

Chapter one

Introduction and literature review

1.1 Introduction

Neonatal sepsis is a generalized bacterial infection during the first four weeks of life associated with general systemic manifestation and positive blood culture.

In 40% of cases it is associated with meningitis and 20-25% of cases with pneumonia or urinary tract infection. Septicemia and meningitis are considered together since etiology and clinical picture are closely similar and are frequently associated. (Gamal.2014)

Neonatal sepsis is one of the important causes of neonatal morbidity and mortality particularly in the developing countries .

The earliest signs of sepsis are often subtle and non-specific and need a high index of suspicion for early diagnosis. Babies with sepsis may present with one or more of the following symptoms and signs :

- (a) Hypothermia or fever (former is more common in low birth weight babies).
- (b) Lethargy, poor cry, refusal to suck.
- (c) Poor perfusion, prolonged capillary refill time.
- (d) Hypotonia, absent neonatal reflexes .
- (e) Bradycardia; tachycardia.
- (f) Respiratory distress, apnea and gasping respiration.
- (g) Hypoglycemia, hyperglycemia.
- (h) Metabolic acidosis.

Specific features related to various systems: Central nervous system (CNS): Bulging anterior fontanelle, blank look, high-pitched cry, excessive irritability, not arousable, comatoid seizures, neck retraction. Presence of these features should raise a clinical suspicion of meningitis

Cardiac: Hypotension, poor perfusion, shock

Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic ileus, necrotizing enterocolitis (NEC).

Hepatic: Hepatomegaly, direct hyperbilirubinemia (especially with UTI)

Renal: Acute renal failure

Hematological: Bleeding, petechiae, purpura, skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge.

Neonatal sepsis is classified into early or late according to the different ages at onset of infection during the neonatal period.

The clinical relevance of this distinction is that early-onset disease is often due to organisms acquired during delivery while, late-onset disease is more frequently caused by organisms acquired from nosocomial or community sources .

Most of the estimated 4 million neonatal deaths per year occur in low and middle income countries. Case fatality rates for neonatal infections remain high among both hospitalized newborns and those in the community .

In developing countries, neonatal mortality is defined as deaths in the first 28 days of life per 1000 live births, from all causes is about 34; most of these deaths occur in the first week of life, most on the first day .

The aims of this study are to determine the hematological changes in neonates diagnosed with neonatal sepsis in Omdurman Maternity Hospital . Neonatal Unit, to identify the possible risk factors for neonatal sepsis, and to look for a correlation between risk factors and occurrence of sepsis .

1.2 Literature review:

1.2.1 BLOOD:

Blood is a mesenchymal tissue and its components are: plasma, red blood cells (erythrocytes, rubricyte) , white blood cells (leucocyte) and platelets.

In a normal healthy person there is a constant breakdown and fresh formation of various blood elements .However, minor daily physiological fluctuation occurs.

The erythrocyte transport the respiratory gases ,oxygen and carbon dioxide, granulocytes and monocytes (Leucocytes) are cell that can get out of the blood vessels and migrate among the cells of many tissues. These cells are important in inflammation and phagocytosis .

Platelets are tiny , a nucleated cells that contain molecules required for hemostasis ,they also provide hemostasis through their ability to adhere ,aggregate and provide a surface for coagulation reactions. (Ramnik , 2010).

1.2.2 Hematopoiesis:

Haematopoiesis : Is the formation of blood cellular components. All cellular blood components are derived from haematopoietic stem cells. In a healthy adult person, approximately 10^{11} – 10^{12} new blood cells are produced daily in order to maintain steady state levels in the peripheral circulation.(Morrison and Kimble ,2006)

1.2.3 Hemopoietic stem and progenitor cells :

Hemopoiesis starts with a common ,pluripotential stem cell that can give rise to the separate cell lineages. The exact phenotype of the human stem cell is unknown but on immunological testing it is CD34+,CD38- and has the appearance of small lymphocytes.

Cell differentiation occurs from the stem cell down erythroid, granulocytic and other lineages via the committed hemopoietic progenitor which are restricted in their developmental potential(. Hoffbrand and Petti ,2001)

1.2.4 Erythropoiesis :

Mature RBCs are derived from committed erythroid progenitor cells through a series of mitotic division and maturation phase.Erythropoiesis occurs in the marrow over a period of four to five days through successive morphologic alterations in the nucleated cell from pronormoblast to the anucleated mature RBC.Stages oferythroblastic(Normoblastic) are Ponormoblast,prominent, early normoblast,intermediate normoblast,late normoblast,reticulocyte and mature red blood cell. (Ramnik , 2010)

1.2.5 Leucopoiesis :

Leukopoiesis is a form of hematopoiesis in which white blood cells (WBC, or leukocytes) are formed in bone marrow located in flat bones in adults and hematopoietic organs in the fetus. White blood cells, indeed all blood cells, are formed from the differentiation of pluripotent hematopoietic stem cells which give rise to several cell lines with more limited differentiation potential

White blood cells (WBCs), also called leukocytes or leucocytes, are the cells of the immune system that are involved in protecting the body against both infectious disease and foreign invaders. All leukocytes are produced and derived from a multipotent cell in the bone marrow known as a hematopoietic stem cell. Leukocytes are found throughout the body, including the blood and lymphatic system. Five different and diverse types of leukocytes exist. (LaFleur,2008)

The number of leukocytes in the blood is often an indicator of disease, and thus the WBC count is an important subset of the complete blood count. The normal white cell count is usually between 4 and $11 \times 10^9/L$. (Hollowell. *et al*,2005)

They make up approximately 1% of the total blood volume in a healthy adult .(Albert,*etal*,2002)

1.2.5.1 Neutrophil (polymorph) :

These cells have characteristic dense nucleus consisting of between two and five lobes and pale cytoplasm , the granules are divided into primary and secondary granules. The life span of neutrophils in the blood is only about 10 hours.

Normal range ($2.5-7.5 \times 10^9/l$) constituting about 65% of total leucocytes in man.

Neutrophils have the ability to ingest and kill microorganism .Mature cell retain the capacity to synthesize RNA and can secret a variety of cytokines in response to stimulation . Neutrophil progress through several morphologically distinct stages of maturation (myeloblast, promyelocyte, myelocyte, metamyelocyte and band form. (Hoffbrand.*et al*,2001)

In neonates normal neutrophil values are age dependent, with a peak during the first 12 to 14 h of age (range, $7,800$ cells/ mm^3 to $14,500$ cells/ mm^3) . During 72 h to 240

h, the values range from 2,700 cells/mm³ (5th percentile) to 13,000 cells/mm³ (95th percentile) in full-term infants. Absolute immature neutrophil counts peaks at 12 h of age, from a maximum value of 1,100 cells/mm³ to 1,500 cells/mm³ at 12 h. In contrast, a maximum normal ratio of immature to total white blood cells (I:T ratio) of 0.16 occurs at birth and reaches a nadir of 0.12 with increasing postnatal age.

(Avecill.*et al*,2004)**1.2.5.2 Eosinophil :**

Eosinophil is a minor species of granulocyte comprising 1-4% of total white blood cells, normal range (0.04-0.44×10⁹/l) the transient time of eosinophil in blood is about 3-8 hours.

The mature eosinophil is larger than the neutrophil and is characterized by numerous large cytoplasmic granules, the nucleus is generally bilobed with occasional third lobe. It plays a role in phagocytosis and respiratory burst and activation by cytokines interleukin -5 (IL-5).

Eosinophils play an important role in mediating hypersensitivity reaction, bronchial asthma, skin inflammation and predominantly provide protection against parasitic infection. (Hoffbrand, *et al*.2001)

1.2.5.3 Basophil :

Basophil and mast cell, basophils comprising 0.2-1% of circulating leucocyte, normal range (0.01-0.1×10⁹/l). The mature basophils have multilobed nuclei and contain numerous prominent granules that stain purple with blue aniline dye due to presence of the highly sulphated proteoglycan and heparin. Mast cell is a basophil located in tissues. Basophils provide a framework for storage of the granule protein, histamine and proteases, and stain positive with peroxidase. Basophils and mast cells play a major role in hypersensitivity disease. (Hoffbrand, *et al*.2001)

1.2.5.4 Monocytes :

are a type of white blood cells (leukocytes). They are the largest of all the leukocytes. They are part of the innate immune system of vertebrates including all mammals (humans included), birds, reptiles, and fish. They are amoeboid in shape, having agranular cytoplasm. Monocytes have unilobed nuclei, which makes them one of the types of mononuclear leukocytes (containing azurophilic granules). The archetypal idea of the nucleus is that it is bean-shaped or kidney-shaped, although

the most important distinction is that it is not deeply furcated into lobes, as occurs in polymorphonuclear leukocytes. Monocytes constitute 2% to 10% of all leukocytes in the human body. They play multiple roles in immune function. Such roles include: (1) replenishing resident macrophages under normal states , (2) in response to inflammation signals, monocytes can move quickly (approx. 8–12 hours) to sites of infection in the tissues and divide/differentiate into macrophages and dendritic cells to elicit an immune response. Half of them are stored in the spleen. (Swirski.*et al* ,2009)

1.2.5.5 Lymphocyte :

Microscopically in a Wright's stained peripheral blood smear, a normal lymphocyte has a large, dark-staining nucleus with little to no eosinophilic cytoplasm. In normal situations, the coarse, dense nucleus of a lymphocyte is approximately the size of a red blood cell (about seven micrometres in diameter. Some lymphocytes show a clear perinuclear zone (or halo) around the nucleus or could exhibit a small clear zone to one side of the nucleus. Polyribosomes are a prominent feature in the lymphocytes and can be viewed with an electron microscope. The ribosomes are involved in protein synthesis, allowing the generation of large quantities of cytokines and immunoglobulins by these cells. It is impossible to distinguish between T cells and B cells in a peripheral blood smear. (Abbas and Lichtman,2003)

Normally, flow cytometry testing is used for specific lymphocyte population counts. This can be used to specifically determine the percentage of lymphocytes that contain a particular combination of specific cell surface proteins, such as immunoglobulins or cluster of differentiation (CD) markers or that produce particular proteins (for example, cytokines using intracellular cytokine staining (ICCS)). In order to study the function of a lymphocyte by virtue of the proteins it generates, other scientific techniques like the ELISPOT or secretion assay techniques can be used . (Charles.*et al*, 2001)

1.2.6 Megakaryocytopoiesis:

is the process by which bone marrow progenitor cells develop into mature megakaryocytes, which in turn produce platelets required for normal hemostasis.(Avecill.*et al*,2004)

1.2.6.1 Megakaryocytic series :

Megakaryocytes are derived from hematopoietic stem cell precursor cells in the bone marrow. They are produced primarily by the liver, kidney, spleen, and bone marrow. These multipotent stem cells live in the marrow sinusoids and are capable of producing all types of blood cells depending on the signals they receive. The primary signal for megakaryocyte production is thrombopoietin or TPO. TPO is sufficient but not absolutely necessary for inducing differentiation of progenitor cells in the bone marrow towards a final megakaryocyte phenotype. Other molecular signals for megakaryocyte differentiation include GM-CSF, IL-3, IL-6, IL-11, chemokines (SDF-1, FGF-4). (Avecill.*et al*,2004)

Thrombopoietin is a glycoprotein hormone produced by the liver and kidney which regulates the production of platelets. It stimulates the production and differentiation of megakaryocytes, the bone marrow cells that bud off large numbers of platelets. (Kaushansky ,2006)

The main function of platelet is to contribute to hemostasis : the process of stopping bleeding at the site of interrupted endothelium, they gathering at the site ,unless the interruption is physically too large , they plug the hole . First platelet attach to substance outside the interrupted endothelium , adhesion. Second they change shape turn on receptor to secret chemical messenger activation. Third, they connect to each other through receptor bridges , that is aggregation. Formation of platelet plug (primary hemostasis) is associated with activation of coagulation cascade resulting in fibrin deposition and linking (second hemostasis) the process may overlap the spectrum is from a predominantly platelet or white plug to a predominantly fibrin clot or red clot.(Hoffbrand *et al* 2005)

1.2.7 Neonatal sepsis:

1.2.7.1 Definition :

Neonatal sepsis (N.S) is a clinical syndrome of systemic illness in infants of 28 days or younger, manifested by systemic sign of infection and/or isolation of bacterial pathogen from blood stream.

It may cause just bacteremia or be association with systemic involvement as meningitis, pneumonia or osteomyelitis. (Edwards , *et al.*2004)

1.2.7.2 Incidence and epidemiology :

In developing countries the neonatal mortality rate range from 17 to 68/1000 live birth in the first 28 days ,and third of these deaths. In developing countries neonatal mortality is 2-5/1000 live birth and 10% is caused by infection . (Verganano. , *et al.*2005)

According to WHO there was an estimated number of neonatal deaths, caused by infection, Of 38200 (3.4%) of all death in Africa in 2004, in Europe the estimated number was 27000 (0.3%) of all deaths . However it is generally assumed that the neonatal mortality in developing countries is–underreporting by atleast 20%). (Myros,2008)

N.S is an important cause of neonatal morbidity and mortality, the overall incidence from 1-5/1000 live birth in term babies, the incidence is higher in low birth (LBW) ,8-9/1000 and much higher in very low birth (VLBW) with early onset sepsis, 15-19/1000 in late onset, nosocomial sepsis as(21%) according to data from national institute of child health and human development neonatal research network. The incidence of early onset sepsis (EOS) has decreased as reduction of group B streptococcus (GBS) infection .

The American Academy of pediatrics (APC) and center for disease control and prevention (CDC) have recommended for sepsis screening and/or treatment for various risk factors ,because the hazard of non-treated or delay treatment to wait for positive blood culture.(Myros , 2008)

1.2.7.3 Classification of neonatal sepsis:

Neonatal sepsis is classified according to the time of onset of the disease ,early onset disease (EOD) and late onset disease (LOD).

This distinction has clinical relevance as EOD is mainly due to bacteria acquired before and during delivery , and LOD to bacteria acquired after delivery from nosocomial or community source. Unfortunately ,there is no consensus as to what age limit apply, making it difficult to compare studies where cases are grouped into EOD and LOD without further details, in most literature on GBS, EOD is 0-6 days and LOD 7-90 day after birth. (Goldsten., *et al.*2005)

Early onset disease (EOD) :

In early onset sepsis bacteria have ascended from the birth canal and invaded the amniotic fluid. The fetus is secondarily infected because the fetal lungs are in direct contact with infected amniotic fluid. These infant have pneumonia and secondary bacteremia/septicemia. In contrast , congenital viral infections and early onset infection with listeria monocytogenes, fetal infection is acquired via placenta following maternal infection .

The risk of early onset infection increased if there has been prolonged or premature rupture of the amniotic membranes, and when chorioamnionitis is clinically evident such as when the mother has fever during ,presentation is with respiratory distress and temperature instability. (Lissaure .2012)

Late onset disease (LOD) :

In late onset the sepsis source of infection is often infant's environment . The presentation is usually non-specific.

Nosocomially acquired infections are an inherent risk in neonatal unit and staff must adhere strictly to effective high hygiene measure to prevent cross –infection.

In neonatal intensive care unit ,the main source of infection are indwelling central venous catheters for parenteral nutrition ,invasive procedures which break the protective barrier of the skin and tracheal tubes, coagulase staphylococcus (staphylococcus epidermidis) the most common pathogen. (Lissaure .2012)

1.2.7.4 Aetiology and predominant pathogens of neonatal sepsis:

In developing countries it appear to be a wide variety of bacteria causing EOD and LOD . In most studies ,Gram –negative organism are predominant .among Gram-negative organisms *klebsiellaspp*, *Escherichia coli*, *pseudomonas spp*and *salmonella spp*. Among gram –positive bacteria staphylococcus aureus , coagulase negative staphylococci (CONS), streptococcus pneumonia and streptococcus pyogenes are the most reported species. (Verganano, *et al.*2005)

This variation may be true, but important confounders may be true ,but important confounder may include different definition of EOD and LOD, different inclusion criteria for studies(including population sampled) inability to culture certain organisms , small number and/or short period of surveillance, the latter may be particularly important , as surveillance may be occurring during or indeed may have been initiated because of an outbreak of a specific pathogen and may not therefore be representative .

Organisms responsible for neonatal infection in developing countries have change the last decades . while *S.Pyogenes*and *S.Pneumoniae* constituted half of the cases at Yale from 1933-1943, no cases caused by these bacteria were detected in period 1989-2003.

Following the introduction of sulfonamides and penicillin ,gram negative bacteria and particularly E- coli , become predominant bacteria in neonatal infection ,and specially the first 24 hours after birth .(Bizzaro ,*et al.*2003)

In the last twenty years gram –positive organism have a dominant both EOD and LOD in termed infants, while E-coli have been more common in premature infants. (Hufngael, *et al.* 2008)

Some recent studies have shown a declining incidence of EOD in infant born after 37 weeks gestational age and also a declining incidence of invasive GBS disease. (Hufnagel ,*et al* 2007)

1.2.7.5 Predisposing factors of neonatal sepsis :

A) Maternal factor :

- 1- Mother infected before delivery e.g. bacterial endocarditis ,septicemia, urinary tract infection.
- 2- Premature or prolonged (>24 hours) ruptures of membrane.
- 3- Mothers with no antenatal care, poor hygiene, low socioeconomic status, cervicitis not treated well , or chorioamnionitis.
- 4 - Recurrent miscarriage .
- 5- Colonization of birth canal with GBS. (Gamal.2014)

B) Neonatal factor :

- 1- Prematurity and low birth weight infant who required hospitalization and manipulation .
- 2- Babies with congenital defect leading to exposure of the internal organs as meningitis or omphaloceles. (Gamal.2014)

1.2.7.6 Clinical features of neonatal sepsis:

- Fever or temperature instability or hypothermia.
- Poor feeding.
- Vomiting.
- Apnoea and bradycardia.
- Respiratory distress .
- Abdominal distention.
- Jaundice.
- Neutropenia.
- Hypo/hyperglycemia.
- Shock.
- Irritability.
- Seizures
- Lethargy. (Lissaure . 2012)

1.2.7.7 Diagnosis of neonatal sepsis :

1- History :

A predisposing factor as prematurity , low birth weight, prolonged rupture of membranes (>24 hours), infected birth canal , septic manipulations during delivery.

Intrapartum maternal fever (>38°C) .

a) Clinical manifestation :

As result of feeding , diarrhea ,convulsion , tachypnea,...etc . (Gamal.2014)

b) Investigation :

-Direct method:

Isolation of microorganisms from blood, CSF, urine, pleural fluid or pus is diagnostic.

Blood culture :

Blood cultures are still the gold standard in the diagnosis of neonatal sepsis. However, obtaining cultures from neonates can be difficult as sample volumes are small and a substantial number of cultures turn out to be contaminated or negative. (Escobar,2005)

- Indirect method (Septic screen) :

The typical complete sepsis workup in a neonate consists of obtaining a complete white blood cell count with differential, a single blood culture, urine cultures, and a lumbar puncture for cell count and culture . (Edwards , *et al.*2004)

CBC:

White blood count and differential. White blood cell (WBC) counts; differential, absolute neutrophil counts; and the ratio of immature to total neutrophils in the blood are widely used as screening tests for neonatal sepsis.

White blood count are more than 30.000 cell/mm³,with increased neutrophils especially immature forms (band neutrophils), the ratio of immature neutrophils (band cells/total neutrophils count is greater than 0.2 .

Typically, neonates with viral infections, including HSV, enteroviruses, and HPeV, havenormal WBC counts or very mild leukopenia.(Gamal.2014)

Platelet counts :

Thrombocytopenia affects up to 35% of all patients admitted in neonatal intensive care unit .The causes of thrombocytopenia in neonates are very diverse and include immune and non-immune disorders . The etiology of thrombocytopenia in neonatescan be categorized into several broad categories including increased platelet destruction, decreased platelet production . Also mechanism of thrombocytopenia in septic neonates is multifactorial .Platelets interact with invading micro- organisms and are critically linked to pro inflammatory innate immune response. (Albertset *al*,2002)

Anemia can occur (may be hemolytic) .(Gamal.2014)

C-reactive protein :

CRP is one of the most widely available; most studied, and most used laboratory tests forneonatal bacterial infection. It is well known that it provides limited sensitivity whendetermined during the early phases of the disease, especially at the initial presentation, butprovides very high negative predictive values and is thus useful for identifying infantsunlikely to be infected or monitoring the response to treatment. (Jayeand Waites,1997)

However, thecurrent literature provides a growing body of evidence suggesting the so far reportedcharacteristics of CRP may not be as suitable for the use in preterm as in term newborns.

Furthermore, the use of CRP in neonatal sepsis is complicated by a nonspecific risethat starts shortly after birth.(Chiesa , *et al*. 2011).

De novo hepatic synthesis starts very rapidly after a single stimulus with serum concentrations rising above 5 mg/l by about 6 hours and peaking around 48 hours. (Pepys and Hirschfield, 2003)

1.2.8 Previous studies:

Christophet *al*, (2012) have measured of the CBC in early-Onset Neonatal Sepsis in USA. Their result was Low white blood cell counts, low absolute neutrophil counts, and high immature-to-total neutrophil ratios which is associated with increasing odds of infection (highest odds ratios: 5.38, 6.84, and 7.97, respectively). Specificity and negative predictive values were high (73.7–99.9% and >99.8%). However, sensitivities were low (0.3–54.5%) for all complete blood cell count indices analyzed. Low white blood cell count, absolute neutrophil count, and high immature-to-total neutrophil ratio were associated with increasing odds of infection, but no complete blood cell count-derived index possesses the sensitivity to rule out reliably early-onset sepsis in neonates.

Farhat *et al* (2014) have a study of Clinical Manifestation and Laboratory Findings of Positive Blood Culture in Iran. They collected 100 records of positive blood culture in the neonates suffering from septicemia. Their result was in one hundred septicemic neonates who had been admitted in the NICU were included in the study (57 male 43 female). There were 72 pre-term cases and 28 term neonates. Low birth weight (LBW) was observed in 75 cases while others were normal. Forty-four subjects had been born via natural vaginal delivery and 56 cases were born via Cesarean section. Moreover, 67 neonates were admitted within the first 24 hours of birth and 31 cases had a normal ESR. The hemoglobin level was normal in 58 cases, while it declined in 42 neonates. WBC was normal in 85 cases, while it saw an increase and decrease in 11 and 4 cases, respectively.

Khair and kheir (2014) have a study in the Prevalence and outcome in a tertiary neonatal unit in Sudan, thirty five (56.5%) of maternal delivery were delivered by emergency caesarean section, forty six (74.2%) of patients mothers did not have prolonged rupture of membranes (PROM), Four (6.5%) had ruptured their membranes for less than 24 h and twelve (19.4%) experienced it for more than 24, twenty four (38.7%) of mothers had a history of diseases, of which UTI was found to be the most common

Sartaj *et al*(2015) investigate the Incidence of Thrombocytopenia and Changes in Various Platelet parameters in Neonates with Blood Culture Positive Sepsis in India .They found thrombocytopenia. (defined as $< 150 \times 10^3 /\mu\text{l}$) in 53/80 (66.25%) of babies with blood culture positive sepsis. Among these babies 28/53 (52.8%) were having mild thrombocytopenia, 18/53(33.9%) were having moderate thrombocytopenia and 7/53 (13.52%) were having severe thrombocytopenia. Thrombocytopenia had 66.25% sensitivity.

Edward *et al*(2015) have a study of Diagnosis of Neonatal Bacterial Infection: Hematologic and Pathologic Findings in Fatal and Nonfatal Cases in Denver One hundred infants hospitalized between 1970 and 1979 received a sepsis work-up, died within 72 hours, and then had a complete autopsy. Abnormalities of the WBC's, NC, and PC with a trend toward leukopenia and neutropenia. In contrast, nonfatal cases of bacterial infection often demonstrated an increase in BC and NC. Although a trend toward multiple CBC abnormalities in infected (and especially fatally infected) patients was noted, some infected patients had no abnormalities and some seriously ill non infected patients had multiple CBC abnormalities. In all, 80% of the infected newborns studied had abnormal pre mortem hematologic counts. one of the 23 non infected infants (P value $<.001$). Megakaryocytopenia developed in four of 23 patients with fatal infection but none of the controls(P $<.001$).

Rationale:

Neonatal sepsis is one of the important causes of neonatal morbidity and mortality. The prevalence of sepsis in Sudan was 17.5% and the mortality was 14.5%. Global deaths occurring in the neonatal period each year account for 41% (3.6 million) of all deaths in children under 5 years. The majority of these deaths occur in low income countries and almost 1 million of these deaths are attributable to infectious causes including neonatal sepsis, meningitis and pneumonia. Furthermore, neonatal mortality for different African countries ranges from 68 per 1000 live births in Liberia to 11 per 1000 live births in South Africa. The diagnosis of infection in neonates is difficult because of the non-specific clinical presentation and the lack of reliable diagnostic tests. Recently there has been great interest in the potential diagnostic value of a range of hematological and immunological surrogate markers of infection. So this study undertaken to contribute to the present knowledge on neonatal sepsis.

Objectives

General objective:

To investigate the hematological changes and potential risk factors in early onset neonate sepsis .

Specific objectives:

- To investigate the changes in Hb, RBCs, Hct and red cell indices in septic neonates.
- To investigate the changes in WBCs in early septic neonates..
- To investigate the changes in PLT in early septic neonates..
- To identify the potential risk factors for early neonate sepsis.