervention on PNM and NNM rates. The study concluded that PNM was 28.2/1000 which was reduced from

38.4/1000 livebirths and NMR was 17.5/1000 live births which was reduced from 21.8/1000 live births and causes of ENM were birth asphyxia (50.2%), followed by prematurity (36%), LBW (15.5%) and congenital malformation (2.1%).

Regarding risk factors of perinatal and neonatal mortality was found that, teenage mothers and mothers over 34 years had twice the risk of having an unfavourable outcome of pregnancy compared to mothers aged 20 - 29 years, primigravida and grandmultipara carried also a similar risk of unfavourable outcome. Mothers of previous history of stillbirth had seven times the risk of having stillbirth in the current pregnancy and more than twice the risk of neonatal death in the current pregnancy[15].

Taha conducted a hospital-based study in central Sudan in six community health centres in the period from April 1989 to March 1990. They estimated NMR ranged between 20.0 and 36.0 per 1000 live birth, and the major cause of neonatal mortality was tetanus neonatorum which constituted about 29% of neonatal deaths[16].

Dafallah and Elhadi carried out a retrospective study in Wad Medani Teaching Hospital, they reviewed all the deliveries and perinatal deaths occurred in the period from January 1985 up

to December 1999, there were 44605 deliveries, of them 2340 were perinatal deaths giving the overall mortality of 52.2/1000 live births. It was declined from 77.8/1000 in 1985 to 29.7/1000 in 1999.

Regarding causes of perinnatal mortality, prematurity was the major cause, it accounted for 950 (40.6%) of perinatal deaths and the second cause of mortality was congenital malformations 412 cases (17.6%), half of them were neural tube defects, then asphyxia 302(12.9%), while infection accounted for only 78 cases (3.4%), maternal problems such as hypertensin, pre-eclampsia, diabetes mellitus, antepartum haemorrhage accounted for 19% of perinatal deaths.[17]

Another hospital based study conducted by Mohamed M.A[18] on risk factors of perinatal mortality in two hospitals (Ibrahim Malik and Aba Yazeed hospitals) in Khartoum states. A total 350 consecutive deliveries in each hospital were studied over a six month period, about 29 were early neonatal deaths for Ibrahim Malik hospital and 27 were early neonatal deaths for Aba Yazeed hospital and the perinatal mortality rates were 104/1000 live birth and 97/1000 live births in the two hospital respectively.

Prematurity accounted for 12.3% and 4.3% of the total deliveries in Ibrahim Malik Hospital and Aba Yazeed Hospital respectively. Birth asphyxia accounted for about half of early neonatal deaths in each studied group. Risk factors of perinatal mortality in both hospitals were found to be maternal age < 20 and > 30 years RR (5.57) and RR (5.51) in Ibrahim Malik compared to RR (63) and RR (37.0) in Aba Yazeed hospital respectively.

Primiparous and multiparous also carried a significant risk in both hospitals RR (11.8) and RR (33) in comparison to RR (48.3) and RR (54.6) in both hospitals respectively.

Other risk factors were maternal illiteracy. Perinatal mortality was found to be decreased with increasing years of education RR (1.32) and decreasing to (0.22)[18].

According to Soba Hospital Annual Perinatal Mortality Report (2001),[19] the total admission to Soba NICU was 365 newborns (17.8%) of the total deliveries, common causes of admission were prematurity (27.1%), infants of diabetic mothers (12.6%), neonatal jaundice (10.7%), neonatal sepsis (9.9%), and congenital malformations (5.5%), 1.9% for birth asphyxia. Causes of perinatal mortality were antepartum foetal death, prematurity,

sepsis and congenital malformations, and the overall mortality was 26.8/1000 live births.

perinatal mortality was 52.6/1000 live birth and the early neonatal mortality was 26.8/1000 live birth. Prematurity was the second cause of perinatal mortality after antepartum fetal death.

In comparison to Police Hospital Perinatal Mortality, the total admission to the NICU were 300 newborns, common causes of admission in the order of prematurity (27.9%), birth asphyxia (20.8%), meconium aspiration syndrome (16.07%), congenital malformations accounted for only 3% and neonatal sepsis for only 1.1%, and the overall mortality was 12% from the total admission.[19] There was similar rate of admission in both NICUs, and similar percentage of prematurity, but they differ in the percentage of birth asphyxia among the admission in Police Hospital, it was 20.8% compared to only 1.9% in Soba NICU, which showed good obstetrical management at Soba Hospital, and the other difference between the two nurseries was in the admission of neonatal sepsis, which accounted for 9.9% in Soba compared to only 1.1% in Police Hospital.

According to the annual perinatal mortality of Omdurman Maternity Hospital, the total admission in 2001 were 1035 cases

and total number of neonatal deaths was 339 cases, which gave neonatal mortality of 23.7%/1000 live births and the pattern of admission was prematurity and RDS constituted 35.5% of total admission, followed by birth asphyxia (17.6%), neonatal sepsis (16.3%) and neonatal jaundice (8.2%), congenital malformation (2.4%).

RDS was the major cause of death which constituted 52% of total deaths, followed by birth asphyxia (24.5%). Neonatal mortality for 2002/2003 were 23.1/1000, 22.3/1000 live births respectively with the major cause of neonatal mortality was RDS.[20]

A recent hospital based study was conducted in Soba University Hospital in the period from December 2003 to June 2004 in early neonatal outcome of preterms. One hundred consecutive live born preterm infants were followed up till their seventh day of birth, it was found that distribution of morbidity among preterms were neonatal jaundice (46%), followed by respiratory distress syndrome (36%), apnea (16%), neonatal infection (14%) and intraventricular haemorrhage (18%). The neonatal mortality was found to be 26% of the total preterm and the survival rates increased with increasing gestational age and

birth weight, and number one cause of early neonatal mortality in the study group was respiratory distress syndrome (46.2%), followed by neonatal sepsis (15.4%), then perinatal asphyxia (11.5%) and congenital malformations (7.7%)[21].

1.2. Causes of neonatal morbidity and mortality:

1.2.1. Prematurity and low birth weight:

Birth weight of the newborn is an important determinant of perinatal and infant mortality. Low birth weight is defined as birth weight of less than 2500g whether born before 37 weeks of gestation (preterm) or small for gestational age[22,23].

In developing countries low birth weight is due to intrauterine growth retardation where in developed countries is mainly due to prematurity[24,25].

The rate of low birth weight in United States is 7.5% at 1997 and for very low birth weight (VLBW) (babies weighing 1,500gm or less at birth) the rate had been 1.1 – 1.4% of all births. VLBW are most often premature i.e. <37 weeks of gestation[3].

The prevalence of LBW in Asia, Bangladesh varies between 23% and 60% and this has presumptive effects on stillbirth and neonatal death.[26] In a cohort study done in a periurban setting in Bangladesh on neonatal mortality of low birth weight infants, it was found that, NMR of LBW infants was 133/1000 live births, of them 112/1000 was early neonatal deaths. Fifty percent of early neonatal deaths occurred within 48 hours and preterm delivery was implicated in three quarters of neonatal deaths. VLBW constituted only 7% of LBW, but had early neonatal mortality of 740/1000 live birth, while early neonatal mortality of weight group 1500-1999 grams constituted 152/1000 live births, and early neonatal mortality of weight group 2000 - 2499 grams was 43/1000 live births[27].

In a study involving 149 consecutive admissions to a nursery in South Africa. It was found that prematurity accounted for 54% of total admission and LBW accounted for 81% of admission and mortality rate was 7% among neonates with more than 37 weeks gestation compared with 20% for those of gestation below 37 weeks (P=0.04). Likewise neonates with lowest birth weight were at highest risk of death[28].

1.2.1.2. Causes of low birth weight:

Intrauterine growth retardation (IUGR) was defined as birth weight of less than 3rd centile for gestational age or below 2 SD from the mean[29].

The causation of IUGR could be due to foetal abnormality e.g. chromosomal abnormality, congenital infections, syndromes or foetal poisoning e.g. alcohol consumption, smoking, ionizing radiation, or maternal factors such as malnutrition, malaria, ill health, or placental abnormality[30].

Causes of preterm birth were foetal causes such as multiple gestation, foetal distress, placental causes such as placental dysfunction, placenta previa or abruptio placentae, uterine abnormality, or maternal causes e.g. pre-eclampsia, chronic illness or infections e.g. UTI or chorioamnionitis, other causes are polyhydramnios, premature rupture of membranes[2].

Taha *et al* in 1989-90 in central Sudan conducted two studies to determine the incidence of LBW and to ascertain the major risk factors which influence birth weight[31].

The incidence of LBW was 18.1% in the community and 8.2% in the hospitals. The ratio of term to preterm LBW was 2.9 in the community but only 1.3 in the hospitals. The study showed two important predictors of LBW and preterm LBW were low

maternal weight and malaria infection during pregnancy. It was found that malaria contributed more to the attributable risk of preterm than term low birth weight. Other risk factors included low socioeconomic status and among the hospital population lack of antenatal care, short birth intervals, poor obstetric history and complications of pregnancy[31].

Elshibly[32]studied 194 consecutive newborns whose weight less than 2500 in Soba University hospital in the period from 1985 - 1987, he found that 65.5% of cases were preterm and 33.5% were IUGR. Only 7.2% of LBW had asphyxia neonatorum and the highest percentage of morbidity was due to infections but RDS and apnoeic attacks although were lesser in frequency were more severe and were attended by high mortality. Sixteen percent of LBW infants died, 61.3% of them were early neonatal deaths[32].

In a study done by Rettwitz[33] in Germany from 1985 to 1999 the latest figure for number of live births in Germany was 770.744 live births in 1999 with a rate of low birth weight of 6.5%. There was rise in LBW concerned mainly infants of < 1500g.This rise in LBW births concerned mainly infants <1500g. In parallel, there was a decrease in early neonatal and infant mortality rates in

all sub groups of LBW infants except for the extremely small infants of < 500g[33].

1.2.1.3. Problems of prematurity and low birth weight:

These were hypoglycaemia, hypothermia, polycythemia, hypocalcaemia, congenital malformations where as 3 - 4% of IUGR will have congenital malformation[34].

1.2.1.4. Respiratory distress syndrome:

Also known as hyaline membrane disease, which is caused by surfactant deficiency and affects mainly preterm infants and it is responsible for the deaths of many preterm infants throughout the world each year, the incidence of RDS is inversely proportional to gestational age. Diagnostic criteria were respiratory distress soon after birth weight with tachypnea more than 60/min, expiratory grunting and sternal and intercostals recession, cyanosis in room air or delayed onset of respiration in very immature babies with the classical chest radiographs of ground glass appearance[35].

Modalities of treatment are surfactant administration, maintenance of normoxemia by head box, assisted ventilation in a form of continuous positive airway pressure (CPAP), which is indicated if recurrent attacks of apnea or if oxygen administration is needed to keep PO_2 > 8k Pa (60 mmHg). Intubation and

positive pressure ventilation (PPV) is indicated if respiratory failure or intractable apnoeic attacks (respiratory failure pH <7.20, $PaCO_2$ >9 kpa or 68 mmHg, PaO_2 < 7 kpa or 53mmHg) in 90% O_2[36].

Complications of RDS were persistent ductus arteriosus, intraventricular haemorrhage, pulmonary complications like pneumonia or pneumothorax, broncho pulmonary dysplasia and long-term neurological sequale.

Other causes of respiratory distress at birth or shortly after birth were transient tachypnoea of newborn, meconium aspiration syndrome, pneumothorax, pneumonia, congenital malformations, congenital heart disease and others causes[36].

In a study done in neonatal intensive care unit in Zimbabwe in 1998, the commonest cause of admission was respiratory distress, and the risk of mortality for those who received mechanical ventilation is 12.29 times greater compared for those who received continuous positive airway pressure (CPAP) by nasal prongs[37].

In a recent study done in Soba Hospital in preterms, it was found that RDS was the main cause of morbidity among the study population and accounted for 46.2% of total deaths[21].

1.2.2. Birth asphyxia:

Is the most common and important cause of preventable cerebral injury occurring in the neonatal period. However, no clinically accepted definition for it. The term is used to imply combination of both hypoxia and hypoperfusion which impairs tissue gas exchange leading to tissue acidosis, almost any organ can be affected[38]. Other definition, asphyxia is considered in newborn with fetal acidosis (pH <7.0), 5-min Apgar score of 0 -3, hypoxic-ischaemic encephalopathy (altered tone, depressed level of consciousness, seizures), and other signs of multi-organ failure[39].

In meta-analysis of studies examining the outcome of neonates with different hypoxic-ischaemic encephalopathy, it appears that grade (I) (irritability, mild hypotonia and poor sucking but no seizures) does not confer an increased risk of death or disability[40]. Other grades were grade II (is lethargy, marked abnormalities in tone and seizures) compared to grade III (which is severe where the newborn will be comatosed, with severe hypotonia with failure to maintain spontaneous respiration, prolonged seizures)[41].

In a comparison of depression of Apgar score with hypoxic-ischaemic encephalopathy grading in predicting outcome,

an Apgar score of 5 or less at 10 minutes was found to be a more specific predictor of death or major neurological sequale than hypoxic-ischaemic encephalopathy grades II, III (95% versus 78%) although it was less sensitive (37% versus 96%)[42].

Risk factors of perinatal asphyxia at Qween Elizabeth Central Hospital, Malawi in 1998, were found to be premature delivery, pre-eclampsia, cephalopelvic disproportion, prolonged second stage labour, foetal distress and APH, assisted delivery[43].

Similar study of risk factors of perinatal asphyxia in Bangkok by Kolatat and Vanpropar[44] concluded that incidence of asphyxia was 9.7% and was highest (26.7%) in infants less than 1000g, and the three common risk factors for asphyxia were abnormal fetal heart pattern, thick meconium stained amniotic fluid and premature delivery[44].

Chondra and Ramji found that asphyxia rate is 36.3/1000 live births and the associated risk factors were prolonged second stage labour OR (9.4), vaginal breech deliveries OR (6.6), elective C/S OR (4.6), PIH OR (2.7), IUGR OR (2.4)[45].

1.2.3. Neonatal sepsis:

Incidence of neonatal sepsis varies from 2.7/1000 live births in developed countries to 10-50/1000 live births in

developing countries though under reporting common in both. Incidence in preterm infants rises up to 1/250 live premature babies. Predisposing factors for sepsis may be maternal, perinatal or environmental. Maternal factors like chorioamnionitis and urinary tract infection increase the risk of infection by three to four folds, prematurity increases the risk of infection by 20 folds, but there is considerable debate about the risk of infection following prolonged rupture of membrane.[46]

Signs and symptoms in the newborn are often non-specific, the most frequent symptoms are lethargy, poor feeding, abdominal distension and the most frequent signs are prolonged capillary filling time, glucose intolerance and unexplained persistent apnoea.[47]

In Europe and North America, gram positive streptococci (GPS) is the most common gram positive bacteria causing neonatal septicaemia, this however, is not the case in most Afro Asian Countries. About 35 - 40% of females genital tract are colonized by GBS and although the vertical transmission rate is approximately 50 - 70%, the attack rate for neonatal infection is less than 0.3%[47].

Neonatal sepsis may be categorized as early onset or late onset sepsis, 85% of newborns with early onset infection present within 24 hours, 5% present at 24 - 48 hours and a smaller percentage of patients present between 48 hours and 6 days of life. Onset is most rapid in premature neonates. Early onset sepsis is associated with acquisition of micro-organisms from the mother, micro-organisms most commonly associated with early onset infection include Gram positive group B streptococcus (GBS), *E. coli*, *Haemophilus influenzae* and *Listeria monocytogenes*.

Late onset sepsis occurred from the seventh day of life and is acquired from care giving environment. Micro-organisms that have been implicated in causing late onset sepsis include *Coagulase-negative staphylococcus*, *Staphylococcus aureus*, *E. coli*, *Klebsiella*, *Pseudomonas*, *Enterobacter*, *Candida,* GBS, *Seratia*. The infant's skin, respiratory tract, conjunctivae, gastrointestinal tract and umbilicus may become colonized from the environment leading to the possibility of late onset sepsis[47].

In United States in 1990s intrapartum antibiotic prophylaxis was recommended to prevent maternal infant transmission of group B streptococcus (GBS) which is a leading

cause of early onset sepsis (sepsis developed in the first week of life), since then early onset GBS disease declined by 70%[48].

In Africa, a study done in neonatal intensive care units in Lome showed that, the most predominant micro-organisms causes early onset-neonatal sepsis was *E.coli*, followed by *S. aureus* and the lethality was 36% with an excess of lethality for *S. aureus* (43%)[49].

In a four year study on neonatal sepsis at neonatal intensive care unit by Leibovitz *et al* in Israel, the incidence of early onset-sepsis was 17% and the main pathogens of early onset-sepsis were *S. agalactiae* (42%) and *E. coli* (32%) and main pathogens of late onset-sepsis developed after seven days were *Klebsiella* SP (31%), coagulase-negative staphylococci (18%) and the overall fatality from neonatal sepsis was 0.8/1000 live birth[50].

1.2.4. Congenital malformations:

Congenital anomalies are major causes of stillbirth and neonatal deaths, early recognition is needed for planning care[40].

In study of infants with congenital anomalies admitted to 17 Canadian neonatal intensive care units,13.7% of total admissions were congenital malformation, which were associated with higher mortality and morbidity[51].

Ali IF in a study of 4152 newborns in Khartoum North and Soba Hospital found that the incidence of congenital malformations was 18/1000, the case fatality rate was found to be 14.7% and the main causes of death were cardiac and CNS anomalies[52].

In a recent study done in Omdurman Maternity Hospital, Sudan the incidence of neural tube defects was 3.48/1000 which is the highest percentage in Africa, and 50% of the cases were myelomeningiocele, 38% were anencephaly[53].

1.2.5. Meconium aspiration syndrome (MAS):

Is defined as respiratory distress following inhalation of meconium before, during or immediately after delivery and the baby had the criteria of respiratory distress i.e. respiratory rate >60/min, grunting expiration, indrawing of the sternum, intercostal spaces and lower ribs during inspiration and cyanosis without O_2. MAS is a disease of term or post-term pregnancy[54,55].

In the large American National Institutes of Health perinatal outcome of more than 50,000 deliveries, where the prevalence of meconium aspiration syndrome was 18.4% compared to 11.5% in the 1970 perinatal mortality survey in United Kingdom[56].

William and Thomas studied risk factors for MAS in newborns who were delivered through meconium stained amniotic fluid, MAS developed in 6.8% of births, 45.8% required ventilatory support. Looking at multiple prediction level, an infant with fetal distress, Apgar <7 at 1 and 5 minutes and thick meconium has 79.8% probability of developing MAS[57].

Bhaskar and Karthikeyan in an Indian study showed risk factors associated with MAS were primiparous, grand multiparous, post term delivery, prolonged rupture of membranes, infants with moderate to severe birth asphyxia[58].

1.2.6. Neonatal jaundice:

Jaundice is observed during the first week of life in approximately 60% of term infants and 80% in preterm infants. Unconjugated bilirubin is neurologically toxic to infants at certain levels. Prematurity, asphyxia, and sepsis increase its effects and increase the susceptibility of brain cells to its toxicity[59].

Hyperbilirubinaemia is either direct or indirect hyperbilirubinanaemia, that is present at birth or in the first 24 hours requires immediate attention and may be due to erythoblastosis fetalis, concealed haemorrhage, sepsis, intrauterine

infections. Jaundice that appears on the second or third day usually is physiological but may represent a more severe form[60].

Neonatal jaundice constituted 45.6% of newborn admitted at a tertiary hospital in Nigeria in a ten years period study (1981-1990) and mortality among them was 14.1%. Neonatal infections constituted 18.0% of total admissions and the mortality about 12.4%[12].

1.2.7. Birth trauma:

It is a potentially avoidable mechanical injury occurring during labour. Birth injury could be soft tissue injuries such as extracranial (caput succedaneum, subaponeurotic haemorrhage, cephalohematoma) or intracranial injuries. Other birth injuries were peripheral nerve injury, e.g. facial nerve damage usually in forceps delivery, neck retraction in breech or shoulder dystotia give Erb's palsy (c_5, c_6 injury) or phrenic nerve palsy (c_3, c_4, c_5) and spinal cord injury. Conditions predisposing to birth injury were numerous e.g. grand-multiparity, very young and old maternal age, twins particularly the second twin, prematurity and low birth weight, instrumental delivery and macrosomia[60].

1.3. Risk factors of early neonatal mortality:

Risk factors associated with early neonatal mortality and morbidity were numerous including demographic social factors e.g. maternal age less than 20 years and more than 40 years, poverty, medical diseases e.g. diabetes mellitus, hypertension, previous pregnancy with stillbirth or neonatal death, pre-eclampsia, APH, polyhydramnios and oligohydramnios, prematurity, congenital malformations, premature labour, Apgar score of less than 4 at 1min and multiple gestations[61].

1.3.1. Maternal age and parity and education:

A retrospective cohort study was conducted for all live births (single tone were 22,546,718; twins 5,35544) in United States in 1985-1986, 1990-1991, 1995-1996. The result showed that maternal age had U-shaped association with mortality among singletons, with highest rates seen at extremes of ages, while among twins there was a steep and inverse relationship between age and mortality with those born to young mothers experiencing the highest mortality rates, 7% of twin births resulted in an infant death for women who were younger than 20 years, 2.7% for those 30-34 years and 2.0% for women 40-49 years[62]

In a hospital-based case control study in Nicaragua, on risk factors for early neonatal deaths. It was found that interaction

between mortality and the mother's versus father's literacy, there was high risk of mortality if the mother is illiterate and the father was literate (odds ratio 7.0, CI 2.6 -19.3), while illiteracy of both parents was associated to a lower risk (OR 4.2, CI 1.0-18.3). The strong association between maternal illiteracy and early neonatal death is striking[63].

Six-hundred twenty-one grand multiparous (parity more than 4) women were prospectively compared with 621 age matched multiparous (parity 2-4) as controls, grand multiparity was associated with low socioeconomic status and low education (OR 6.4, 95%; CI 4.5- 9.0), poorer antenatal care (OR 6.4, 95%; CI 1.5- 6.1). Grandmultipara had more previous intrauterine and perinatal deaths (OR 3.2, 95%; CI 2.0-5.0). They had fewer intrapartum complications e.g. instrumental deliveries (OR 0.31; 95% CI 0.16 - 0.59), arrest of cervical dilatation (OR 0.19, 95% CI 0.06 - 0.66)[64].

1.3.2. Maternal social class and effect of ANC:

Chatterjee and others studied biosocial factors influencing early neonatal mortality, they found early neonatal mortality was higher among illiterate mothers (odds ratio 3.9) and those living in

rural and slum areas (OR 3 and 2.8). Also early neonatal mortality is higher in those who did not receive ANC OR 28[65].

1.3.3. Effect of adverse outcome of the previous pregnancy:

In the study done in Sudan, in East Nile province it was found that compared to mothers whose last outcome had resulted in a live birth, mothers with previous stillbirth had seven times the risk of stillbirth and more than twice the risk of neonatal mortality in the current pregnancy[15].

Risk factors for neonatal death were primiparity (OR 2.18), previous stillbirth (OR 3.19), prolonged labour (OR 2.80) in a study done by Leach and others[10] while increase risk of neonatal mortality was found to be male sex and twin delivery in Ethiopian study [9].

1.3.4. Multiple pregnancy:

Twin pregnancy account for about 2% of births but 9% of perinatal deaths and between 20% - 30% of twin will born preterm with more neonatal mortality than foetal deaths[66].

Most, but not all, studies have shown that second born twin was at high risk of death and morbidity[67,68].

In retrospective study in Zambia to determine risk factors of perinatal mortality in twin gestation, it was found that risk factors associated with perinatal mortality were birth weight less than 2000 gm (47%), retained second twin (36%), primiparity (28%), foetal malpresentations (25%)[69].

Kleimmsan, *et al* studied perinatal mortality among United States multiple births and singletons for 1960 and 1983 using the linked birth/ infant death data sets. They found that the twin mortality rates were four to five times that of singletons.[70]

1.3.5. Apgar score and early neonatal mortality:

Apgar score had been used to assess the condition and prognosis of newborn infants throughout the world for several decades. In a study done by Heller and others showed that low Apgar score of 0-3 at 1,5,10 minutes in term baby is a risk factor for early neonatal mortality compared with scores 7-10 at 1,5,10 minute and they were superior to umbilical blood pH in predicting early neonatal mortality[71].

Another study done by Brain and Donald, they studied 13,399 infants of 26-36 weeks of gestation and 132, 228 born at

term. The neonatal mortality rate was (for preterm group) 315/1000 for 5-minute Apgar 0-3 as compared with 5/1000 for the same infants with 5-minute Apgar 7-10 while for term group neonatal mortality was 244/1000 for 5-minute Apgar of 0-3 as compared to 0.2/1000 for 5-minute Apgar 7-10 and the risk of neonatal death in term infants with 5-minute Apgar of 0-3 was eight times the risk in term infants with umbilical artery blood pH values of 7.0 or less[72].

JUSTIFICATIONS

1. Many developing countries have high neonatal mortality and morbidity of which Sudan is not an exception.
2. Most predisposing factors to neonatal mortality and morbidity are preventable.

3. Few hospital-based studies were done, few studies have been done to evaluate the effect of nurseries in mortality figures.

OBJECTIVES

1. To determine the incidence of early neonatal outcome in Omdurman Maternity Hospital Nursery Unit.
2. To describe the pattern of early neonatal morbidity in Omdurman Maternity Hospital Nursery Unit.

3. To evaluate the risk factors associated with early neonatal morbidity and mortality.

MATERIALS AND METHODS

2.1. Study design:

A prospective, case control, hospital based study.

2.2. Study area:

The study was conducted in Omdurman maternity hospital.

2.3. Study duration:

From the first of August 2004 till the first of January 2005.

2.4. Study population and sample size:

2.4.1. Study population:

Study population included neonates delivered at OMH and were admitted to OMH Nursery Unit in three days a week (Saturday, Monday and Wednesday), while the control group included neonates delivered in the same hospital in the nearest time of the case, they were not matched to the case by sex, gestation or weight.

2.4.2. Sample size:

Sample size was calculated using Epi-info statcalc-sample size calculation for unmatched case-control studies. A size of 202 cases and 202 controls was found to be sufficient to detect a ratio of 2.5 or more with a power of 80% at a significance level of 0.05 and proportion of exposure to the control of 0.08. These estimates of (odd's ratio and proportion in controls) are based on the results of a study on the effect of a past history of early neonatal death on the risk of perinatal mortality.[18]

2.5. Inclusion criteria:

2.5.1. Cases: these included neonates admitted to OMH-nursery in 3 days a week (Saturday, Monday and Wednesday) in the period of the study.

2.5.2. Controls: the control group included neonates delivered at the nearest time in the same hospital and were not admitted to the nursery unit.

2.6. Exclusion criteria:

- All neonates whose parents refuse to participate in the study.
- Neonates who could not be reached after being discharged because of no access either by using telephone or those living far away.
- Neonates who were discharged from the postnatal ward and readmitted into the nursery.

2.7. Research technique:

2.7.1. Consent:

A written consent was obtained from OMH administrator. An informed verbal consent was obtained from the parents.

2.7.2. Research tools:

Detailed questionnaire pertaining to neonates and their mothers were used; each questionnaire included maternal data, history of pregnancy, mode of delivery, Apgar score, complications and need for resuscitation of the newborn at birth, as well as full clinical examination of the neonate including weight, length and head circumference.

A non-stretchable tape was used to measure both length and head circumference of the newborn and the measurement was taken to the nearest 0.1cm. The weight of the newborn was measured by Salter scale and the reading was taken to the nearest 10gm. Weight and head circumference centiles were determined using centile charts for

gestational age. Gestational age was calculated using last menstrual period and Parkin method.[73]

Investigations done to each neonate in the study group were Hb%, blood grouping of the mother and the baby.

Specific investigations were done according to the case, full blood count and clotting profile for neonates with bleeding tendency, total serum bilirubin and differential with Coomb's test for neonatal jaundice, CXR for neonates with respiratory distress, except for neonates with respiratory distress syndrome who were diagnosed clinically according to clinical criteria of RDS only,[35] since there was no radiological facilities in Omdurman Maternity Hospital and those newborns were usually very ill to be mobilized outside the hospital. Cranial U/S for hydrocephalus and clinical evidence of intraventricular haemorrhage and blood culture for suspected neonatal sepsis, i.e. neonates with signs of septicaemia such as hyperthermia, hypothermia, lethargy, refusal or poor feeding, looking ill. For those of signs of septicemia, 1-3 ml of blood was taken under aseptic precautions for blood culture using

Bactec computerized blood culture system for detection of bacterial growth.

Causes of admission to the nursery and clinical diagnosis would be recorded in the questionnaire.

Neonates were followed up until their seventh day of life or death, those who were discharged from the nursery before completed their seventh day of life, were seen in refer clinic every Wednesday.

For those who died relevant cause of death, time of death would be recorded.

For the control group, neonates were followed up by telephone till their seventh day and morbidity and mortality will be registered.

2.7.3. Research team:

The author who filled the questionnaire, examined the neonates and follow up the cases till discharge, death, as well as follow up at refer clinic in OMH Nursery Unit.

Oncall doctors who admitted neonates during their night duty and died before being seen by the author.

2.8. Data analysis:

Data collected were entered in the computer, analyzed using the SPSS and epi-info systems. Results were tested for significance using odd's ratios to calculate the relative risk (RR). A chi-squire was used, a probability of < 0.05 was considered to be significant.

2.9. Funds:

The research was done with self-resources, without external funds.

RESULTS

3.1. Newborns characteristics:

3.1.1. According to multiple pregnancy:

Eleven cases from the study group were twin deliveries comprising 10.9% (**Fig.1a**), in comparison to 5 cases in the control group (5.9%) (**Fig.1b**).

3.1.2. Gender:

Male predominated the studied population 116 (57.4%) while female represented 86 (42.6%). In the control group male represented 109 (54.0%) and female represented 93 (46.0%) (**Fig.2**).

3.1.3. Gestational age:

Distribution of the study group by gestational ages was shown in (**Fig. 3**). Those with gestational age between twenty seven weeks and thirty weeks were 15 (7.4%) and between thirty one and thirty three were 19 (9.4%), while those who were between thirty four to thirty six were 40 (19.8%). Between thirty-seven and thirty-nine were 57 (28.2%) and between forty and forty-two were 71 (35.2%).

3.1.4. Birth weight:

In the study group only one newborn was below one kilogram in weight (0.5%) while newborns with weights from 1-1.49kg were 24 (11.9%), those between 1.5-1.99kg were 43(21.3%), those with weights 2-2.49kg were 24 (11.9%), those with weights from 2.50-2.99kg constituted 37 (18.3%), those from

3.00-3.49kg were 32 (15.8%), and from 3.50-3.99kg were 23 (11.4%) while those of 4kg or more were 18 (8.9%) (**Fig. 4**).

In comparison to the control group where there were no cases below birth-weight of 1.50kg. Those having their weight between 1.5-1.99 were 3 (1.5%), those between 2.00-2.49kg were 5 (2.6%) those between 2.5-2.99 were 39 (20%), those between 3.00-3.49 were 102 (50.5%) while those with weight range of 3.50-3.99kg were 46 (23.6%) and those whose weight of 4 kg or more were 7 (3.6%).

There was significant difference in birth weight distribution between the study group and the control group (P= 0.0001).

3.2. Paternal characteristics:

3.2.1. Paternal education:

Figure 5 shows most of fathers in the study group were in the group of 10-14 years of education (33.7%) followed by education of 5-9 years (31.7%). While illiterate fathers constituted 13.9%, which was equal to the number of fathers who had education of more than 14 years, and the lowest percentage for those who were educated for 1- 4 years (6.9%). In comparison to the control group where also the level of education of 10-14 years also accounted for the highest percentage (46.0%) followed by fathers who were educated to more than 14 years (28.7%), then 5-9 years of education (20.8%) and the lowest is for the illiterate group (2.5%) and fathers of 1- 4 years education constituted (2.0%).

Statistically there was significance difference between the study group and the control group in respect to duration of education.

3.2.2. Paternal occupation:

Most of the cases had fathers who were unskilled labourers (41.6%), followed by fathers who were civil employees (23.3%) and those fathers who were professionals and merchants were of lowest percentage in the case group constituting (0.5%)

and (7.4%) respectively. When compared to control group, most of the fathers were of civil employee (36.1%) followed by unskilled labourers (22.3%), those who were merchants were about (13.9%) and the professionals accounted about (3.0%) from the control group as shown in (**Fig. 6**).

There was significance difference between the study group and the control group in respect of father's occupation (P= 0.001).

3.3. Maternal characteristics:

3.3.1. Maternal age:

The most common maternal age range found among the study group was from 20 - 29 years (54.5%), followed by age group 30-39 years (37.6%) and the ages of less than 20 years and more than 40 years showed smallest percentage (5.9%) and (2.0%) respectively. In contrast to control group, which showed that, mothers age less than 20 years constitute (6.4%), while those in the age group of 20 -29 years constituting 53.5% and for

those in the age group of 30 -39 were 38.6%, and more than 40 years were 1.5%, and there was no statistically significant difference between the study group and control regarding the maternal age (P= 0.973) (**Fig. 7**).

3.3.2. Maternal education:

There was high percentage of maternal illiteracy in the study group compared to control group 14.8% compared 4.5%. While more percentage of increase in years of education in control group compared to study group this was seen clearly in mothers whose level or education was more than 14 years was found about 27.9%, in comparison to 9.9% in the study group. There was significant difference between two groups (P= .0001) (**Fig. 8**).

3.3.3. Complications of pregnancy:

Regarding complications during pregnancy, 75.7% of mothers in the study group had no pregnancy complications, while 90% of mothers in the control group had no complications. Major complications include pregnancy induced hypertension, diabetes mellitus, antepartum haemorrhage which constituted 7.9%, 7.5%, 6.4% of the study group respectively, compared to 6.4%, 2.0%, 0.5% of the control group respectively. There was a significant

difference between the two groups with regard to pregnancy complications (P= 0.0003), (**Table 1**).

3.3.4. Mode of delivery:

Concerning the mode of delivery, 103(51%) of the mothers in the study group were delivered vaginally, compared to 126 cases (62.4%) in the control group, while 85 mother (42.1%) delivered by caesarean section, compared to 67 cases (33.1%) in the control group. Only 14(6.9%) mothers had instrumental delivery compared to 9(4.5%) in the control group. There was no significant difference between the two groups concerning the mode of delivery (P= 0.13) (**Table 2**).

Table 1: Distribution of study and control groups according to complications of pregnancy (n= 404)

Complications	Study group		Control group	
	n	%	n	%
No complications	153	75.7	182	90.1
Pregnancy induced hypertension	16	7.9	13	6.4
Diabetes mellitus	15	7.5	04	2.0
Antepartum haemorrhage	13	6.4	01	0.5
Anaemia	02	01.0	01	0.5
Others	03	1.5	01	0.5

Total	**202**	**100.0**	**202**	**100.0**

P < 0.0003

Table 2: Distribution of study and control groups according to mode of delivery (n=404)

Mode of delivery	**Study group**		**Control group**	
	n	%	n	%
Normal vaginal delivery	103	51.0	126	62.4
Ventose	01	0.5	01	05
Forceps	13	6.4	08	4.0
Caesarean section	85	42.1	67	33.1
Total	**202**	**100.0**	**202**	**100.0**

P < 0.13

3.4 Social characteristics

3.4.1 Family income:

Distribution according to monthly income showed that the highest percentage in the study group was for the income between 10,000 - < 25,000 Sudanese Dinnars, while for the control group the highest percentage was for the income of 25,000 - 50,000 Dinnars. The lowest percentage was for the income range from 75,000 - < 100,000 for both control and study group. The difference was statistically significant (P = 0.0001) (**Table 3**).

3.4.2 Water supply:

More than half of the study group had their water supply from tape water (pipe in the house), i.e. 57.4%, compared to the majority of control group (80.7%), and 33.7% of the studied population used to buy water (classified as others) compared to

only 10.9% of the control group and the difference was statistically significant (P = 0.0001) (**Fig. 9**).

3.4.3 Types of latrines:

The majority of studied population (89.6%) used to have pit latrines compared to 80.7% of the control group, while only 8.4% of the study group used to have siphon compared to 18.4% of the control group and this difference was found to be significant (P < 0.05) (**Fig. 10**).

Table 3: Distribution of study and control groups according to monthly income (n= 404)

Monthly income (SD)	Study group		Control group	
	n	%	n	%
5,000 - < 10,000	15	7.4	20	9.9
10,000 - < 25,000	85	42.1	40	19.8
25,000 - < 50,000	74	36.6	84	1.6
50,000 - < 75,000	15	7.4	41	20.3
75,000 - <100,000	06	3.0	06	3.0
> 100,000	07	3.5	11	5.4
Total	**202**	**100**	**202**	**100**

P < 0.0001

SD = Sudanese Dinars

3.5 Effects of antenatal care:

5.9% of mother in the study group did not attend any antenatal care services compared to only 1% of the control group. 78.2% of the mothers in the study group attended ANC between 1-9 times, compared to 66.3% in control group. While those who attended more than 9 visits were 15.8% for study group compared to 32.7% in the control group. Those differences were statistically significant ($P < 0.0001$) (**Table 4**).

3.6 Effect of past history of neonatal death:

A positive history of neonatal death was detected in 19(9.4%) families of the study group compared to 3(1.5%) in the control group. The difference between the two groups was statistically significant ($P = 0.006$) (**Table 5**).

3.7. Causes of morbidity:

The most common cause of admission to the nursery was prematurity, it accounted for 79 (39.1%), 39(19.3%) were admitted with birth asphyxia. This was followed by neonatal jaundice for which 25(12.4%) were admitted, congenital malformations was the

reason for admission in 23 (11.4%), while as neonatal sepsis accounted for 13 cases (6.4%) and birth trauma for 9 cases (4.5%) and meconium aspiration syndrome for 8 cases (4.0%) (Table 6**).**

Table 4: Distribution of study and control groups according to ANC attendance (n=404)

No. of ANC visit	Study group		Control group	
	n	%	n	%
Not attended	12	5.9	2	1.0
Attended 1-9 visits	158	78.2	134	66.3
Attended > 9 visits	32	15.8	66	32.7
Total	**202**	**100.0**	**202**	**100.0**

P < 0.0001

ANC = Antenatal Care

Table 5: Distribution of study and control according to past history of neonatal deaths (n = 404)

Past history of neonatal deaths	Study group		Control group	
	n	%	n	%
No past history	183	90.6	199	98.5
Past history	19	09.4	3	1.5
Total	**202**	**100.0**	**202**	**100.0**

P < 0.0001

Table 6: Causes of morbidity among the study group (n = 202)

Causes of morbidity	n	Percentage
Prematurity	79	39.1
Birth asphyxia	39	19.3
Congenital malformation	23	11.4
Neonatal jaundice	25	12.4
Neonatal sepsis	13	06.4
Birth trauma	09	04.5
Meconium aspiration syndrome	08	04.0
Others*	44	21.8

** Others: were cases of infant of diabetic mother, precious babies for observation, haemorrhagic disease of newborns, aspiration pneumonia, congenital pneumonia.*

3.8. Outcome of study group: -

One hundred and forty seven neonates were alive in the study group (72.8%), while the mortality was recorded in 55 cases (27.2%).

From the survivors 131 (64.9%) were discharged with a follow up, while 13 (6.4%) were discharged, being referred to other units, and 3(1.5%) babies remained in the nursery after the seventh day of age (**Fig. 11**). Compared to a mortality of only 0.5% in control group (**Fig. 12**).

3.9. Incidence of early neonatal mortality:

The total number of live births in Omdurman Maternity Hospital during the period of the study was 8314 live births. Early neonatal deaths in this study were 55. So early neonatal mortality in this study was estimated to be found to be 6.6/1000 live births.

3.9.1. Early neonatal mortality of singleton and multiple births: -

There were 22 twin newborns (resulting from 11 pregnancies), Ten of them died constituting 18.2% of the whole

deaths and 45.5% of twin deaths. This was in contrast to 45 deaths from singleton pregnancy, which constituted about 81.8% from total deaths, but only 28.0% of deaths were due to single pregnancies (**Table 7**). There was statistically difference regarding multiple pregnancy (P = 0.042).

3.8.2. Early neonatal mortality by infant gender, gestational age and birth weight: -

3.8.2.1. Infant gender:

Though males out number the females in the study group 116 males (57.4%) compared to 86 females (42.6%) (**Fig. 2**), early neonatal mortality was almost the same in the two groups. Twenty-nine (25%) of male neonates died compared to 26 (30.2%) for females. There was no statistically significant difference between males and females regarding early neonatal mortality (P = 0.409) (**Fig. 13**).

3.9.2.2. Gestational age:

Regarding gestational age as a cause of early neonatal mortality, all neonates of gestational age from 27 - 30 weeks died (100%), while 11 (57.9%) of 31 -33 weeks died and 10 (25%) of 34-36 weeks were early neonatal death. Those whose gestational age lies between 37- 39 weeks were 57 (10.5%), only

6 of them were early neonatal deaths, while as those from 40 - 42 weeks were 71 cases, and 13 (18.3%) of them were early neonatal deaths (P = 0.0001) (**Fig. 14**).

3.9.2.3. Early neonatal mortality by birth weight:

When regarding the relation of birth weight to early neonatal mortality we found that only one newborn below 1 kg and he died (100%), while 24 neonates were found in the weight group from 1.0 - 1.49 kg and of those 20(83.3%) were early neonatal deaths. Those in weight group from 1.50 - 1.99 kg were 43 cases and 12 (27.9%), were early neonatal deaths, while 24 neonates in the weight group from 2.0 - 2.49 kg, 8 (33.3%) were died. In the weight groups of 2.5 - 2.99 kg, 3.0 - 3.49, 3.5 - 3.99 and of 4 kg or more had early neonatal mortality of 16.2%, 9.4%, 8.7% and 16.7% were found respectively (P= 0.0001) (**Fig. 15**).

3.10. Time of early neonatal mortality:

Sixty percent of the early neonatal deaths occurred in the first 48 hours of admission, while 40% in the remaining 5 days (**Fig. 16**).

Table 7: Early neonatal mortality of singleton and multiple births

Multiple Pregnancy	Alive n (%)	Early neonatal deaths n (%)	Total n (%)
Twin newborn	12 (54.2)	10 (45.5)	22 (100)
Single newborn	135 (75.0)	45 (25.0)	180 (100)
Total	**147**	**55**	**202**

$P < 0.042$

3.11. Causes of early neonatal mortality:

The main cause of early neonatal deaths in the study group was prematurity which accounted for 31 cases (56.4%). The second cause was congenital malformations and accounted for 11 cases (20.0%). Those were followed by asphyxia in 8 (4.5%) cases, and sepsis in 2 (3.6%) cases (**Table 8**).

3.11.1. Causes of early neonatal mortality:

3.11.1.1. The prematurity and early neonatal mortality

Prematurity accounted for 79 cases (39.1%) of the study group, 31 cases of the early neonatal deaths were due to prematurity. Respiratory distress syndrome was reported in 22 (27.8%) preterm infants. Nineteen out of those 22 preterms died due to RDS, and this is constituted 22.7% of whole preterms. The rest of preterms babies were 57 preterms, of them 12 newborns died and constituted 15.2% of whole preterms. Causes of death of these preterms were asphyxia, hypothermia, hypoglycaemia, neonatal sepsis and jaundice (**Table 9**).

Table 8: Causes of early neonatal mortality among study group (n = 55)

Causes of early mortality	Frequency	Percentage
Prematurity	31	56.4
Congenital malformation	11	20.0
Asphyxia	08	14.5

Sepsis	02	03.6
Others*	03	05.5
Total	**55**	**100.0**

** Others: 2 cases of necrotizing enterocolitis, 1 case of multiple haemangioma and thrombocytopenia.*

Table 9: Causes of death of preterm babies (n =31)

Causes of deaths	n (%)
Respiratory distress syndrome	19 (61.3)
Birth asphyxia	03 (9.6)
Hypothermia	02 (06.5)
Hypoglycemia	02 (6.5)
Neonatal sepsis	02 (06.5)

Neonatal jaundice	02 (06.5)
Total	**31 (100.0)**

3.11.2. Early neonatal mortality and congenital malformation:

Pattern of early neonatal mortality due to congenital malformations in the study group showed that, central nervous system congenital malformations were the commonest cause of death being due to neural tube defects (7.4%) and 3.6% for congenital hydrocephalus and both constituted half of deaths from congenital malformations (**Table 10**).

3.11.3. Early neonatal mortality and neonatal sepsis:

Thirteen cases (6.4%) were suspected to have neonatal sepsis, but only 6 cases (46.2%) had positive blood cultures, of those early neonatal mortality occurred in 2 cases (15.4%). *Klebsiella pneumoniae and Staph. aureus* were the organisms isolated from these cultures (**Fig. 17**).

Table 10: Pattern and mortality of congenital malformations in OMH Nursery Unit (n = 23)

Pattern of congenital malformations	Alive	Died	Total	%
Neural tube defects	1	4	5	7.4
Congenital hydrocephlus	1	2	3	3.6
Syndromes	3	1	4	1.8
Skeletal dysplasia	1	2	3	3.6
Cleft lip + palate	2	0	2	0.0

Choanal atresia ± other malformations	1	1	2	1.8
Others*	3	1	4	1.8
Total	**12**	**11**	**23**	**20**

** hypospadius + absence urethral opening, Hydropsfetalis and gastrochiesies.*

3.12.Relative risk of early neonatal deaths by newborn gestational age and birth weight:

3.12.1. Gestational age:

When preterm neonates (less than 37 weeks of gestation) were compared with term neonates (of 37 or more of gestation) the relative risk of early neonatal mortality was found to be 2.8 (P = 0.001).

3.12.2. Birth weight:

Concerning weight of newborn, when the group of 2.50- 2.99 kg was taken as a reference group, neonates of the birth weight 1 - 1,49 kg had a relative risk of 5.18 (C1: 5.03 -

12.44) of early neonatal mortality. For birth weight of 1.5 - 1.99 kg the relative risk of early neonatal mortality was found to be 0.92 (C1: 1.16 - 1.47).

3.12.3. Relative risk of early neonatal mortality by maternal age and education:

Mothers who were less than 20 years of age when compared with a reference group of 20 - 29 years of age, it was found that the relative risk of early neonatal mortality was 0.806.

When comparing illiterate mothers with educated one, the relative risk of early neonatal mortality for illiteracy was 0.66 (C1: 0.86 - 1.11) (P = 0.218).

3.12.4. Relative risk of early neonatal mortality by antenatal care visits:

Considering the number of antenatal visits, only 12 mothers had not attended any ANC, three of their infants were early neonatal deaths, mothers who had attended one to four visits, and mothers who had attended more than four visits were 190 mothers, 52 of their newborns were early neonatal deaths, RR 0.74 (C1 1.03 - 1.45) (P = 0.23) (**Table 11**).

Concerning presence of a past history of neonatal death about 182 mothers from the study group had no past history of

neonatal deaths, and 47 of their newborns were early neonatal deaths. Twenty mothers had a positive history of neonatal death and 8 of their newborns were early neonatal deaths. The relative risk was found to be 0.78 (C1: 1.07 - 1.47) (**Table 12**).

Table 11: Early neonatal outcome by (ANC) visits

ANC visit	**Alive**	**Died**	**Total**
	n (%)	**n (%)**	**n (%)**
Not attended ANC	9 (5.4)	3 (5.5)	12 (5.4)
Attended	138 (94.6)	52 (94.5)	190 (94.6)
Total	**147 (100.0)**	**55 (100.0)**	**202 (100.0)**

P = 0.5

ANC = Antenatal Care

Table 12: Early neonatal outcome by past history of neonatal deaths

Past history of neonatal death	Alive n (%)	Died n (%)	Total n (%)
No	135 (9.8)	47 (85.5)	182 (90.1)
Yes	12 (8.2)	8 (14.5)	20 (9.9)
Total	**147 (100.0)**	**55 (100.0)**	**202 (100.0)**

P = 0.23

DISCUSSION

In a five months period, 202 newborns admitted to the Omdurman Maternity Nursery Unit and a control group of 202 neonates were taken at the same time. The gender distribution in the two groups was comparable with a predominance of male newborns.

According to distribution by multiple births, the percentage of twin cases was 10.9% in the study group in comparison to 5.9% in the control group. This could be due to the high percentage of prematurity, which is a risk factor for multiple pregnancy.

The prematurity accounted for 39.1% of cases, which was a high percentage of preterm admission, it was higher than percentage of prematurity reported in Soba and Police hospitals which were 27.1% and 27.9% respectively,[20] but less than results obtained in South Africa, where the admission due prematurity was 54%[29] and more than the results obtain from Nigerian study (18.2%)[13].

Maternal age which was dominantly found in this study 20 - 29 years in both the study and control group (54.5%) and (53.5%)

respectively. This was due to the fact that, this was the age of maximum reproduction. Other age groups < 20 years, 30 - 39 and >40 years showed similar percentages in both groups.

Maternal education when studied showed that the percentage of maternal illiteracy in the study group was 14.8% compared to 4.5% in the control, while more mothers were found with increasing years of education in the control group especially when duration of education is more than 14 years. Where 27.9% of the mothers in the control group were found compared to 9.9% in the study group. This could be explained by the fact that mothers from the periurban area around Omdurman usually present to hospital if they had complications with pregnancy are expected to have lower educational level. In this study, illiteracy, of mothers had no significant effect on early neonatal mortality (P = 0.218, RR = 0.66). This situation was the same in Pakistan, where in a study in neonatal unit showed that maternal risk factors like maternal age, parity, illiteracy had no effect on neonatal mortality compared to pregnancy related factors such as antepartum haemorrhage and toxaemia,[66] but that was different from a study done in Nigeria, which showed a striking relation between maternal illiteracy and neonatal mortality (OR 7.0)[64] This result is also different from a previous Sudanese study of perinatal mortality in two hospitals, which was found to decrease with increasing years of education (RR 1.32

decreased to 0.22)[18].

Most of the cases studied showed that their fathers were educated for 10 - 14 years, and the percentage of illiteracy and fathers education of more than 14 years, both being 13.9%. While in the control group there was a lower percentage of paternal illiteracy (2.5%) and high percentage of fathers educated for more than 14 year (20.8%). The difference between the two groups could also be due to the periurban area that is covered by Omdurman Maternity Hospital, and the same explanation applied for paternal occupations in the study group, most of the fathers were unskilled labourers (41.6%) compared to only 22.3% in control group, while the professional and merchants were more in the control group compared with study group, 3.0%, 13.9% versus 0.5% and 7.4 % respectively. Those differences could be attributed to decrease level of education in the study group compared to control group.

Only 12 (5.9%) mothers in the study group did not attend ANC compared to two mothers in the control group. Lack of ANC was not detected as a risk for neonatal mortality in this study (RR 0.74). This is different from studies done in Northern Brazil[5] and Pakistan[8], both of which showed an inadequate ANC to be a risk factor for early neonatal mortality. The same was reported in India, where mothers who did not receive ANC had an increase risk of early neonatal death (OR 28)[66].

In 85.5% of cases of neonatal deaths, there was no past history of neonatal deaths as only 14.5% had past history of neonatal death, so there was no statistically significant association between early neonatal mortality and presence of neonatal deaths. This is not the case in a Sudanese study carried out in the East Nile Province at a community level, which showed that a past history of neonatal deaths carried twice risk of having another neonatal death[15]. This difference of the results could be explained by the small size of the sample of this study.

4.1. Pattern of morbidity:

Prematurity is the main cause of admission to the nursery (39.1%), followed by birth asphyxia (19.3%), neonatal jaundice and a relatively high percentage (11.4%) of congenital malformations. Neonatal sepsis comes lower on the list of pattern of diseases, and this could be explained by the fact this study includes only neonates delivered at Omdurman Maternity Hospital, and neonates delivered outside the hospital had been an exclusion criteria. The pattern of morbidity in this study is similar to other study i.e. prematurity and its main complication RDS constituted the major cause of morbidity and mortality in many countries such as Brazile, Turky, Gambia and Sudan[5,6,10,17]. Where in Pakistan the pattern is different, neonatal

sepsis being the commonest cause of neonatal morbidity followed by birth asphyxia and prematurity.

Regarding gestational age, newborns whose gestational age was <30 weeks had a 100% mortality rate, neonates whose gestational age lie in the range of 31-33 weeks, and 34 - 36 weeks, when compared to newborns of gestation of more than 37 weeks as a reference group had a relative risk of 2.8, i.e. preterms of less than 37 weeks gestation had 2.8 times the risk of early neonatal mortality. This is comparable to a study done in Africa, where mortality rate for neonates with ≥ 37 weeks gestation was only (7%) compared to 20% for newborns of gestation less than 37 weeks.[29]

Regarding the birth weight there had been only one newborn below 1 kg and he died. There were 24 neonates in the weight group of 1-1.49 kg and of those 20 were early neonatal deaths constituting 83.3%, and also constituted 9.9% of the all neonatal deaths. Those from 1.5 - 1.99 kg were 43 cases and of those 12 were early neonatal deaths (27.9%), constituted 5.9% of the whole study group. This showed that, there was a decrease in the percentage of neonatal deaths as the birth weight increases, and this supported the fact that neonates with lowest birth weight at highest risk of death.[29]

4.2. Causes of early neonatal mortality:

Causes of early neonatal mortality in Omdurman Maternity

Hospital were prematurity in 56.4%, followed by congenital malformation in 20%, while asphyxia constituted 14.5% and neonatal sepsis (3.6%) of early neonatal deaths. This was different from a community study conducted in Sudan, ten years ago, where causes of early neonatal mortality were birth asphyxia in 50.2%, low birth weight in 15.5%, congenital malformation in only 2.1%.[15] Another study in Central Sudan revealed that the major cause of neonatal mortality was tetanus neonatorum, which constituted 29%.[16] Our results were different from a study done in two hospitals in Khartoum State, which revealed that birth asphyxia constituted half of early neonatal deaths in those hospitals.[18] But our result were similar to the study conducted in Wad Madani, where prematurity was found to be the major cause of perinatal mortality and found in 40.6%, followed by congenital malformations in 17.6%, birth asphyxia in 12.9% and neonatal sepsis was in only 3.4%.[17]

Congenital malformations was constituted one fifth of early neonatal mortality (20.0%) and this high percentage could be attributed to the presence of a large proportion of neural tube defects, in five cases constituting 21.2% of whole congenital malformations and were associated with a high mortality. This was uniform with a recent study done in Omdurman Maternity Hospital, which revealed that the incidence of neural tube defects was 3.48/1000 live birth and their

perinatal mortality was 82.5%[54].

CONCLUSION

- Prematurity was the major cause of admission to Neonatal Care Unit in Omdurman Maternity Hospital, followed by birth asphyxia and the common causes of death were prematurity, congenital malformations and birth asphyxia.

- Early neonatal mortality of this study group was found to be 27.2%, while in the control group was 0.5%.
- Early mortality was significantly associated with multiple births and small gestational, as mortality rates increases with the decrease of the gestational age.
- Birth weight was also significantly associated with early neonatal mortality, where it increases as the birth weight decreases, gender was found to have no effect on mortality rates.
- Risk factors of early neonatal mortality were found to include gestational age of less than 37 weeks with a relative risk of 2.8 (RR 2.8).
- Other risk factors include birth weight of less than 1.5 kg with a relative risk of 5.18 when compared to weight of 2.5 -2.99 kg.
- Maternal factors such as age, illiteracy, the number of antenatal care visits, a past history of neonatal deaths were not found to be risk factor for early neonatal mortality in the study.

RECOMMENDATIONS

According to my findings and conclusion, I recommended the following:

- Improving neonatal care units services by supply with the recent technology and equipment for better management of newborns specially the preterm babies.
- To reduce the early neonatal mortality in preterms we recommended introduction of ventilators, CPAP, endotracheal tubes and other equipments necessary for management of RDS and other respiratory problems. Introduction of surfactant therapy for management of respiratory distress syndrome is essential.
- Continuous training of nursery staff on neonatal resuscitation programes.

- In order to reduce the percentage of birth asphyxia. I recommend good collaboration with the colleagues in the departments of obstetrics and gynaecology.
- Development of a clear protocol for management of the commonest neonatal problems in Neonatal Nursery Unit, including lines of management, doses of drugs, fluid requirement and time and amount of feeding.

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بسم الله الرحمن الرحيم

QUESTIONNAIRE

Early Neonatal Morbidity and Outcome in Omdurman Maternity Hospital Nursery Unit

- Serial No.: …….. ***- Tel No: ……***

1. Name :……

Date of birth: ……

Age (in days): ……

4. Sex: *1. Male* *2. Female*

5. Residence: ……

6. Father's name :……

7. Father's education (in years) ……

8. Father's occupation: *8.1. Professional* *8.2 Merchant* *8.3. Civil employee* *8.4. Skilled labourer* *8.5. Non-skilled labourer* *8.6. Others*

9. Mother's age (in years) ☐☐

10. Mother's education (in years) ☐☐

11. Mother's occupation: *11.1. Professional* *11.2 Merchant* *11.3. Civil employee* *11.4. Skilled labourer* *11.5. Non-skilled labourer* *11.6. Housewife* *11.7. Others*

12. Parents consanguinity: *11.1. First degree relatives* *11.2 Far cous* ☐☐ *11.3. Not related*

13. No. of ANC visits ☐☐

14. Social status: ……

15. Family monthly income (in dinars): ……

16. No. of rooms in the house: ……

17. No. of persons/room: ……

18. Water supply: *18.1 Nile* *18.2. Well* *18.3 Pipe in* *18.4. Pipe our* *18.5. Others ……* ☐

19. Type of latrine: *19.1 Siphon* *19.2. Private pit latrine* *19.3. Communal pit latrine* *19.5. Open space* ☐

20. No. of pregnancies: ☐☐

21. No. of live births ☐☐

22. No. of stillbirths: ☐☐

23. No. of abortions ☐☐

24. No. neonatal deaths (first 4 weeks of life): ☐☐

25. No. of childhood deaths (more than 4 weeks) ☐☐

26. Outcome of last pregnancy: *26.1 Term infant alive* *26.2. Term died* *26.3. Preterm alive* *26.4. Preterm died* *26.5. Stillbirth* *26.6. Abortion* *26.7. Others ;……*

☐☐

27. Cause of death of the last neonatal death:

27.1 Birth asphyxia 27.2. L.B.W

27.3. Prematurity 27.4. Congenital malformations

27.5. Infections (sepsis, meningitis, tetanus)

27.6. Others (specify);…….. ☐☐.

28. Duration of pregnancy (in weeks):

29. Maternal disease: *Medical: ……*

Obstetrical: …… ☐☐

31. Mode of delivery:

31.1. NVD 31.2. Ventose delivery

31.3. Forceps delivery 31.4. C/S delivery

32. If C/S: *1- Emergency 2- Elective* ☐☐

33. Indication of C/S: *……*

34. Complications of pregnancy:

34.1. APH 34.2. PIH

34.3. Anaemia 34.4. Others (specify)

35. Complications of labour: ☐☐

35.1. Birth asphyxia 35.2. Birth trauma

35.3. Premature rupture of membrane

35.4. Others (specify) …… ☐☐

37. Maternal outcome: *37.1. Alive 37.2. Died* ☐☐

38. Apgar score: *38.1. I minute* ☐

38.2. 5 minutes ☐

38.3. 10 minutes ☐

39. Need of resuscitation: *39.1 Yes 39.2. No* ☐

40. Duration of resuscitation (in minutes): *……* ☐

41. Type of resuscitation: *1- Drying, tactile stimulation*

2- O2 by face and mask.

3- Ambu bag ventilation. ☐

4- Intubation and ventilation.

5- Drugs - specify: ……

42. Gestational assessment by Parkin method (attached paper):

……weeks.

43. Anthropometry:

Weight

……kg……centilr.

Length

……cm……centilr.

HC

……cm……centilr.

44. Abnormal physical findings:

……

45. Relevant investigations:

……
……
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……
……
……

46. Final diagnosis: *……*
……

47. If died in the nursery what is the cause of mortality:

Primary cause:……

Secondary cause:……

48. Follow up:

……
……

Calculation of mean gestational ages from the total scores of skin texture, skin colour, breast size and ear firmness.

Score	Gestational age in weeks
1	27
2	30
3	33
4	34 - 1/2
5	36
6	37
7	38 - 1/2
8	39 - 1/2
9	40
10	41
11	41 - 1/2
12	42

Source: Reference No. 73

Parkin JM, Yey EN, Clowes JS. Rapid assessment of gestational age of birth. Arch Dis Child 1976; 51; 259 - 63.

Calculation of mean gestational ages from the total scores of skin texture,
skin colour, breast size and ear firmness.[73]

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Scoring system for rapid assessment

	0	1	2	
Skin texture. Tested by picking up a fold of abdominal skin between finger and thumb, and by inspection	Very thin with a gelatinous feel	Thin and smooth	Smooth and of a medium thickness, irritation rash and superficial peeling may be present	Slight thic feeling wit and peelin on the han
Skin colour. Estimated by inspection when	Dark red	Uniformly pink	Pale pink, through the	Pale: no w

the baby is quiet.			colour may vary over different parts of the body, some parts may be very pale	except on t and soles
Breast : size. Measured by picking up the breast tissue between finger and thumb	No breast tissue palpable	Breast tissue palpable on one or both sides, neither being more than 0.5 cm in diameter	Breast tissue palpable on one or both sides, one or both begin 0.5 cm -1 cm in diameter.	Breast tiss one or both cm in dian
Ear firmness tested by palpation and folding of the upper pinna	Pinna feels soft and is easily folded into bizarre positions without sprining back into position spontaneous	Pina feels soft along the edge and is easily folded but returns slowly to the correct position spontaneously	Cartilage can be felt to the edge of the pinna thought it is thin in places and the pinna sprinings back readily after being folded	Pinna firm cartilage e periphery, immediate folding