"PROSPECTIVE STUDY ON THE ASSOCIATION BETWEEN CORD BLOOD VITAMIN D LEVELS AND EARLY ONSET NEONATAL SEPSIS''

By
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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA.

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE
IN
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Under the Guidance of

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Dr. Rajitha. B

ABSTRACT:

BACKGROUND:

Vitamin D is a fat-soluble vitamin. Very few foods naturally contain vitamin D (fatty fish livers are the exception), so dermal synthesis is the major natural source of the vitamin. Dietary intake or dermal synthesis is physiologically inactive and requires enzymatic conversion to active metabolites. By way of its endocrine actions, Vitamin D plays a significant role in bone mineralization and calcium metabolism. The recent research focused on Vitamin D on its role in extra skeletal manifestations including immunity. Many studies have been conducted to investigate the role of Vitamin D deficiency in acute respiratory tract infections. Only few studies and less literature is available on role of Vitamin D in neonatal sepsis hence this study was conducted to determine the relationship between cord blood vitamin D levels and early onset sepsis (EOS).

OBJECTIVES:

1. To measure cord blood vitamin D levels in term neonates with and without Early onset sepsis
2. To find out the association between cord blood Vitamin D levels and Early onset sepsis.

MATERIALS AND METHODS:

A Prospective observational study included 107 neonates with any one or more maternal risk factors. Detailed maternal history and neonatal examination were done and recorded. Cord blood Vitamin D levels, sepsis screen and blood culture were sent. Neonates were divided into EOS positive group and EOS negative group, or healthy neonates based on sepsis screen. EOS group was subdivided into probable sepsis (only sepsis screen positive) and definitive

sepsis(culture positive) group. The study is to find the association of cord blood vitamin D levels and EOS.

RESULTS:

Our study included 107 neonates who met the inclusion criteria.

Among study population cord blood Vitamin D levels were deficient in 47.7% neonates, insufficient in 42.1% neonates and sufficient in only 10.3% neonates.

In the study population of 107 neonates, 53.3% had EONS, with just 2% having sufficient Vitamin D levels; the remaining 37% and 61% had insufficiency and deficiency, respectively, whereas neonates without EOS had sufficiency at 20%, deficiency at 32%, and insufficiency at 48%. With a p value of 0.001, there was a significant correlation between cord blood Vitamin D levels and EOS.

CONCLUSION:

In our study, we found statistical significance between cord blood Vitamin D levels and EOS, with a p value of 0.001. Maternal sun exposure and infant birth weight had a significant association with Cord blood Vitamin D levels, whereas there was a negative correlation between cord blood Vitamin D levels and maternal age, maternal oral Vitamin D intake, socioeconomic status, and neonate gender.

LIST OF ABBREVATIONS

GLOSSARY	ABBREVIATIONS
Vit D	Vitamin D
EOS	Early Onset Sepsis
LOS	Late Onset Sepsis
7 DHC	7- dehydrocholesterol
UV	Ultraviolet
DBP	Vitamin D Binding Protein
VDR	Vitamin D Receptor
DC	Dendritic Cells
SARS-CoV-2	Severe Acute Respiratory Syndrome Corona Virus 2
CBC	Complete blood count
CRP	C-reactive protein
25(OH)D	25 Hydroxyvitamin D
IOM	Institute of Medicine
NOF	National Osteoporosis Foundation
IOF	International Osteoporosis Foundation
AGS	American Geriatrics Society
ng/mL	nanogram/milliliter
nmol/L	Nanomoles/Liters
GBS	Group B Streptococcus
E coli	Escherichia coli
CONS	Coagulase Negative Staphylococci
APC	Antigen Presenting Cells
MHC	Major Histocompatibility Complex
TNF α	Tumour Necrosis Factor alpha
IL	Interleukin
TLR	Toll-Like Receptor
TLC	Total Leucocyte Count

ANC	Absolute Neutrophil Count
m ESR	micro Erythrocyte Sedimentation Rate
I/T ratio	Immature to total neutrophil ratio
mm/hour	millimeters/hour
mg/dl	milligram/deciliter
CD	Cluster Differentiation
DNA	Deoxyribo Nucleic Acid
CSF	Cerebrospinal fluid
RLJH&RC	R L Jalappa Hospital &Research Centre
CL	Confidence Level
IEC	Institutional Ethics Committee
SDUMC	Sri Devaraj Urs Medical College
SDUAHER	Sri Devaraj Urs Academy of Higher Education and Research
ABG	Arterial blood gas analysis
HRP	Horseradish Peroxidase
EDTA	Ethylenediamine tetraacetic acid
SD	Standard Deviation
IQR	Inter Quartile Range

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INTRODUCTION

Vitamin D is an essential nutrient representing a group of fat soluble secosteroids with key endocrine functions. It is synthesised in the skin on sun exposure. Vitamin D is critical in bone metabolism and calcium homeostasis as well as acting as an important regulator in extra skeletal metabolic processes, cardiovascular and immune system. Many observational and laboratory studies have observed the anti-inflammatory properties of vitamin D, including direct regulation of endogenous antimicrobial peptide production.[1] It was suggested that it might have a role in the optimal functioning of the innate immune system by inducing antimicrobial peptides, cathelicidin (ll-37) in epithelial cells, neutrophils and macrophages[2]. Recently, it has been well established that low levels of circulating vitamin D levels have been shown to be strongly associated with infectious diseases.

New-borns are more susceptible to infections as both innate and adaptive immune systems are not entirely developed. Neonatal sepsis is broadly defined as a systemic inflammatory response occurring in the first 4 weeks or 28 days of life as a result of a suspected or proven infection. Early onset sepsis (EOS) is defined as blood stream infection ≤72 hours of age. Despite major advances in neonatal intensive care, neonatal sepsis is still a major cause of morbidity and mortality contributing to 23% of all neonatal deaths[3].

EOS is usually acquired vertically from the mother and manifests shortly after birth. Clinically, symptoms are generally subtle but sepsis may rapidly progress and worsen and may cause death in few hours to days. Early recognition and initiation of antimicrobial therapy is of great importance in order to prevent morbidity and mortality. Considering the high mortality and serious morbidity associated with neonatal sepsis, a diagnostic marker with a very high sensitivity and negative predictive value approaching 100% is desirable.

However, none of the current diagnostic markers are sensitive and specific enough to influence the judgment to withhold antimicrobial treatment[4]. The relationship between Vitamin D deficiency and infections has been demonstrated in children and neonates[3]. However, no studies have been conducted in and around Kolar District (Karnataka). Hence, this prospective study was done to determine the possible association between neonatal Vitamin D levels and development of EOS in term neonates.

OBJECTIVES

1. To measure the cord blood vitamin D levels in term neonates with and without EOS.

2. To find out the association between cord blood vitamin D levels and EOS.

REVIEW OF LITERATURE

Vitamin D3 (cholecalciferol) is taken in the diet or is synthesized in the skin from its precursor 7- dehydrocholesterol (7-DHC) by exposure to ultraviolet (UV) irradiation. Primarily created, cholecalciferol goes through conversion at two stages, one at the liver in the presence of 25 hydroxylase enzyme and the other by the enzyme 1α hydroxylase in the kidneys, before it becomes a hormonally active form - calcitriol {1α,25-dihydroxyvitamin D3; $1,25(OH)_2D3$}[5].

History:

Vitamin D discovery is dated as early as 1914 when American researchers Elmer McCollum and Marguerite Davis found a substance which had anti rachitic property in cod liver oil . In 1925, it was established that when 7-DHC is irradiated with light, a form of a fat-soluble vitamin is produced (now known as D_3).Alfred Fabian Hess showed "light equals vitamin D". The structure of vitamin D2 was deduced in 1931 by Askew et al. The structure of vitamin D3 was determined through synthetic means by Windaus et al. In 1971–72, the further metabolism of vitamin D to active forms was discovered[6]. Both 25(OH) D and 1, $25(OH)_2$ D were identified by a team led by Michael F. Holickin the laboratory of Hector DeLuca[7]**.** Vitamin D was discovered with many other vitamins and is classed as a vitamin even now. However, findings from the second half of the 20th century showed that vitamin D is truly a prohormone and not a vitamin[6].

Sources of vitamin D:

Vitamin D is produced endogenously in the skin from sun exposure and also obtained from foods that naturally contain vitamin D, like cod liver oil and fatty fish (e.g., salmon,

mackerel, and tuna), UV-irradiated mushrooms, foods fortified with vitamin D, and supplements[8]– Figure 1.

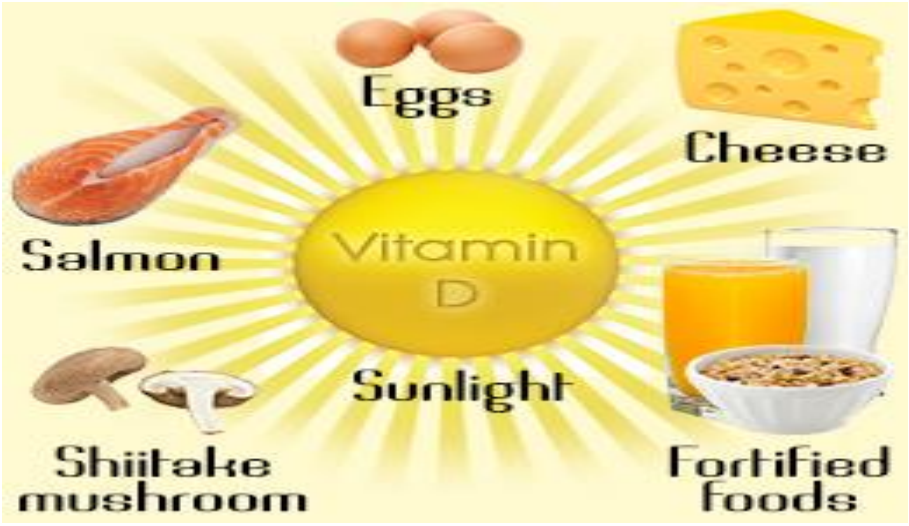


Figure 1: Sources of Vitamin D

Synthesis of Vitamin D:

During exposure to sunlight, 7-DHC in the skin is converted to pre-vitamin D3. The 7-DHC is present in all the layers of human skin. Approximately 10,000 to 20,000 IU of vitamin D is produced in 30 minutes of whole-body exposure, in the skin of most vertebrate animals, including humans. Once pre-vitamin D3 is synthesized in the skin, it undergoes a heat-induced membrane-enhanced isomerization to vitamin D3. Cutaneous vitamin D3 production is influenced by skin pigmentation, sunscreen use, time of day, season, latitude, altitude, and air pollution. Once formed, vitamin D3 is ejected out of the keratinocyte plasma membrane and is drawn into the dermal capillary bed by the vitamin D binding protein (DBP). Vitamin D that is ingested is incorporated into chylomicron which is released into the lymphatic system, and enters the venous blood where it binds to DBP and lipoproteins and transported to the liver. Vitamin D2 and vitamin D3 are 25-hydroxylated by the 25-hydroxylase

(CYP2R1) to produce the major circulating vitamin D metabolite, 25(OH) D which is used to determine a patient's vitamin D status. This metabolite undergoes further hydroxylation by the 25(OH) D- 1α-hydroxylase (CYP27B1) in the kidneys to form the secosteroid hormone 1α, 25- dihydroxyvitamin D [1, 25(OH)$_2$D] [1].

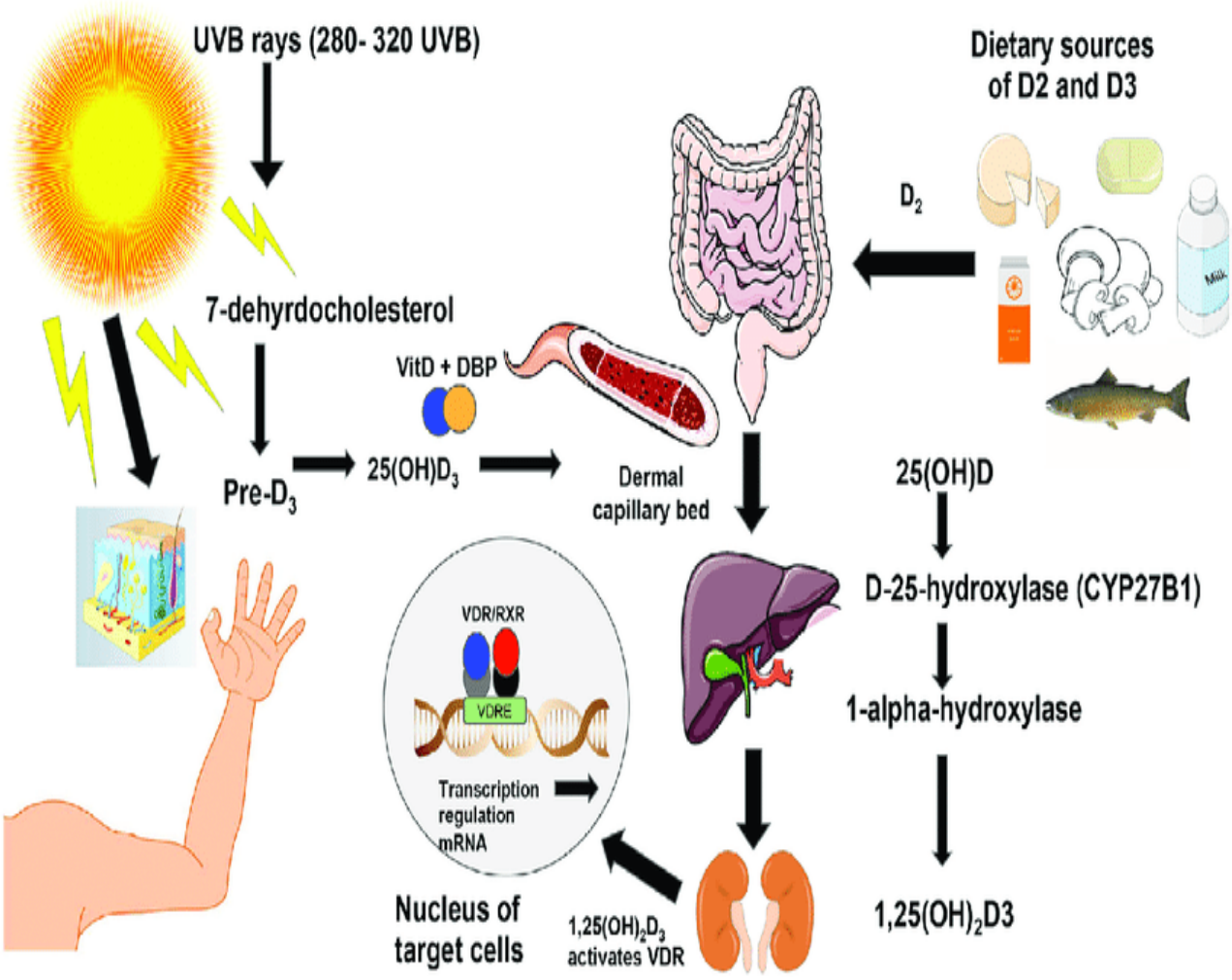


Figure 2: Role of Vitamin D as an immune modulator:

The potential role of vitamin D in the immune system is proposed after the discovery of vitamin D receptor (VDR) in macrophages, dendritic cells (DC) and activated T and B lymphocytes, and the ability of these cells to express CYP27B1[9] – Figure 2. However, it is still unclear whether increasing the level of vitamin D in the circulation has an effect on the

local paracrine function. Also, despite the optimal level of vitamin D in circulation, the metabolism capacity can vary among individuals, as proposed in the case of certain genetic polymorphisms in VDR and vitamin D metabolizing enzymes[10].

The causal link between poor vitamin D status and autoimmune diseases or infections in humans remains unclear. Vitamin D has major effects on nearly all cells of the immune system. Antigen-presenting cells, such as dendritic cells, macrophages, and T and B cells, express the vitamin D receptor (VDR). Thus, the VDR-vitamin D endocrine system can modulate most aspects of the innate and acquired immune system (and even mast cells) when challenged by extreme deficiency or exposure to high 1,25-dihydroxyvitamin D (or its analogues)

The active form of vitamin D, 1,25-dihydroxyvitamin D, is an inhibitor of dendritic cell maturation and functions as an immune modulator, reducing activation of the acquired immune system. Therefore, vitamin D deficiency could theoretically increase the risk of autoimmune diseases, which has been reported in some studies[10,11].

A causal relationship between vitamin D and infection has not been firmly established, and vitamin D supplementation for the case of prevention of infection alone is not warranted. Although vitamin D reduces activation of the acquired immune system, it activates the innate immune system, particularly monocytes and macrophages[10]. Exposure of monocytes and/or macrophages to bacterial infections upregulates VDR and 1-alpha-hydroxylase expression and, after 48 hours, increases the production of several natural defensins (at least in human monocytes) capable of decreasing the intracellular survival of such mycobacteria[12]. In addition, there is a hypothesis that common virologic infections have a marked seasonal variation because of the seasonal variation of the vitamin D status.

In view of the wide variety of infectious diseases, additional studies are needed to better define which target group might benefit from vitamin D supplementation. There is growing interest in the role of vitamin D as a facilitator of the innate immune response during SARS-CoV-2 infection.

There are several observational studies suggesting an association between poor maternal vitamin D status and adverse pregnancy outcome and also in various infectious diseases[13].

The best laboratory indicator of vitamin D adequacy is the serum 25(OH)D concentration. The lower limit of normal for 25(OH)D levels varies depending on the geographic location and sunlight exposure of the reference population (range 8 to 15 ng/mL). However, there is no consensus on the optimal 25(OH)D concentration for skeletal or extra-skeletal health[14].

Vitamin D status in relation to 25OH levels

The best laboratory indicator of vitamin D adequacy is the serum 25(OH)D concentration. The lower limit of normal for 25(OH)D levels varies depending on the geographic location and sunlight exposure of the reference population (range 8 to 15 ng/mL). However, there is no consensus on the optimal 25(OH)D concentration for skeletal or extra-skeletal health[14].The IOM (Institute of Medicine) concluded that a serum 25(OH)D concentration of 20 ng/mL (50 nmol/L) is sufficient for most individuals, but other experts (Endocrine Society, National Osteoporosis Foundation [NOF], International Osteoporosis Foundation [IOF], American Geriatrics Society [AGS]) suggest that a minimum level of 30 ng/mL (75 nmol/L) is necessary in older adults to minimize the risk of falls and fracture[15].

The Endocrine Society defined vitamin D deficiency as 25(OH)D level of 20 ng/mL or less, vitamin D insufficiency as 21 to 29 ng/mL, and vitamin D sufficiency as 30 ng/mL or greater

for children – Table 1. It suggested that maintenance of a 25(OH)D level of 40 to 60 ng/mL is ideal (this takes into account assay variability) and that up to 100 ng/mL is safe[14].

Table 1: US Endocrine Society of Classification[14]

Vitamin D levels	Status
Deficient	≤20 ng/mL
Insufficient	21-29ng/mL
Sufficient	≥30ng/mL
Toxicity	>150ng/mL

Neonatal Sepsis:

Sepsis is an important cause of morbidity and mortality among newborn infants. Although the incidence of sepsis in term infants is low, the potential for serious adverse outcomes is of such great consequence, that caregivers should have a low threshold for evaluation and treatment for possible sepsis in neonates. Most infection related deaths occur in low income and middle-income countries, due to poor hygiene and sub optimal practices. Sepsis related mortality is prevented by prevention of sepsis itself[16].

The incidence of neonatal sepsis reported to be around 38 per 1000 intramural live births in tertiary care institutions. Septicaemia was the commonest clinical condition with an incidence of 24 per 1000 live births[17]. Meningitis was diagnosed in 0.5 per 1000 live births. Neonatal sepsis, the most common cause of neonatal mortality contributing to 23% of all neonatal

deaths[16]. Klebsiella pneumoniae was most isolated pathogen (31.2%), followed by Staphylococcus aureus (17.5%) among the intramural live births. Among extramural babies admitted for neonatal problems, Klebsiella pneumoniae was the commonest organism (36.4%), followed by Staphylococcus aureus (14.3%) and Pseudomonas (13.2%)[18].

Definition:

"Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection with or without the presence of a bacterial pathogen from the bloodstream"[18]. A consensus definition for neonatal sepsis is lacking[19].

Sepsis is classified according to the infant's age at the onset of symptoms as follows:

Early-onset sepsis (EOS) is defined as the onset of symptoms before three days of age, that is infections within the first 72 hours of life[20].

Late-onset sepsis (LOS) is generally defined as the onset of symptoms at age greater than 72 hours of life[20].

Infants with EOS typically present with symptoms during their birth hospitalization. Term infants with LOS generally present to the outpatient setting or emergency department unless comorbid conditions have prolonged the birth hospitalization[21].

Pathogenesis of Neonatal Sepsis:

Early-onset infection – Early-onset infection is usually due to vertical transmission by ascending contaminated amniotic fluid or during vaginal delivery from bacteria in the mother's lower genital tract. Maternal chorioamnionitis (or intraamniotic infection) is a well-recognized risk factor for EOS. Maternal group B streptococcal (GBS) colonization is

another important risk factor. Use of forceps during delivery and electrodes placed for intrauterine monitoring also involved in the pathogenesis of EOS because they penetrate the neonatal defensive epithelial barriers[22].

Late-onset infection – Late-onset infections can be acquired by the following mechanisms:

-Vertical transmission, resulting in initial neonatal colonization that evolves into later infection.

-Horizontal transmission from contact with care providers or environmental sources.

Disruption of the intact skin or mucosa, which can be due to invasive procedures (eg, intravascular catheter), increases the risk of late-onset infection. LOS is uncommonly associated with maternal obstetrical complications[23].

Metabolic factors including hypoxia, acidosis, hypothermia, and inherited metabolic disorders (eg, galactosemia), are likely to contribute to risk for and severity of neonatal sepsis (including both early- and late-onset). These factors are thought to disrupt the neonate's host defences [23].

Maternal factors associated with an increased risk of EOS in the neonate, particularly GBS infection, include chorioamnionitis (intraamniotic infection), intrapartum maternal fever, maternal GBS colonization, preterm delivery, and prolonged rupture of the membranes[24].

Micro-organisms causing sepsis in new born and their antibiotic sensitivity may change over time and differ between countries. In developed countries, the organisms isolated in EOS are GBS and E coli. The organisms isolated in LOS include Coagulase negative staphylococci (CONS) followed by GBS and Staphylococci aureus[25]. Whereas, in developing countries, Gram negative organisms are more common (mainly Klebsiella, E. coli and Pseudomonas)

and among Gram-positive organisms, Staph aureus, CONS, Streptococcus pneumoniae, and Streptococcus pyogenes are isolated[26].

Essentially, the definitions try to delineate a cut-off point beyond which the origin of infections is usually nosocomial (LOS), rather than intrapartum (EOS). The incidence of EOS has declined from 3-4 cases/1000 live births to 0.8-1/1000 live births in the post GBS prophylaxis era[27].

Neonatal immunity is deficient at multiple steps. Invading pathogens first come into contact with the antigen presenting cells (APCs) like the monocytes, macrophages and Langerhans cells of skin. However, neonatal APCs have defective expression of major histocompatibility complex II (MHC II) and co-stimulatory molecules, resulting in reduced presentation to CD4 + cells. Further, neonates exhibit a skewed response to stimulation by pathogens, marked by predominance of Th2 polarizing anti-inflammatory cytokines such as interleukin (IL-10 rather than the usual Th1 polarizing cytokine response such as tumour necrosis factor alpha (TNF α), IL-12 and interferon. This deficient pathogen recognition and activation of immune system is being targeted with toll-like receptor agonists (TLR 8 agonists) in vitro[28].

Several obstetric and neonatal factors have been identified that have association with increased risk of neonatal infection[29]. Based on few studies from India, the following risk factors are identified:

- Spontaneous prematurity
- Foul smelling liquor
- Rupture of membranes for greater than 24 hours of life
- Single unclean or > 3 sterile vaginal examinations during prolonged labour.
- Prolonged labour > 24 hours; first and second stage of labour > 24 hours
- Perinatal asphyxia with APGAR score < 4 at 1 minute

Infants with any of the two risk factors are subjected to sepsis screen and infants with foul smelling liquor and prolonged rupture of membranes are warranted to start intravenous antibiotics. If the sepsis screen is negative then there is a need to repeat after 12 to 24 hours[29].

Clinical features:

The earliest onset of signs is usually nonspecific:

- Hypothermia or fever
- Lethargy, poor cry and refusal to suck
- Poor perfusion and prolonged capillary filling time
- Hypotonia and absent or decreased reflexes
- Bradycardia or tachycardia
- Respiratory distress, apnoea or gasping respiration
- Hypoglycaemia or hyperglycaemia
- Metabolic acidosis

Systemic manifestations:

- Central nervous system: Bulging anterior fontanelle, vacant stare, high pitched cry, excess irritability, stupor, coma, seizures, neck stiffness or retraction. Any of these clinical features should raise a suspicion of meningitis.
- Cardiovascular system: Hypotension, poor perfusion or shock
- Gastrointestinal system: Feed intolerance, vomiting, diarrhoea, abdominal distension and paralytical ileus

- Hepatic: Hepatomegaly and direct hyperbilirubinemia
- Renal: Acute renal failure
- Haematological: Bleeding, petechia and purpura.
- Skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge.

EOS is usually a multisystem disease predominantly with respiratory symptoms, characterized by a sudden onset and fulminant course progressing rapidly to septic shock and death.

Investigations:

Sepsis screen needs to be done in all neonates with clinical suspicion of sepsis[29-32]:

Various components of sepsis screen include Total leucocyte count, absolute neutrophil count (ANC), immature to total neutrophil ratio, micro erythrocyte sedimentation rate (m ESR), C-reactive protein (CRP) [29] – Table 2.

Table 2: Components of sepsis screen and the cut off values

Components	Values
Total leucocyte count	Less than 5000/mm
Absolute neutrophil count	Low counts as per Manroe chart in term babies
Immature to total neutrophil ratio	>0.2
Micro Erythrocyte sedimentation rate	>15mm/hour
C-Reactive protein	>1 mg/dl

If any of the above two criteria are met, then the sepsis screen is positive.

Definitive Sepsis is isolating the organism in the blood and is the gold standard test for diagnosis of sepsis and needs to be done prior to starting antibiotics. A positive blood culture with sensitivity of the isolated organism is the best guide to antimicrobial therapy[29].

Other biomarkers include Procalcitonin, serum amyloid A, hepcidin, CD64, CD 11b, IL 1, IL 6, IL 8, TNF α, E selectin etc[33].

Molecular assays: Molecular pathogen detection methods are based on hybridisation or amplification of pathogen DNA, can be completed in less than 12 hours, and have better sensitivity than cultures[34].

The incidence of meningitis varies and the symptoms of sepsis and meningitis overlaps, so it is quite possible to have meningitis in sepsis. Cerebrospinal fluid (CSF) analysis is based on the results the course and duration of antibiotics are decided[35].

Recent studies:

In a case control study to determine the possible association between neonatal vitamin D deficiency and development of early onset sepsis in term neonates Ashwani Kumar et al. observed that among 100 term neonates with early onset sepsis, 77% had deficient vitamin D levels (≤20 ng/ml), 23% had insufficient levels (21-29 ng/ml) and none had sufficient levels. Among the healthy controls, 41% of neonates had deficient Vitamin D levels, 28% had insufficient levels and 31% neonates had sufficient levels. Mean serum Vitamin D level was significantly lower in the cases compared to that of controls[3].

Cetinkaya et al observed the association between maternal and neonatal Vitamin D levels and early onset sepsis in term neonates. The study population included 100 neonates of whom 50 neonates had early onset sepsis and 50 were healthy controls. There was no significant difference between the two groups in terms of sex, birthweight, gestational age, birth season, mode of delivery and Apgar scores. No significant difference was detected with respect to maternal demographic features including maternal age and perinatal comorbidities between the two groups. Educational status was significantly lower in the study group and mothers had never or irregularly used Vitamin D supplementation. Vitamin D levels were significantly lower in term infants with early onset sepsis along with their mothers suggesting that lower vitamin D levels are associated with EOS. Neonatal Vitamin D levels positively correlated with maternal Vitamin D levels[36].

In a case control study on serum Vitamin D levels in term neonates with early onset sepsis, Khaing et al. recruited 40 cases with early onset sepsis and 40 healthy neonates as controls. Cord blood Vitamin D level was estimated. There was no significant difference between two groups in terms of birth weight and sex. Likewise, there was no significant difference with regard to maternal age, race, birth season and also mode of delivery. All the neonates (100%) in the sepsis group (cases) had deficient levels of Vitamin D while in the control group, 65% of neonates had deficient levels and 2.5% had sufficient levels. Cord blood vitamin D levels in among cases were significantly lower than that of controls[37].

Saboute et al investigated the association between maternal Vitamin D serum levels and neonatal early onset sepsis in new-borns. Out of 64 neonates, 32 had early onset sepsis while 32 were healthy. Maternal Vitamin D levels were also estimated. Maternal serum Vitamin D

levels inversely correlated with the occurrence of neonatal sepsis, suggesting that Vitamin D had protective effects against neonatal sepsis. They also observed a significant correlation between maternal vitamin D supplement intake during pregnancy and lower risk for neonatal sepsis. They suggested that intake of vitamin D supplement during pregnancy could decrease the risk of early neonatal sepsis[38].

In a case-control study, the relationship between maternal and infant vitamin D levels and late onset sepsis was investigated by Betyul S B et al. Cases consisted of 46 neonates with late-onset sepsis and 46 controls were neonates with hyperbilirubinemia. Birth weight, gestational week, gender, and mode of delivery were similar between the groups. Maternal demographics like maternal age, pregnancy related diseases, educational status of the mother, scarf use and consanguineous marriage rates were similar between the two groups. They observed that Vitamin D supplementation during pregnancy was significantly lower in mothers of neonates with sepsis compared to the control group. They also observed significant low levels of serum Vitamin D levels among neonates and mothers among the cases. In their study, Vitamin D cut off value of 15.45 ng/ml (sensitivity: 91.3 %, specificity: 71.7 %, area under the curve: 0.824, $p < 0.001$) determined the risk of late-onset sepsis among neonates[2]

MATERIAL AND METHODS

Study site: This study was conducted in the Department of Paediatrics at R L Jalappa Hospital &Research Centre (RLJH&RC), Kolar, Karnataka.

Source of data: Neonates born to mother with risk factors for sepsis admitted in RLJH&RC were included in the study.

Study design: A prospective observational study conducted from February 2020 to April 2021.

Sampling method: All the eligible subjects fulfilling the inclusion criteria were recruited and the end of study period.

Sample size:

Sample size was estimated by using the proportion of deficient Vitamin D levels in EOS was 73% from the study by Kochar et al[39] using the formula

Sample Size = $\underline{\mathbf{Z}_{1-\alpha/2}{}^2 \, P\,(1-P)}$

d^2

$\mathbf{Z}_{1-\alpha/2}$ = is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type1 error ($P<0.01$) it is 2.58). In majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

P= Expected proportion in population based on previous studies or pilot studies

d= Absolute error or precision

P = 73% or 0.73

q = 27% or 0.27

d = 10% or 0.010

Using the above values at 95% Confidence Level (CL), a sample size of 76 subjects were included in the study. Considering 10% non -response a sample size of 76 + 7.6 ≈ 84 subjects or more were included in the study.

Method of collection of Data:

- **Inclusion criteria:** All term neonates (gestational age from 37 weeks to <42 weeks) with 1 or more of the following maternal risk factors:

✓ Foul smelling liquor

✓ Rupture of membranes > 18 hours

✓ Single unclean or > 3 sterile vaginal examinations during labour.

✓ Prolonged labour >24 hours

✓ Maternal UTI

- **Exclusion Criteria**: New-borns with

1. Congenital anomalies
2. Suspected metabolic disease.

Ethical considerations: Study was approved by Institutional Ethics Committee (IEC). Informed written consent was taken. The risks and benefits involved in the study and the voluntary nature of participation were explained before obtaining consent. Confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

• This study was conducted in RLJH affiliated to Sri Devaraj Urs Medical College (SDUMC), a constituent college of Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER).

• Subjects fulfilling the inclusion criteria were enrolled after obtaining informed consent.

Maternal data was collected and following delivery, neonatal characteristics like gestational age, birth weight, APGAR score were noted. Complete physical examination was performed, and findings were recorded.

Definitions:

Socio-economic status was classified according to Kuppuswamy classification[40] - Table 3

Table 3: Kuppuswamy's socio-economic status scale 2019

Score	Socio economic class
26-29	Upper (I)
16-25	Upper middle (II)
11-15	Lower middle (III)
5-10	Upper lower (IV)
<5	Lower (V)

Maternal sun exposure: Maternal sun exposure to sun light for at least 10 minutes /day during afternoon hours in the absence of purdahs (as prevalent in some cultures) was taken as exposed to sunlight[41].

Septic screen was considered positive when 2 or more of the following parameters were present[29]:

1. Total leukocyte count: < 5000/mm^3 or more than 24,000/mm.
2. Absolute neutrophil count: low count as per Monroe chart for term infant.
3. Immature or band cells to total neutrophil ratio: >0.2
4. Micro ESR: >10mm 1st hour
5. CRP: >1mg/dL.

Neonates were divided into two groups based on the results of Sepsis screen and Blood culture. Neonates with a positive septic screen and/or blood culture were taken as **EOS positive group** and those with a negative septic screen and/or blood culture were taken as **No sepsis group or EOS negative group**[29]**.**

Early onset sepsis group was further subdivided into **Probable sepsis**[29] (septic screen positive only) and **Definitive sepsis**[29] (septic screen and blood culture positive)

The following investigations were done for all the neonates:

- Cord blood Vitamin D levels (immediately after delivery)
- Complete blood count (CBC); CRP (C- Reactive Protein); Blood culture and sensitivity (within 6 hours of life)- Venous sample.

The following investigations were done as and when required:

- Arterial blood gas analysis (ABG).
- Chest X-ray.

- Lumbar puncture.

Blood Sampling:

Cord blood Vitamin D level: Two millilitres of cord blood sample was collected under aseptic condition using plain vacutainer, allowed to clot and the serum was separated by centrifugation stored at -20^{o}Celsius until analysis. The sera were processed in VITROS ECi/ECiQ System Kit in Biochemistry Lab affiliated to RLJH centre.

Working Principle*:* Vitamin D estimation was done by Chemiluminescence immune assay which involves release of 25-OH Vitamin D in the sample from the binding protein using a low Ph denaturant and the subsequent competition of the free 25-OH Vitamin D with horseradish peroxidase (HRP) labelled 25-OH reagent for monoclonal anti Vitamin D is bound to the wells. Unbound materials were removed by washing. The bound HRP conjugate was measured by luminescent reaction which is indirectly proportional to 25-OH Vitamin D.

Vitamin D levels were classified as per the Endocrine Society recommendations in which vitamin D deficiency was defined as a 25(OH)D level of 20 ng/mL or less, 21 to 29 ng/mL as insufficient and 30 ng/mL or greater as sufficient[14,41] - Table 4.

Table 4: Classification of Vitamin D Status [14,42]

Vitamin D Levels	Status
Deficient	≤20 ng/mL
Insufficient	21-29ng/mL
Sufficient	≥30ng/mL
Toxicity	>150ng/mL

CBC: Venous blood sample (2 ml) was collected in EDTA vacutainer and CBC was done by automated Haematology Analyser Sysmex Autoloader Processing.

CRP: Venous blood sample (2 ml) was collected in a sterile tube without anticoagulant and allowed to clot at room temperature. Serum was separated and stored at $+2^0$ to 4^0 Celsius. CRP was done using Diagnostic Reagent Kit in the microbiology lab of RLJH&RC, ARKRAY Healthcare Pvt Ltd.

Blood Culture:

Venous blood sample (2 ml) was collected using aseptic technique in a container having specific media (chocolate agar, Mac Conkey Agar etc) for aerobic and anaerobic organisms (yellow cap). Bottles were loaded into Bact/ALERT equipment. It was considered as positive if there was a beep or if the screen showed yellow light and was considered as negative if the screen showed green after 7 days.

Statistical Analysis:

Data were coded and recorded in MS Excel spread sheet. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive analysis was discussed in the form of mean, standard deviation (SD), median and inter quartile range (IQR) for continuous variables. Frequencies and percentages were used for categorical variables. Graphical representation of bar charts and pie charts were used for categorical data.

Chi square test was used as a test of significance for more than 2 group comparisons of categorical data. Fischer exact test was used in expected frequency in the contingency tables for <5 with >25% of the cells. Statistical significance was kept at p value <0.05.

RESULTS

This study was carried out at RLJH & RC, a tertiary care teaching hospital of SDUMC.

A total of 107 neonates were included in the study.

Table 5: Distribution of Neonates according to Maternal Age (n = 107)

Maternal Age	Frequency	Percentage	95% CI
18-25 Years	48	44.9	35.3% - 54.8%
26-30 Years	50	46.7	37.1% - 56.6%
31-35 Years	9	8.4	4.2% - 15.8%

Figure 3: Bar diagram representing distribution of Neonates according to Maternal Age (n = 107)

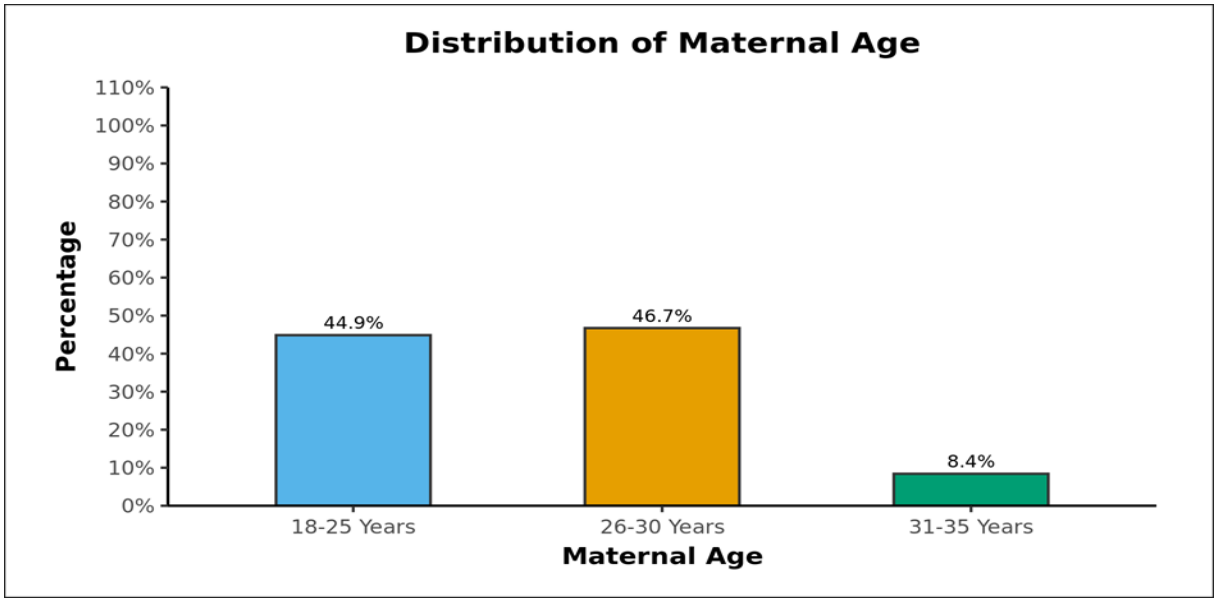
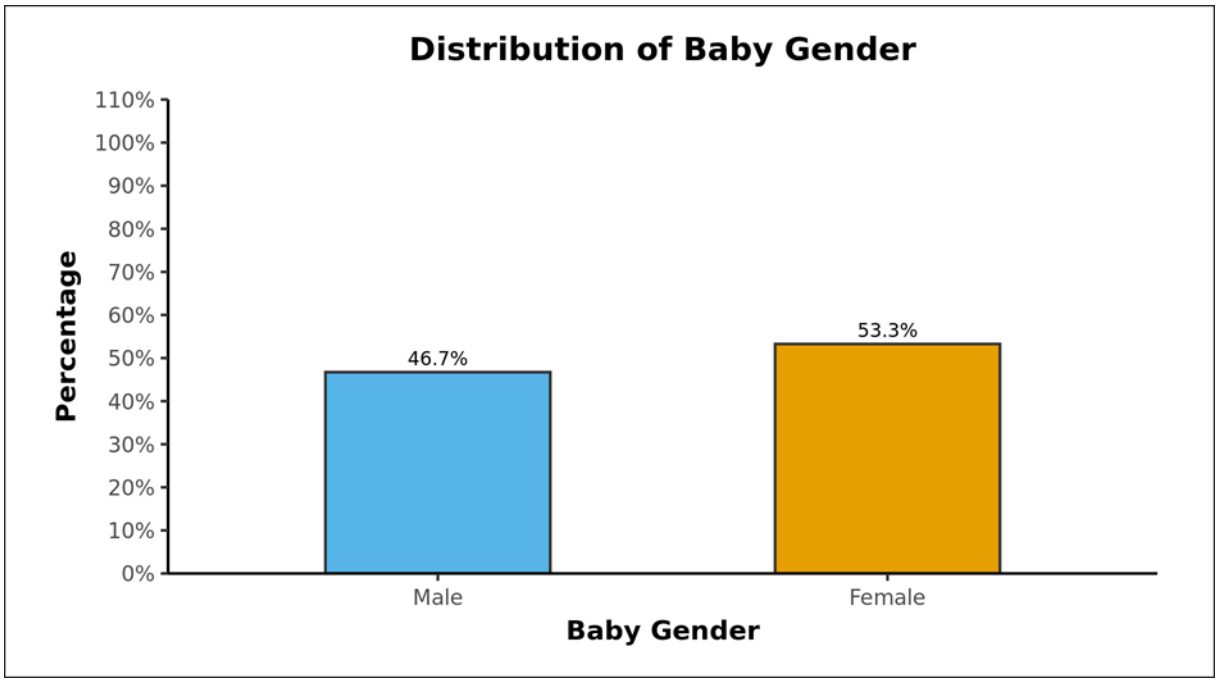


Table 5 and Figure 3 depict the distribution of participants according to maternal age. It was noted that 44.9%, 46.7% and 8.4% of the mothers were in the age groups of 18-25 years, 26-30 years and 31- 35 years respectively.

Table 6: Distribution of Neonates according to Gender (n = 107)

Gender	Frequency	Percentage	95% CI
Male	50	46.7	37.1% - 56.6%
Female	57	53.3	43.4% - 62.9%

Figure 4: Bar diagram depicting distribution of Neonates according to Gender of the Neonates (n = 107)



There was a preponderance of females (53%) with a female to male ratio of 1.14:1 – Table 6 & Figure 4

Table 7: Distribution of Neonates according to Socio-economic Status (n = 107)

Socio-Economic Status	Frequency	Percentage	95% CI
Upper Middle	38	35.5	26.7% - 45.4%
Lower Middle	46	43.0	33.6% - 52.9%
Upper Lower	17	15.9	9.8% - 24.5%
Lower	6	5.6	2.3% - 12.3%

Figure 5: Bar diagram depicting Distribution of Neonates according to Socio-economic Status (n=107)

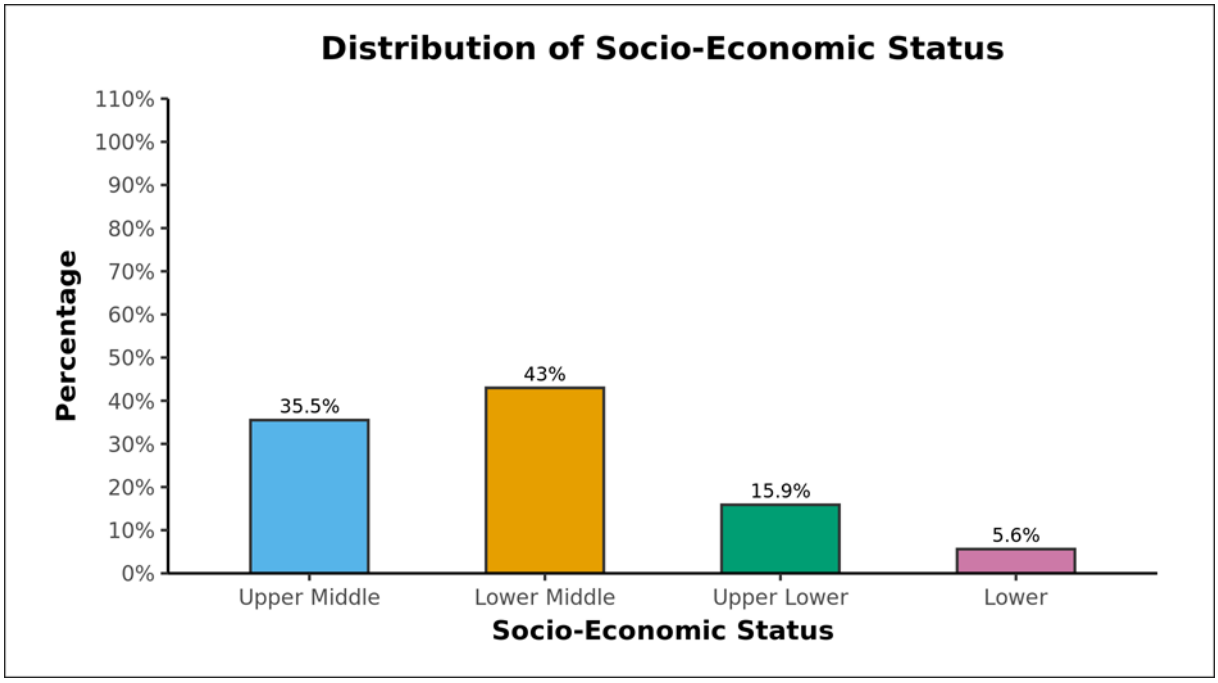


Table 7 & Figure 5 depict the distribution according to socio-economic status. It was observed that majority (43%) belonged to lower middle class while 35.5%, 15.9% and 5.6% belonged to upper middle class, upper lower class and lower class respectively.

Table 8: Distribution of Neonates according Maternal Sun Exposure (n = 107)

Sun Exposure	Frequency	Percentage	95% CI
Present	49	45.8	36.2% - 55.7%
absent	58	54.2	44.3% - 63.8%

Figure 6: Bar diagram depicting distribution of Neonates according to Maternal Sun Exposure (n=107):

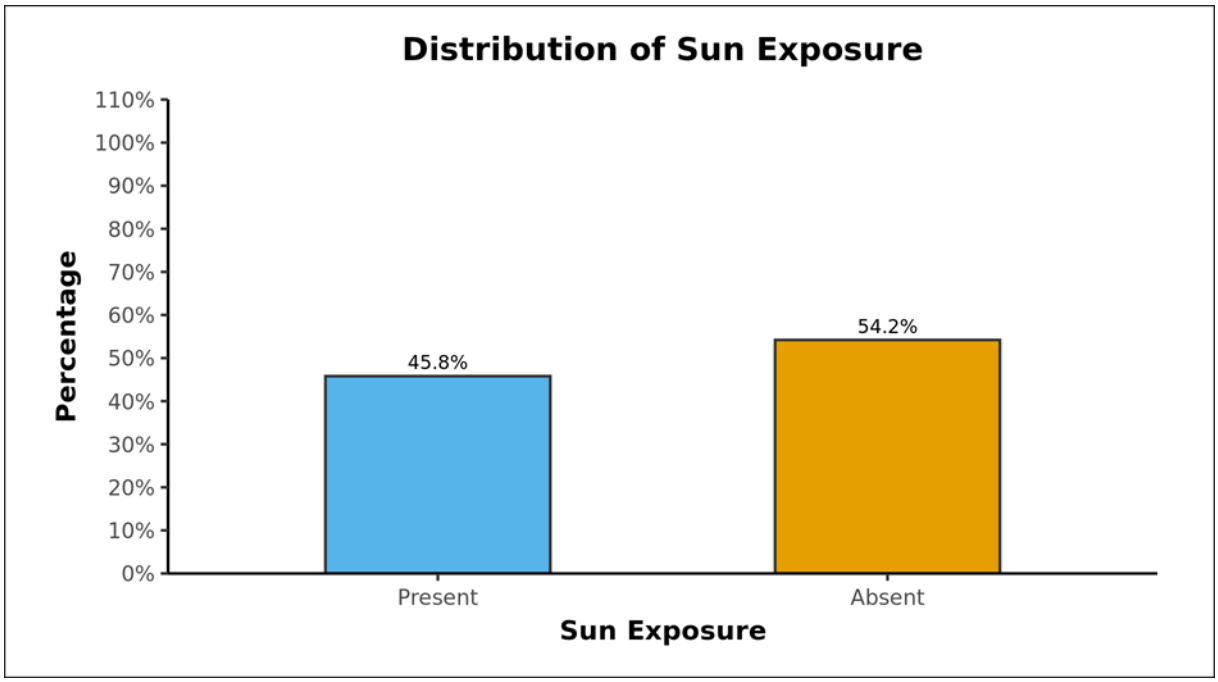
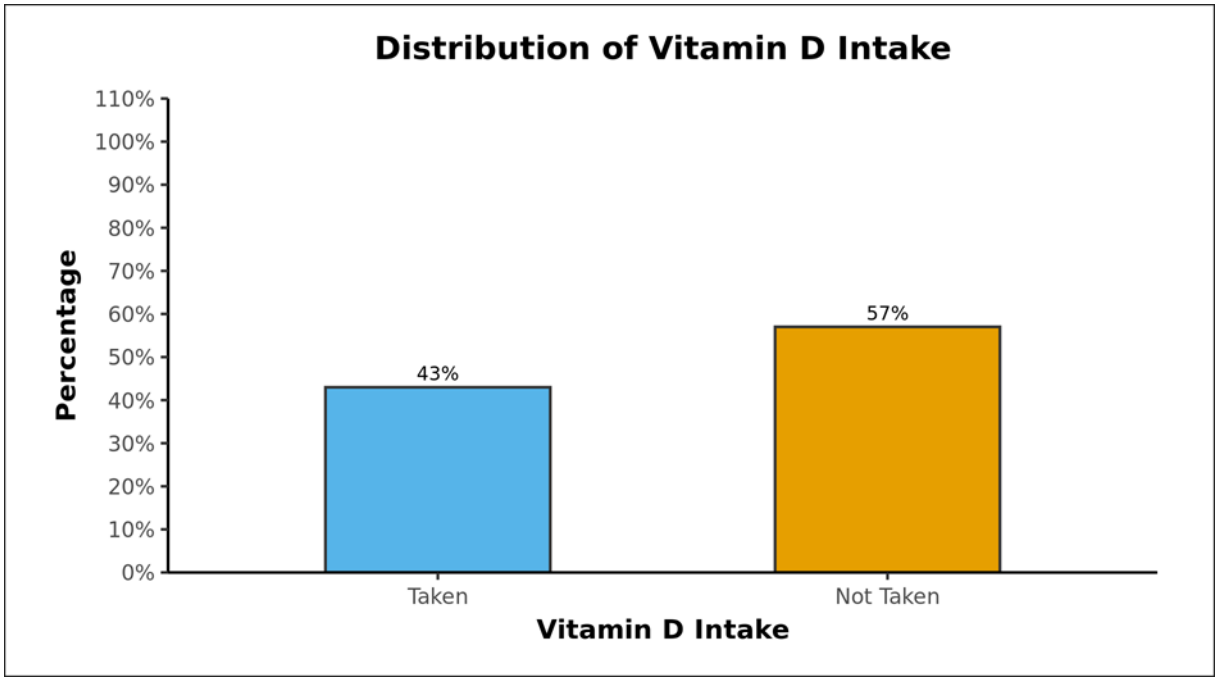


Table 8 and Figure 6 depict that 45.8% mothers had sun exposure and the rest did not have enough exposure.

Table 9: Distribution of Neonates according to Oral Maternal Vitamin D Supplementation (n = 107)

Vitamin D Supplementation	Frequency	Percentage	95% CI
Supplemented	46	43	33.6% -52.9%
Not supplemented	61	57	47.1% - 66.4%

Figure 7: Bar Diagram showing Distribution of Neonates according to Oral Maternal Vitamin D Supplementation (n=107)

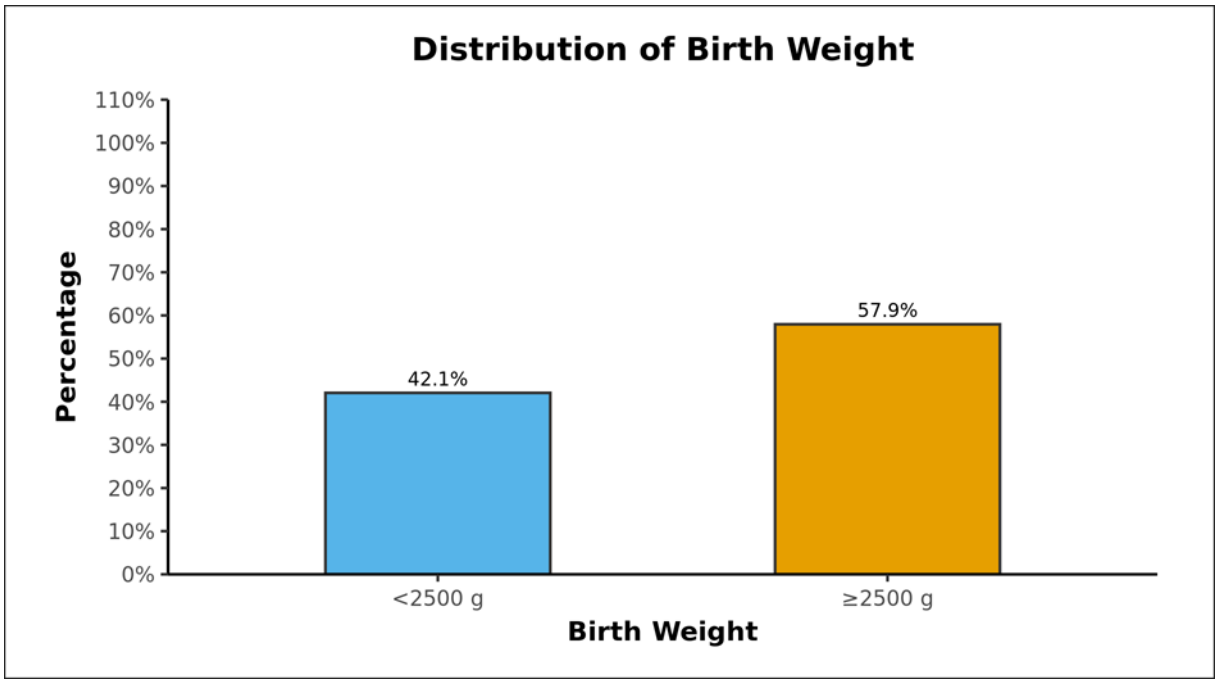


In the present study, 43% of mothers had taken oral Vitamin D supplementation during pregnancy while the remaining 57% did not – Table 9 & Figure 7.

Table 10: Distribution of Neonates according to Birth Weight (n = 107)

Birth Weight	Frequency	Percentage	95% CI
<2500 grams	45	42.1	32.7% - 52.0%
≥2500 grams	62	57.9	48.0% - 67.3%

Figure 8: Bar Diagram representing Distribution of Neonates according to Birth Weight

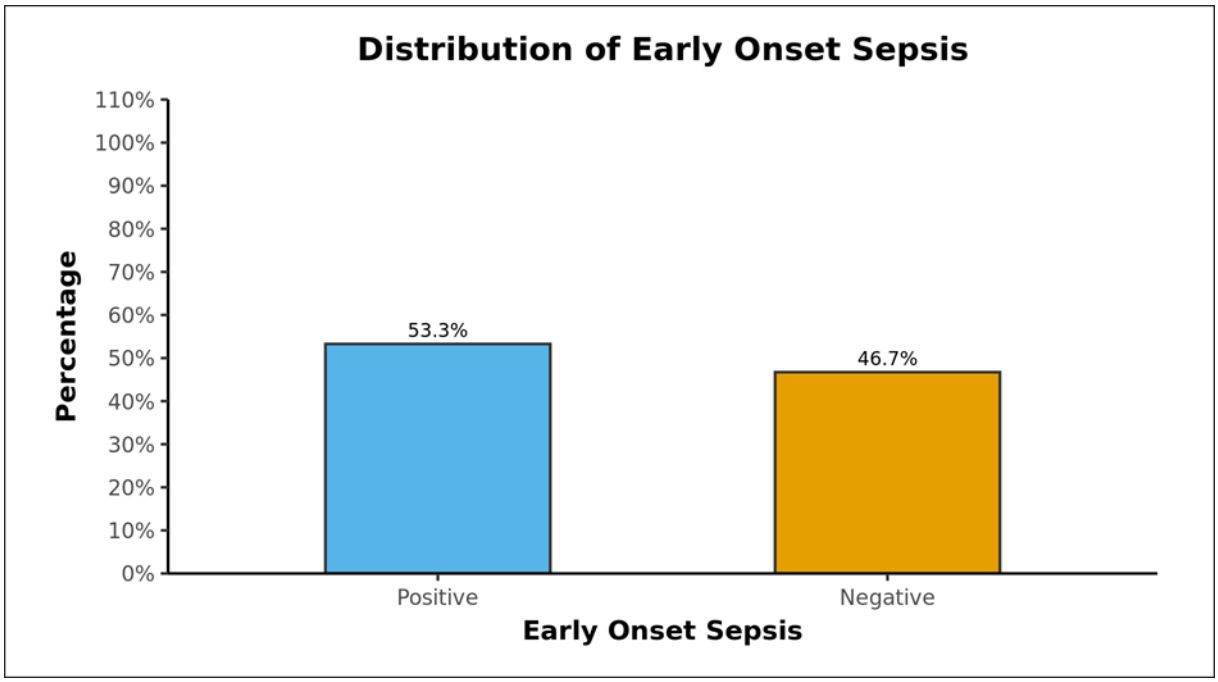


Majority (57.9%) of neonates weighed ≥2500 grams while 42.1% of the neonates had low birth weight as shown in Table 10 & Figure 8.

Table 11: Distribution of Neonates according to EOS and No Sepsis (n = 107)

Early onset sepsis	Frequency	Percentage	95% CI
Positive	57	53.3	43.4%-62.9%
Negative	50	46.7	37.1%-6.6%

Figure 9: Bar Diagram representing Distribution of Neonates according to EOS and No Sepsis

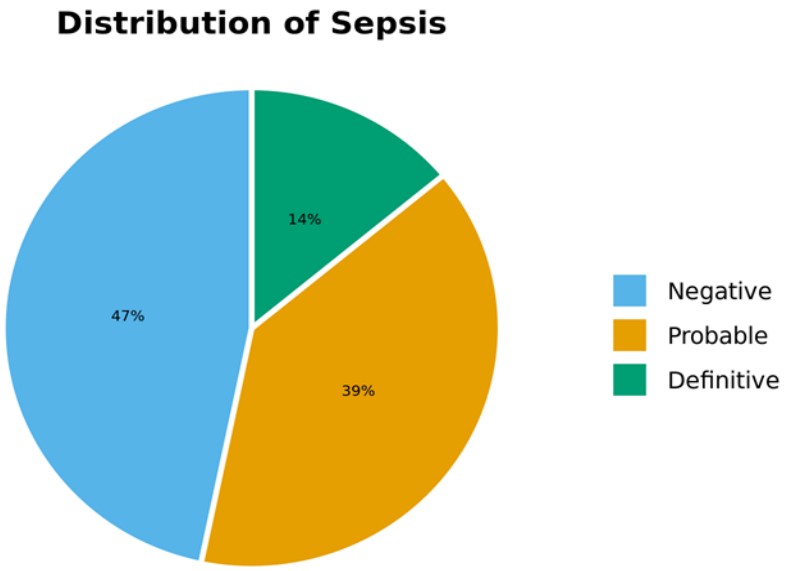


Out of 107 neonates, 57(53.3%) had EOS while 50 (46.7%) neonates did not have sepsis – Table 11 & Figure 9.

Table 12: Distribution of Neonates according to Probable Sepsis, Definitive Sepsis and No Sepsis (n = 107)

Status of Sepsis	Frequency	Percentage	95% CI
No Sepsis	50	46.7	37.1% - 56.6%
Probable Sepsis	42	39.3	30.1% - 49.2%
Definitive Sepsis	15	14.0	8.3% - 22.4%

Figure 9: Pie diagram showing Distribution of Neonates according to Probable Sepsis, Definitive Sepsis and No Sepsis

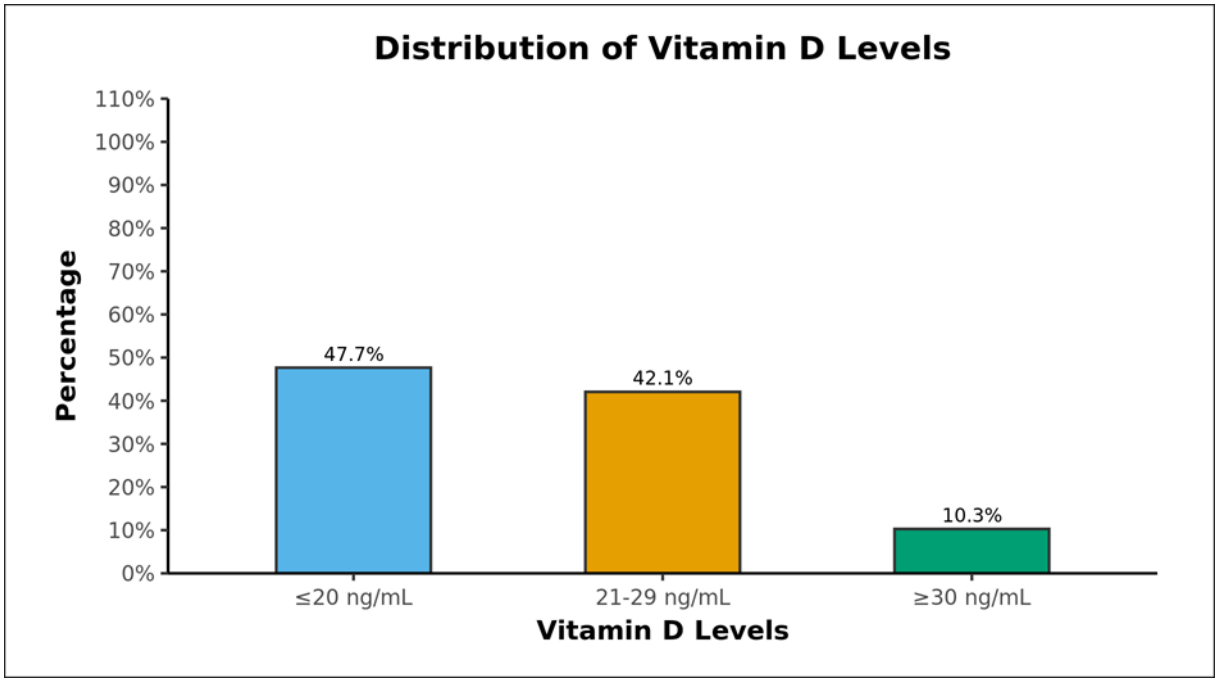


Out of 107 neonates, 39.3% and 14% had probable sepsis and definitive sepsis respectively while 46.7% had no sepsis -Table 12 & Figure 9.

Table 13: Distribution of Neonates according to Cord Blood Vitamin D Levels (n = 107)

Vitamin D Levels	Frequency	Percentage	95% CI
≤20 ng/mL (Deficient)	51	47.7	38.0% - 57.5%
21-29 ng/mL (Insufficient)	45	42.1	32.7% - 52.0%
≥30 ng/mL (Sufficient)	11	10.3	5.5% - 18.0%

Figure 10: Bar diagram showing Distribution of Neonates according to Cord Blood Vitamin D levels (n=107)



In the present study, it was observed that only 10.3% of neonates had sufficient levels of Vitamin D. Deficient levels and insufficient levels of Vitamin D was present in 47.7% and 42.1% respectively – Table 13 & Figure 10.

Table 14: Central tendency of Vitamin D levels in EOS Positive and Negative Groups.

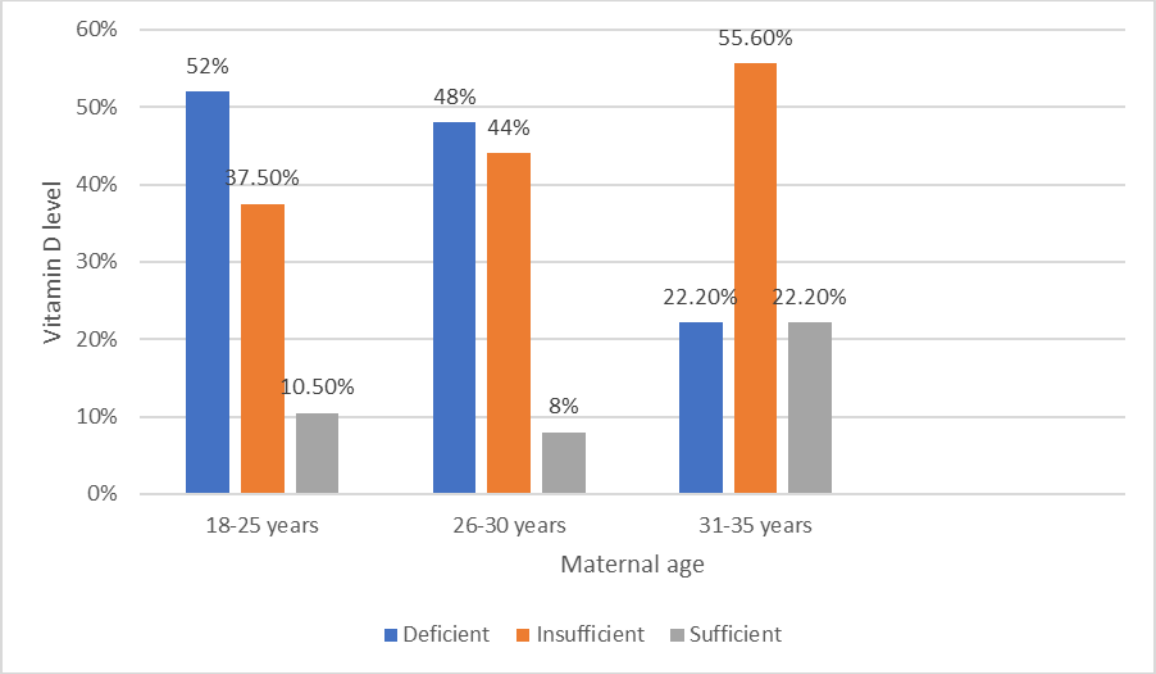
Vitamin D level (ng/ml)	EOS Positive	EOS Negative
Mean (± SD)	19.48(± 4.40)	23.60 (± 6.63)
Median (IQR)	18 (16-22)	23.5 (18-26)
Range	13-34	14-42

In the present study, mean Vitamin D values in EOS positive and negative groups were 19.48 (± 4.40) ng/ml and 23.60 (± 6.63) ng/ml respectively. The median (IQR)in EOS positive and negative groups were 18 (16-22) ng/ml and 23.5 (18-26) ng/ml respectively – Table 14.

Table 15: Association between Cord Blood Vitamin D Levels and Maternal Age

Maternal Age (Years)	Vitamin D Levels				Fisher's Exact Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
18-25	25 (52.0%)	18 (37.5%)	5 (10.5%)	48(100%)	3.594	0.390
26-30	24 (48%)	22 (44%)	4 (8%)	50 (100%)		
31-35	2 (22.2%)	5 (55.6%)	2 (22.2%)	9 (100%)		
Total	51	45	11	107		

Figure 11: Association between Cord Blood Vitamin D Levels and Maternal Age



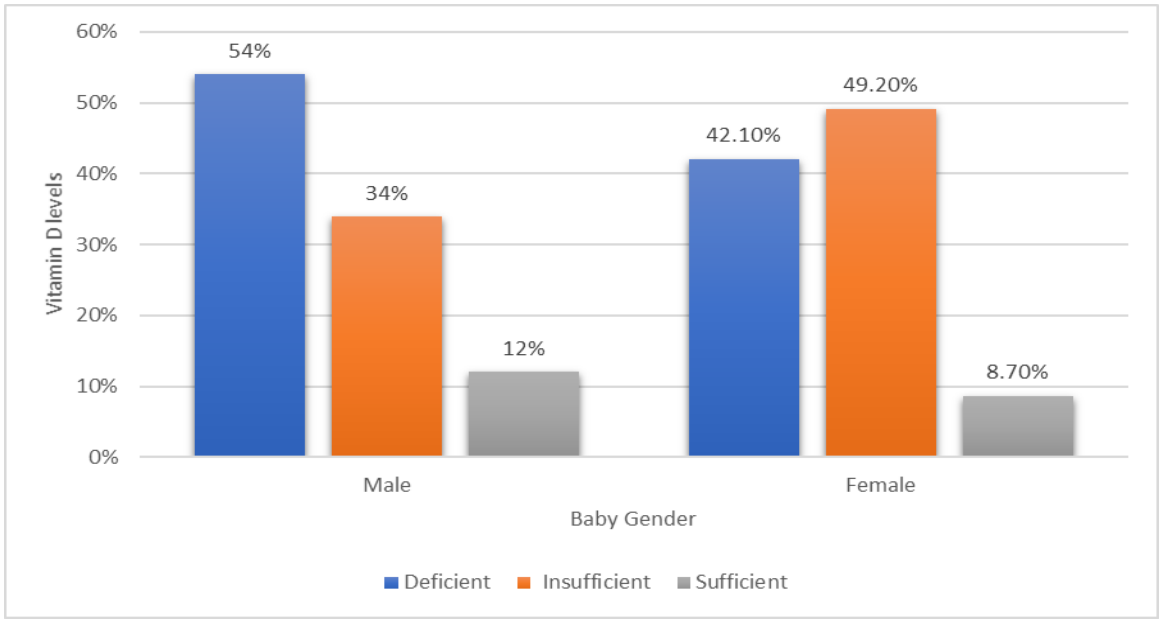
Among mothers in the age group of 18-25 years, cord blood Vitamin D levels were deficient and insufficient in 52% and 37.5% respectively while it was sufficient in 10.5%. In the maternal age group of 26-30 years, cord blood Vitamin D levels were deficient, insufficient, and sufficient in 48%, 44% and 8% respectively. In the maternal age group of 31-35 years, cord blood Vitamin D levels were deficient, insufficient, and sufficient in 22.2%, 55.6% and 22.2% respectively.

Fisher's exact test was used to explore the association between cord blood Vitamin D levels and maternal age. There was no significant difference between the various groups in terms of maternal age – Table 15 & Figure 11.

Table 16: Association between Cord Blood Vitamin D Levels and Gender

Gender	Vitamin D Levels				Chi-Squared Test	
	<20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
Male	27 (54%)	17 (34%)	6 (12%)	50 (100%)	2.509	0.285
Female	24 (42.1%)	28 (49.2%)	5 (8.7%)	57 (100%)		
Total	51	45	11	107		

Figure12: Association between Cord Blood Vitamin D Levels and Gender



Among male neonates, 54% had vitamin D deficiency, 34% had insufficiency and 12% had sufficiency whereas in female neonates deficient and insufficient vitamin D levels were 42.1% and 49.2% respectively, while sufficient vitamin D levels were present in 8.7%. There was no statistical difference between gender and cord blood Vitamin D levels – Table 16 & Figure 12.

Table 17: Association between Cord Blood Vitamin D Levels and Socio-economic Status

Socio-Economic Status	Vitamin D Levels				Fisher's Exact Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
Upper Middle	17 (44.7%)	18 (47.3%)	3 (8%)	38 (100%)	4.597	0.722
Lower Middle	22 (47.8%)	17 (37%)	7 (15.2%)	46 (100%)		
Upper Lower	10 (58.8%)	6 (35.2%)	1 (6%)	17 (100%)		
Lower	2 (33.4%)	4 (66.6%)	0 (0.0%)	6 (100%)		
Total	51	45	11	107		

Figure 13: Association between Cord Blood Vitamin D Levels and Socio-economic Status

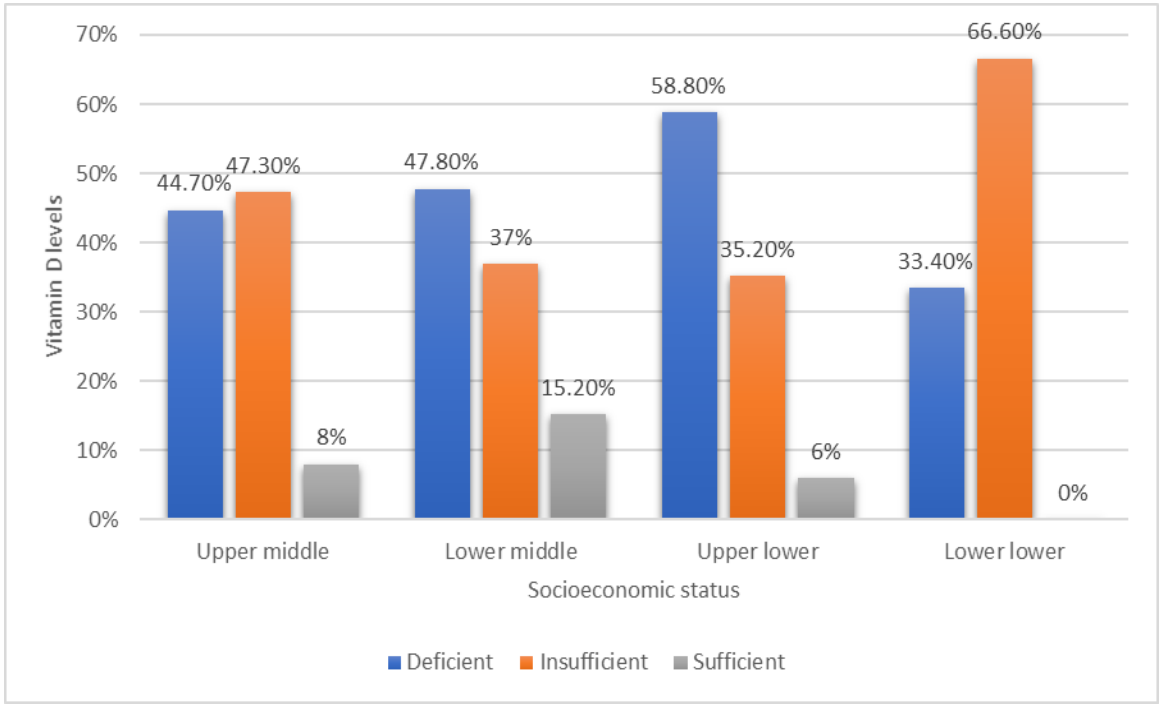


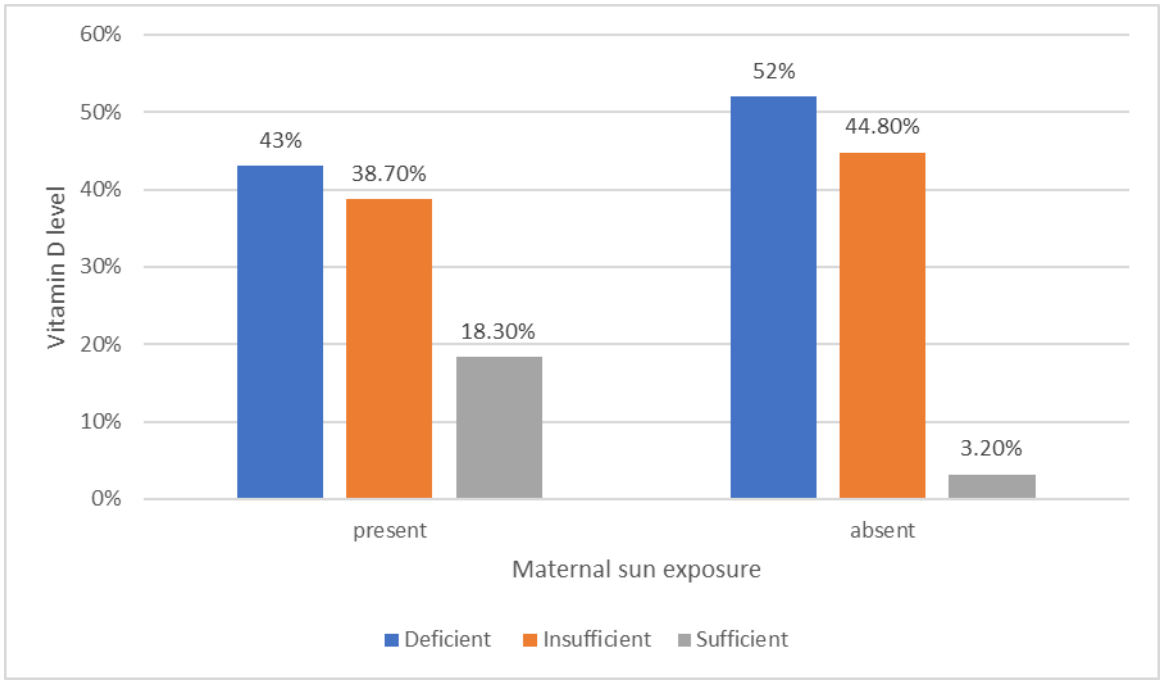
Table 17 & Figure 13 depict the association between cord blood Vitamin D levels and socio-economic status. It was observed that in upper middle class and lower middle class, sufficient

levels of vitamin D were 8% and 15.2% respectively whereas in upper lower class only 6% of neonates had sufficient vitamin D levels and none in lower class. Majority of neonates belonged to deficient and insufficient levels in all the classes of socioeconomic status. No significant association between cord blood Vitamin D levels and socio-economic status was observed.

Table 18: Association between Cord Blood Vitamin D Levels and Maternal Sun Exposure

Maternal Sun Exposure	Vitamin D Levels				Chi-Squared Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
Present	21 (43%)	19 (38.7%)	9 (18.3%)	49 (100%)	6.420	0.040
Absent	30 (52%)	26 (44.8%)	2 (3.2%)	58 (100%)		
Total	51	45	11	107		

Figure 14: Association between Cord Blood Vitamin D Levels and Maternal Sun Exposure



Among 49 neonates with maternal sun exposure, 18.3% had sufficient vitamin D levels while 38.7% and 43% had insufficient and deficient levels respectively. Out of 58 neonates born to mothers who did not have adequate sun exposure, only 3.2% neonates had sufficient vitamin D levels while 44.8% and 52% had insufficient and deficient vitamin D levels respectively. There was a significant statistical association between the cord blood Vitamin D levels and maternal sun exposure with a p value of 0.040 – Table 18 & Figure 14

Table 19 Association between Cord Blood Vitamin D Levels and Maternal Vitamin D supplementation.

Vitamin D Supplementation	Vitamin D Levels				Chi-Squared Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
Taken	23 (50%)	17 (37%)	6 (13%)	46 (100%)	1.191	0.551
Not Taken	28 (46%)	28 (46%)	5 (8%)	61 (100%)		
Total	51	45	11	107		

Figure 15: Association between Cord Blood Vitamin D Levels and Maternal Oral Vitamin D Supplementation

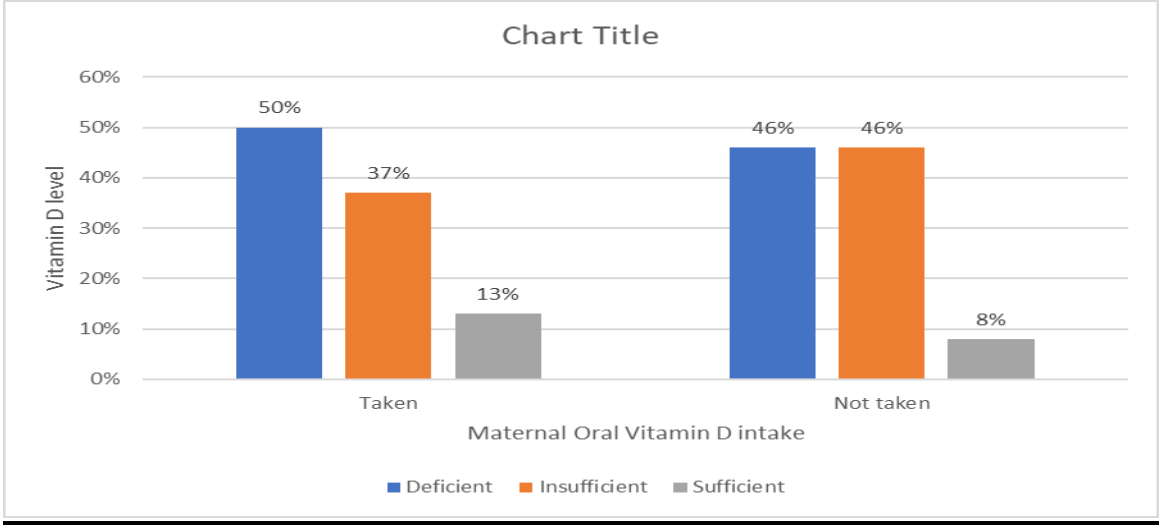
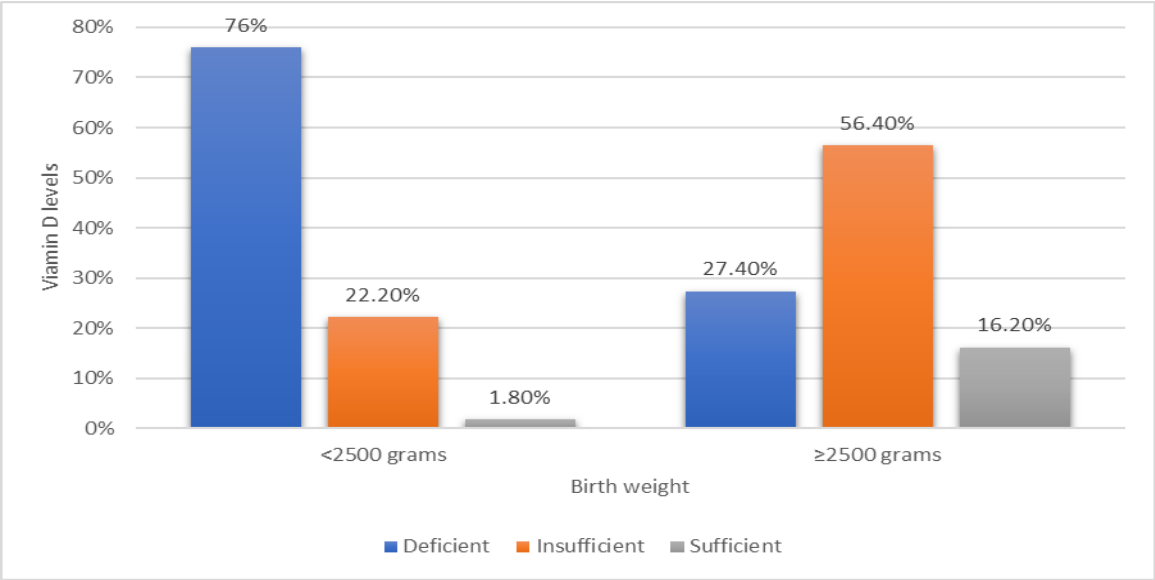


Table 19 & Figure 15 depict the association between cord blood Vitamin D levels and maternal oral Vitamin D supplementation. It was observed that out of 46 neonates with maternal oral Vitamin D supplementation, 50% had vitamin D deficiency, 37% had insufficient levels while only 13% had sufficient levels. Out of 61 neonates without maternal oral Vitamin D supplementation, 46% had deficient and insufficient vitamin D levels each, while 8% neonates had sufficient levels. There was no significant association between cord blood vitamin D levels and maternal oral vitamin D supplementation (p value of 0.551).

Table 20: Association between Cord Blood Vitamin D Levels and Birth Weight

Birth Weight	Vitamin D Levels				Chi-Squared Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
<2500 grams	34 (76%)	10 (22.2%)	1 (1.8%)	45 (100%)	24.845	<0.001
≥2500 grams	17 (27.4%)	35 (56.4%)	10 (16.2%)	62 (100%)		
Total	51	45	11	107		

Figure16: Association between Cord Blood Vitamin D Levels and Birth Weight

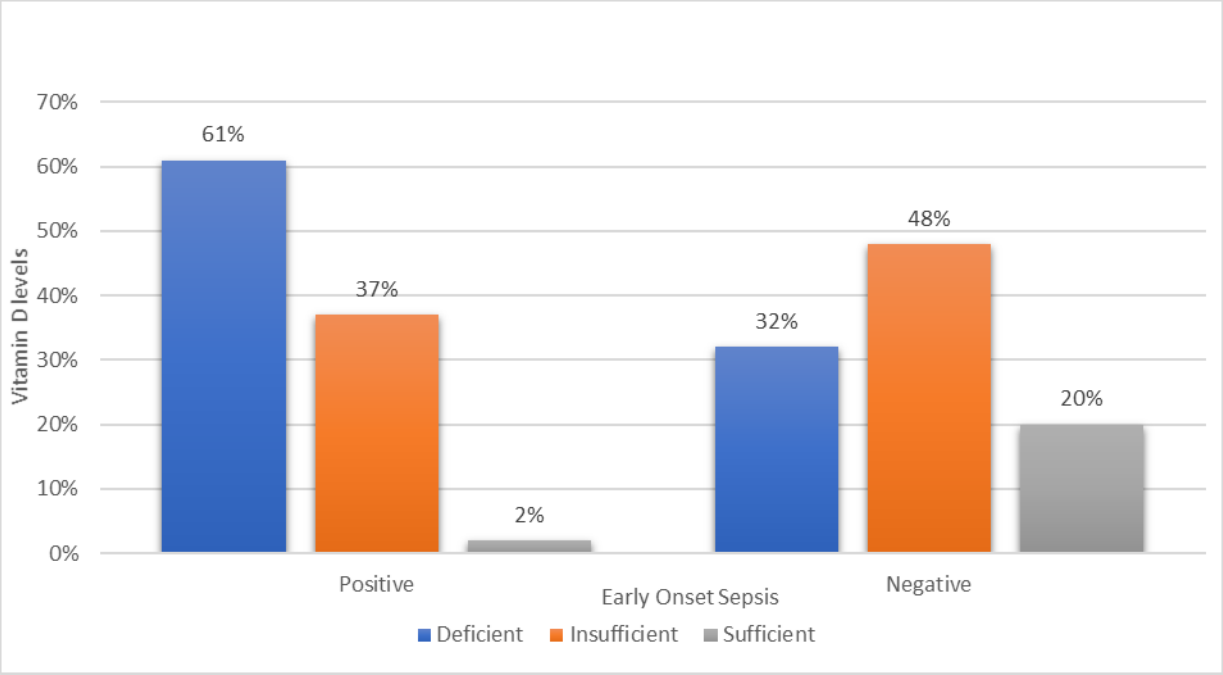


In the present study, it was observed that out of 45 neonates with low birth weight, only 1.8% had sufficient vitamin D levels while 76% and 22.2% had deficient and insufficient levels of Vitamin D. Among the neonates with normal birth weight, 16.2% had sufficient levels, while 27.4% and 56.4% had deficient and insufficient levels respectively. There was a significant association between cord blood vitamin D levels and birthweight with a p value of <0.001. - Table 20 & Figure 16.

Table 21: Association between Cord Blood Vitamin D Levels and EOS

EOS	Vitamin D Levels				Chi-Squared Test	
	≤20ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
Positive	35 (61%)	21 (37%)	1 (2%)	57 (100%)	14.245	<0.001
Negative	16 (32%)	24 (48%)	10 (20%)	50 (46.7%)		
Total	51	45	11	107		

Figure 17: Association between Cord Blood Vitamin D Levels and EOS

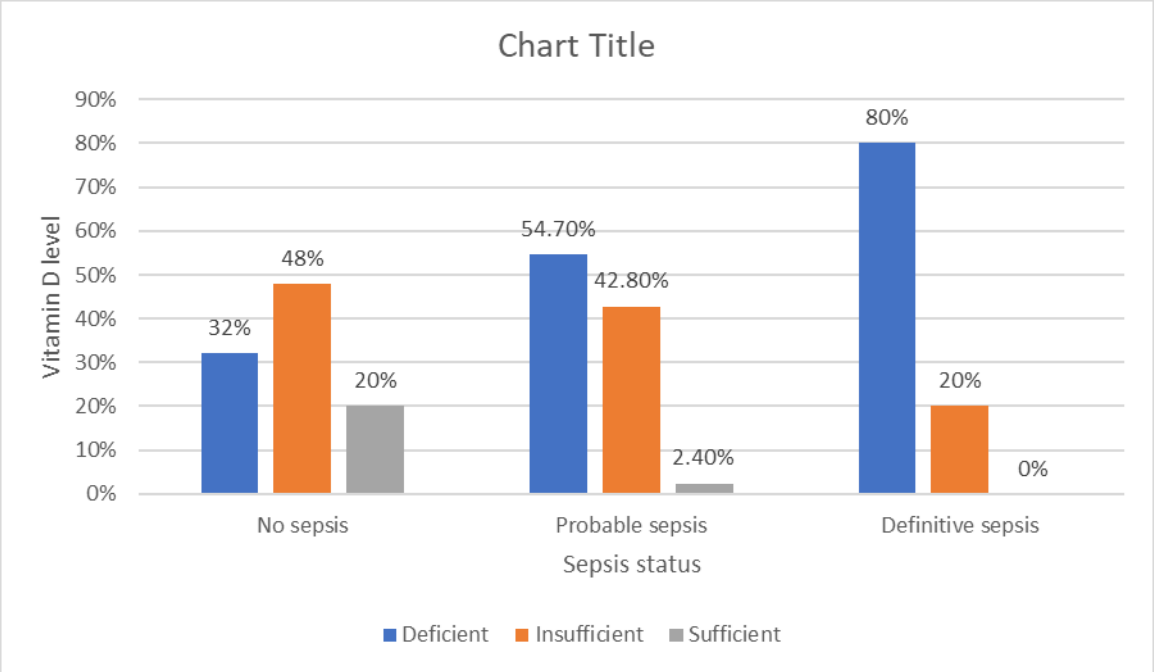


Out of 57 neonates with EOS, it was observed that 61% had deficient levels of Vitamin D while out of 50 neonates without EOS only 32% had deficient vitamin D levels. Among neonates with EOS, 37% had insufficient levels of Vitamin D while among neonates without EOS, 48% had insufficient levels. Sufficient levels of Vitamin D among neonates with EOS was only 2% while among neonates without EOS, it was 20%. There was a statistical significance between cord blood Vitamin D levels and EOS with a p value of <0.001 – Table 21 & Figure 17.

Table 22: Association between Cord Blood Vitamin D levels and No sepsis , Probable Sepsis and Definitive Sepsis

Status of Sepsis	Vitamin D Levels				Fisher's Exact Test	
	≤20 ng/mL (Deficient)	21-29ng/mL (Insufficient)	≥30ng/mL (Sufficient)	Total	$\chi 2$	P Value
No Sepsis	16 (32%)	24 (48%)	10 (20%)	50 (100%)	17.156	0.002
Probable Sepsis	23 (54.7%)	18 (42.8%)	1(2.4%)	42 (100%)		
Definitive Sepsis	12 (80%)	3 (20%)	0 (0.0%)	15 (100%)		
Total	51	45	11	107		

Figure 18: Association between Cord Blood Vitamin D levels and No Sepsis, Probable Sepsis and Definitive Sepsis



Out of 42 neonates with probable sepsis, 54.7% and 42.8% had deficient and insufficient levels of cord blood Vitamin D respectively while it was sufficient in only 2.4%. In the definitive sepsis group, 80% had deficient levels of Vitamin D and 20% had insufficient levels. None of the neonates in the definitive sepsis group had sufficient Vitamin D levels. Among neonates without sepsis, 32%, 48% and 20% had deficient, insufficient, and sufficient levels of Vitamin D respectively. Fisher's exact test was used to explore the association between cord blood Vitamin D levels and Definitive Sepsis, Probable Sepsis and No Sepsis. There was a statistical significance between cord blood Vitamin D levels and the various groups (p value of 0.002) – Table 22 & Figure 18.

DISCUSSION

Vitamin D is a fat-soluble vitamin that has an important role in immune function apart from calcium metabolism. Vitamin D plays a crucial role in promoting innate and adaptive immunity. Low cord blood Vitamin D levels were found to be associated with decreased antimicrobial activity resulting in risk of sepsis[11]. The present study was conducted at a tertiary care centre to find the association between cord blood Vitamin D levels and EOS.

Cord blood Vitamin D levels and EOS: In the present study, it was observed that majority (89.8%) of neonates had low levels of cord blood Vitamin D (deficient levels in 47.7% and insufficient levels in 42.1%) while only 10.3% of neonates had sufficient levels. Out of 107 neonates, 57(53.3%) had EOS and 50 (46.7%) had no sepsis.

Out of 57 neonates with EOS, it was observed that low levels of cord blood Vitamin D were present in 98% of neonates (61% and 37% - deficient and insufficient levels respectively) while only 2% had sufficient levels which was statistically significant. Cetinkaya et al[36] also observed that both maternal and neonatal Vitamin D levels among neonates with EOS were significantly lower compared to those in control group. All the neonates with sepsis had deficient Vitamin D levels as reported by Khaing et al[37]and Kumar et al[3]. Poonam et al[42] also observed that majority (80%) of neonates with sepsis had low levels of neonatal Vitamin D which is in agreement with the findings of our study.

In the present study, mean cord blood Vitamin D levels in EOS positive and negative groups were 19.48± 4.40 ng/ml and 23.60± 6.63 ng/ml respectively implying that mean Vitamin D levels are lower in the sepsis group compared to the group without sepsis. Cetinkaya et al[36] also reported lower maternal (Mean±SD 22.2±6.8 ng/ml) and neonatal (Mean±SD8.6±3.1 ng/ml) Vitamin D levels among neonates with EOS. Similar results were reported by Gamal

et al [4]. The mean values however could not be compared as, cord blood Vitamin D estimation was done in the present study, while maternal and neonatal Vitamin D estimation was done by Cetinkaya et al[36] and Gamal et al [4]

All the above studies showed a positive association between Vitamin D levels and EOS which is similar to our study. This is explained by vitamin D immune modulation effects which can stimulate the inflammatory mediators and boost the innate immunity.

Cord blood Vitamin D levels and Maternal Age:

In the present study, in the maternal age group of 18-25 years, cord blood Vitamin D levels were deficient and insufficient in 52% and 37.5% respectively while it was sufficient in 10.5%. In the maternal age group of 26-30 years, cord blood Vitamin D levels were deficient, insufficient and sufficient in 48%, 44% and 8% respectively. In the maternal age group of 31-35 years, cord blood Vitamin D levels were deficient, insufficient, and sufficient in 22.2%, 55.6% and 22.2% respectively. However, there was no significant statistical association between maternal age and cord blood Vitamin D levels which is in agreement with a study done by Khaing et al [37]. Similarly, there was no significant association between maternal age and neonatal and maternal Vitamin D levels among septic neonates as reported by SabouteM et al[38] and Kumar et al [3].

Cord blood Vitamin D levels and Gender of Neonates:

In our study population, deficient levels of cord blood Vitamin D were present in 54% and 42.1% of male and female neonates respectively. Insufficient levels were present in 34% and 49.2% of male and female neonates respectively. Sufficient levels of cord blood Vitamin D were present in 12% of male neonates and 8.7% of female neonates. There was no statistical

difference between gender and cord blood Vitamin D levels which was similar to studies done by Khaing et al[37], Cetinkaya et al[36], Gamal et al [4].

Cord blood Vitamin D levels and Socio-economic Status:

In the present study, it was observed that in the lower class, 33.4% of neonates had Vitamin D deficiency, 66.6% of neonates had insufficiency and none had sufficient Vitamin D levels whereas in upper lower class only 6% of the neonates had sufficient levels with 58.8% and 35.2% of the neonates had deficient and insufficient Vitamin D levels respectively. Among the neonates from upper middle and lower middle class the sufficient Vitamin D levels was 8% and 15.2% respectively, however there was no significant association between cord blood Vitamin D levels and socio-economic status. Cetinkaya et al[36] observed that educational status in the sepsis group was lower compared to that of the healthy controls.

One of the strongest predictors of vitamin D deficiency is socioeconomic status. This status is represented by low family income, increased family size and parents' educational levels. Household income level plays an important role in vitamin D deficiency. Low-income families unable to access fortified foods and dietary supplements that contain vitamin D are more likely to have vitamin D deficiency than families with good income.

Cord blood Vitamin D levels and Maternal Sun Exposure:

Almost half (45.8%) of the mothers had adequate exposure to sun while the remaining did not have enough exposure. This can be explained by the cultural practices in some communities who cover most of their skin when outdoors. In our study, among neonates with maternal sun exposure, 43% had deficient Vitamin D levels, 38.7% had insufficient and 18.3% had sufficient levels whereas, among neonates without adequate maternal sun exposure, 52% had Vitamin D deficiency, 44.8% had insufficiency and only 3.2% had sufficiency. There was a

significant statistical association between the cord blood Vitamin D levels and the maternal sun exposure with a p value of 0.040. A similar positive association between maternal sun exposure and cord blood Vitamin D levels was reported by Cetinkaya et al[36].

Covering the skin is a risk factor for vitamin D deficiency. Populations typically at risk for low sun exposure are institutionalized individuals, deeply pigmented people living in low ultraviolet settings such as high latitudes, and those who, for religious or cultural reasons, cover their entire body surface when they are outdoors.

Cord blood Vitamin D levels and Maternal Oral Vitamin D supplementation:

In the present study, only 43% of mothers had taken oral Vitamin D supplementation during pregnancy. In the mothers with Vitamin D supplementation in pregnancy 50% of neonates had deficient Vitamin D levels, 37% had insufficient and 13% had sufficient Vitamin D levels whereas in the neonates without maternal oral Vitamin D supplementation only 8% had sufficient Vitamin D levels. However, there was no statistical significance between cord blood Vitamin D levels and maternal oral Vitamin D supplementation during pregnancy. In contrast to our study, Cetinkaya et al[36] reported a significant correlation between cord blood Vitamin D levels and maternal Vitamin D intake which implies that optimal amount of Vitamin D intake is necessary to have adequate levels of Vitamin D levels and prevent its deficiency.

Vitamin D supplementation in a single or continued dose during pregnancy increases serum vitamin D concentrations as measured by 25-hydroxyvitamin D at term. Vitamin D supplementation during pregnancy has been suggested to safely improve pregnancy and infant outcomes. However, the clinical significance is yet to be determined in preventing neonatal infection.

Cord blood Vitamin D levels and Birth Weight:

Majority (57.9%) of neonates weighed ≥2500 grams while 42.1% of the neonates had low birth weight in our study. In the low birth weight neonates 76% had Vitamin D deficiency, 22.2% had insufficiency and only 1.8% had sufficient Vitamin D levels while in the neonates with normal birth weight only 27.4% had deficient Vitamin D levels with 56.4% having insufficiency and 16.2% had sufficient Vitamin D levels. There was a statistical significance between cord blood Vitamin D levels and birth weight. However, on the contrary, Khaing et al[37], Kumar et al[3] and Cetinkaya et al[36] did not observe any statistical significance between birthweight and cord blood Vitamin D levels.

The positive correlation between low birth weight and low levels of cord blood Vitamin D in our study can be explained by the fact that, Vitamin D has a key role in fetal growth by its interaction with parathyroid hormone and Ca2+ homeostasis. Maternal hypovitaminosis D may impair fetal growth and cause adverse pregnancy outcomes including intrauterine growth restriction and neonatal low birth weight. Insufficient prenatal levels of Vitamin D have great effects on poor bone mineralization which have significant association with small for gestational age births. However, further research is required to find the relationship between the Vitamin D levels, low birth weight and intrauterine growth restriction.

CONCLUSION

- Vitamin D has multiple effects on neonatal health including prevention of neonatal sepsis. In our study, the mean cord bold Vitamin D levels in neonates with EOS was 19.48(± 4.40) ng/ml whereas it was 23.6(± 6.63) ng/ml in neonates without sepsis. There was a statistical significance between low cord blood Vitamin D levels and EOS. Supplementation of Vitamin D during pregnancy can increase the Vitamin D levels of mothers and the off springs. This could boost the immune system of neonates and decrease neonatal mortality that might be associated with neonatal sepsis.

- In our study, there was significant association between maternal sun exposure and cord blood Vitamin D levels. Education regarding adequate sun exposure and Vitamin D supplementation should be reinforced in antenatal clinics to pregnant mothers.

- There was a significant association between low cord blood Vitamin D levels and low birth weight. Modifying maternal nutrition behavior and their Vitamin D levels could be beneficial on pregnancy outcomes in terms of birth weight.

LIMITATIONS

- Vitamin D levels in the mothers could not be measured to correlate with cord blood Vitamin D levels.
- Small sample size.

SUMMARY

- A prospective observational study was done at RLJH &RC over a period of 1 year 2 months from February 2020 to April 2021 on "Association between cord blood Vit D levels and EOS in term neonates".
- A total of 107 neonates who fulfilled the inclusion criteria were included in the study.
- Majority (91.6%) of neonates belonged to maternal age group of 18-30 years.
- There was a female preponderance (53%) with a female to male ratio of 1.14:1.
- Majority (43%) of neonates belonged to lower middle class (socio-economic status) while (21.5%) belonged to upper lower and lower class.
- Adequate maternal sun exposure was present in 45.8% of neonates.
- Maternal oral Vit D supplementation during pregnancy was present in 43%.
- Majority (57.9%) of neonates weighed ≥2500 grams while the remaining (42.1%) had low birth weight (<2500 grams).
- Low level of cord blood Vit D was present in 89.8% (deficient 47.7 %+ insufficient 42.1%) of neonates.
- Vitamin D cord blood levels were significantly low in mothers without adequate sun exposure and low birth weight infants.

- There was no statistical significance between cord blood Vitamin D levels and maternal age, gender of neonates, socioeconomic status, and maternal Oral Vitamin D supplementation.
- Out of 107 neonates, 57 (53.3 %) had evidence of sepsis, while 50 (46.7%) did not have sepsis. Out of 57 neonates with EOS, 42 had probable sepsis and 15 had definitive sepsis.
- The mean Vitamin D cord blood level in the EOS positive group was 19.48 (± 4.40) ng/ml whereas it was 23.60 (± 6.63) ng/ml in EOS negative group.
- Among 57 neonates with EOS, it was observed that 98% had low levels (deficient in 61% and insufficient in 37%) of cord blood Vitamin D and sufficient levels were present in only 2% which was a statistically significant with a p value of <0.001.
- Out of 42 neonates with probable sepsis 97.5% had low levels of vitamin D and all the neonates with definitive sepsis had Vitamin D deficiency with a statistical significance of p value of <0.002. We, therefore, conclude that low levels of vitamin D are associated with EOS.

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PROFORMA

PROSPECTIVE STUDY ON THE ASSOCIATION BETWEEN CORD BLOOD VITAMIN D LEVELS AND EARLY ONSET NEONATAL SEPSIS.

SI NO:

NAME OF MOTHER:

AGE:

OCCUPATIONAL HISTORY:

UHID NO:

ADDRESS:

EXPOSURE TO SUNLIGHT:

TIME OF BIRTH:

MODE OF DELIVERY:

INDICATION OF LSCS:

LIQUOR STATUS:

MATERNAL RISK FACTORS:

H/O PROM

FEVER

UTI

CRP

NO OF VAGINAL EXAMINATIONS

PROLONGED LABOUR

VAGINAL SWAB CULTURE:

FOUL SMELLING LIQUOR:

MATERNAL SUN EXPOSURE:

MATERNAL VITAMIN D INTAKE:

GESTATIONAL AGE:

DYSMORPHIC FEATURES:

DATE OF ADMISSION:

PARAMETERS OBTAINED AT BIRTH:

HEART RATE:
RESPIRATORY RATE:
TEMPERATURE:
SATURATION :
CAPILLARY FILLING TIME:
NEONATAL REFLEXES:

CRY: SUCK: TONE:

ACTIVITY: APGAR SCORE AT 1 MINUTE AND 5MINUTES

PARAMETERS IN NEONATES:

PARAMETER	**VALUES**
CRP	
TOTAL LEUCOCYTE COUNT	
ABSOLUTE NEUTROPHIL COUNT	
I/T RATIO	
MICRO ESR	
PLATELET COUNT	

BLOOD CULTURE:

VITAMIN D LEVEL:

INFORMED CONSENT FORM

Date:

I, Mr/Mrs _____ have been explained in my own vernacular language that my child _____ will be included in the study**, PROSPECTIVE STUDY ON THE ASSOCIATION BETWEEN CORD BLOOD VITAMIN D LEVELS AND EARLY ONSET NEONATAL SEPSIS**

Ihereby give my valid written informed consent without any force or prejudice for recording the observations of clinical and haematological parameters . The nature and risks involved have been explained to me, to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I provide consent voluntarily to allow my child as a participant in this research. I hereby **give consent to provide history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc**. For academic and scientific purpose the operation / procedure, etc may be video graphed or photographed. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc responsible for any untoward consequences during the procedure / study. A copy of this informed consent form and patient information sheet has been provided to the participant.

_____

(Signature & Name of Pt. Attendant)

_____

(Signature/Thumb impression & Name of Patient/Guardian)

(Relation with patient)

Witness :

_____

(Signature & Name of Research person/doctor)

PROSPECTIVE STUDY ON THE ASSOCIATION BETWEEN CORD BLOOD VITAMIN D LEVELS AND EARLY ONSET NEONATAL SEPSIS

PATIENT INFORMATION SHEET

Principal investigators :Dr. RAJITHA . B /Dr. SUDHA REDDY .V.R

I, Dr. RAJITHA .B , Post graduate student in Department of Paediatrics at Sri Devaraj Urs Medical College, will be conducting a study titled **PROSPECTIVE STUDY ON THE ASSOCIATION BETWEEN CORD BLOOD VITAMIN D LEVELS AND EARLY ONSET NEONATAL SEPSIS** for my dissertation under the guidance of Dr. SUDHA REDDY .V.R , Professor and HOD of Department of Paediatrics. The participants of this study i.e. include term neonates.

You will not be paid any financial compensation for the participating in this research project.

All the data will be kept confidential and will be used only for research purpose by this institution. You are free to provide consent for the participation of your child in the study. You can also withdraw your child from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.

Name and Signature of the Principal Investigator

Date:

Place : Kolar.

ಮಾಹಿತಿನೀಡಿದಒಪ್ಪಿಗೆನಮೂನೆ

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ _____

ನನ್ನಮಗುವನ್ನುಅಧ್ಯಯನದಲ್ಲಿಸೇರಿಸಲಾಗುವುದುಎಂದುವಿವರಿಸಲಾಗಿದೆ,

ಕಾಡ್ಜ್ಡ್ವಿಟಮಿನ್ದಿಮಟ್ಟಗಳುಮತ್ತುನವಜಾತಶಿಶುವಿನಆರಂಭಿಕಹಂತಗಳನಡುವಿನಸಂಬಂಧದಬಗ್ಗೆಪ್ರಾಸ್ಪೆಕ್ಟಿವ್ಸ್ ಡಿ
ಕ್ಲಿನಿಕಲ್ಮತ್ತುಹೆಮಟೊಲಾಜಿಕಲ್ನಿಯತಾಂಕಗಳಅವಲೋಕನಗಳನ್ನುದಾಖಲಿಸಲುನಾನುಯಾವುದೇಬಲಅಥವಾಪೂರ್ವಾಗ್ರಹವಿ
ಲ್ಲದೆನನ್ನಮಾನ್ಯವಾದಲಿಖಿತತಿಳುವಳಿಕೆಯನ್ನುನೀಡುತ್ತೇನೆ.

ಒಳಗೊಂಡಿರುವಸ್ವಭಾವಮತ್ತುಅಪಾಯಗಳನ್ನುನನಗೆವಿವರಿಸಲಾಗಿದೆ, ನನ್ನತೃಪ್ತಿ.

ನಡೆಸುತ್ತಿರುವಅಧ್ಯಯನದಬಗ್ಗೆನನಗೆವಿವರವಾಗಿವಿವರಿಸಲಾಗಿದೆ.

ನಾನುರೋಗಿಯಮಾಹಿತಿಹಾಳೆಯನ್ನುಓದಿದ್ದೇನೆಮತ್ತುಯಾವುದೇಪ್ರಶ್ನೆಯನ್ನುಕೇಳಲುನನಗೆಅವಕಾಶವಿದೆ.

ನಾನುಕೇಳಿದಯಾವುದೇಪ್ರಶ್ನೆಗೆನನ್ನತೃಪ್ತಿಗೆಉತ್ತರಿಸಲಾಗಿದೆ.

ನನ್ನಮಗುವನ್ನುಈಸಂಶೋಧನೆಯಲ್ಲಿಪಾಲ್ಗೊಳ್ಳುವಂತೆಅನುಮತಿಸಲುನಾನುಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದಒಪ್ಪಿಗೆಯನ್ನುನೀಡುತ್ತೇನೆ
. ಇತಿಹಾಸವನ್ನುಒದಗಿಸಲು, ದೈಹಿಕಪರೀಕ್ಷೆಗೆಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆಒಳಗಾಗಲು,

ತನಿಖೆಗೆಒಳಗಾಗಲುಮತ್ತುಅದರಫಲಿತಾಂಶಗಳುಮತ್ತುದಾಖಲೆಗಳನ್ನುವೈದ್ಯರು /

ಸಂಸ್ಥೆಇತ್ಯಾದಿಗಳಿಗೆಒದಗಿಸಲುನಾನುಈಮೂಲಕಒಪ್ಪಿಗೆನೀಡುತ್ತೇನೆ.

ಶೈಕ್ಷಣಿಕಮತ್ತುವೈಜ್ಞಾನಿಕಉದ್ದೇಶಕ್ಕಾಗಿಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ,

ಇತ್ಯಾದಿಗಳನ್ನುವೀಡಿಯೊಗ್ರಾಫ್ಅಥವಾಛಾಯಾಚಿತ್ರಮಾಡಬಹುದು.

ಎಲ್ಲಾಡೇಟಾವನ್ನುಪ್ರಕಟಿಸಬಹುದುಅಥವಾಯಾವುದೇಶೈಕ್ಷಣಿಕಉದ್ದೇಶಕ್ಕಾಗಿಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ /

ಅಧ್ಯಯನದಸಮಯದಲ್ಲಿಯಾವುದೇಅಹಿತಕರಪರಿಣಾಮಗಳಿಗೆನಾನುವೈದ್ಯರು /

ಸಂಸ್ಥೆಇತ್ಯಾದಿಗಳನ್ನುಜವಾಬ್ದಾರರನ್ನಾಗಿಮಾಡುವುದಿಲ್ಲ.

ಈತಿಳುವಳಿಕೆಯುಳ್ಳಒಪ್ಪಿಗೆನಮೂನೆಯಪ್ರತಿಯನ್ನುಮತ್ತುರೋಗಿಯಮಾಹಿತಿಹಾಳೆಯನ್ನುಭಾಗವಹಿಸುವವರಿಗೆಒದಗಿಸಲಾಗಿ
ದೆ.

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(ಪಂ. ಅಟೆಂಡೆಂಟ್ನಸಹಿಮತ್ತುಹೆಸರು)

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(ಸಹಿ/ಹೆಬ್ಬೆರಳಿನಗುರುತುಮತ್ತುರೋಗಿಯ/ರಕ್ಷಕರಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನಸಂಬಂಧ)

ಸಾಕ್ಷಿ:

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(ಸಂಶೋಧನಾವ್ಯಕ್ತಿ/ವೈದ್ಯರಸಹಿಮತ್ತುಹೆಸರು)

ಕಾಡ್ಬ್ೆಡ್ಡಿಟಮಿನ್ದಿಮಟ್ಟಗಳುಮತ್ತುಆರಂಭಿಕನಿಯೋನೇಟಲ್ಸೆಪ್ಸಿಸ್ನಡುವಿನಸಂಬಂಧದಕುರಿತುಪ್ರಾಸ್ಪೆಕ್ಟಿವ್ಸ್ಟಡಿ

ರೋಗಿಯಮಾಹಿತಿಹಾಳೆ

ಪ್ರಧಾನತನಿಖಾಧಿಕಾರಿಗಳು: ಡಾ. ರಜಿತಾ. ಬಿ/ಡಾ. ಸುಧಾರೆಡ್ಡಿ .ವಿ.ಆರ್

ನಾನು, ಡಾ. ರಜಿತಾ .ಬಿ , ಶ್ರೀದೇವರಾಜ್ಅರ್ಸ್ಮೆಡಿಕಲ್ಕಾಲೇಜಿನಲ್ಲಿಪೀಡಿಯಾಟ್ರಿಕ್ಸ್ವಿಭಾಗದಸ್ನಾತಕೋತ್ತರವಿದ್ಯಾರ್ಥಿನಿ, ನನ್ನಅಧ್ಯಯನದಅಡಿಯಲ್ಲಿನನ್ನಅಧ್ಯಯನದಅಡಿಯಲ್ಲಿಕಾಡ್ಬ್ೆಡ್ಡಿಟಮಿನ್ದಿಲೆವೆಲ್ಸ್ಮತ್ತುಆರಂಭಿಕಪ್ರವೇಶದನಡುವಿನಸಂಬಂಧದ ಕುರಿತುಪ್ರಾಸ್ಪೆಕ್ಟಿವ್ಸ್ಟಡಿಎಂಬಅಧ್ಯಯನವನ್ನುನಡೆಸುತ್ತಿದ್ದೇನೆ. ಡಾ. ಸುಧಾರೆಡ್ಡಿ .ವಿಆರ್, ಪ್ರಾಧ್ಯಾಪಕರುಮತ್ತುಪೀಡಿಯಾಟ್ರಿಕ್ಸ್ವಿಭಾಗದ HOD.
ಈಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸುವವರುಅಂದರೆನವಜಾತಶಿಶುಗಳುಸೇರಿದ್ದಾರೆ.

ಈಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿಭಾಗವಹಿಸಿದ್ದಕ್ಕಾಗಿನಿಮಗೆಯಾವುದೇಹಣಕಾಸಿನಪರಿಹಾರವನ್ನುಪಾವತಿಸಲಾಗುವುದಿಲ್ಲ.

ಎಲ್ಲಾಡೇಟಾವನ್ನುಗೌಪ್ಯವಾಗಿಇರಿಸಲಾಗುತ್ತದೆಮತ್ತುಈಸಂಸ್ಥೆಯಿಂದಸಂಶೋಧನಾಉದ್ದೇಶಕ್ಕಾಗಿಮಾತ್ರಬಳಸಲಾಗುತ್ತದೆ. ಅಧ್ಯಯನದಲ್ಲಿನಿಮ್ಮಮಗುವಿನಭಾಗವಹಿಸುವಿಕೆಗೆಒಪ್ಪಿಗೆನೀಡಲುನೀವುಸ್ವತಂತ್ರರಾಗಿದ್ದೀರಿ.
ಯಾವುದೇಕಾರಣಗಳನ್ನುನೀಡದೆನೀವುಯಾವುದೇಸಮಯದಲ್ಲಿನಿಮ್ಮಮಗುವನ್ನುಅಧ್ಯಯನದಿಂದಹಿಂಪಡೆಯಬಹುದು.
ಭಾಗವಹಿಸಲುನಿಮ್ಮನಿರಾಕರಣೆಯುಈಸಂಸ್ಥೆಯಲ್ಲಿಯಾವುದೇಪ್ರಸ್ತುತಅಥವಾಭವಿಷ್ಯದಕಾಳಜಿಗೆನಿಮ್ಮನ್ನುಪೂರ್ವಾಗ್ರಹಮಾಡುವುದಿಲ್ಲ.

ಪ್ರಧಾನತನಿಖಾಧಿಕಾರಿಯಹೆಸರುಮತ್ತುಸಹಿ

ದಿನಾಂಕ:

ಸ್ಥಳ: ಕೋಲಾರ.

KEY TO MASTER CHART

ABBREVATIONS

S.No: Serial Number

UHID: Unique Hospital Identification Number

PROM : Premature Rupture Of Membranes

UTI: Urinary Tract Infection

LSCS: Lower Segment Cesarean Section

CRP: C Reactive Protein

A - S.No

B – UHID

C – Maternal age (Years)

D – Baby gender

E – Maternal risk factors

F – Socio-Economic status

G – Sun exposure

H – Vitamin D intake

I – Parity

J – Birth weight (Kg)

K – Heart rate (BPM)

L – Mode of delivery

M – Respiratory rate(CPM)

N – APGAR (1 Minute)

O – APGAR (5 Minutes)

P – Neonatal Reflexes

Q – Gestational Age (weeks)

R – Total leucocyte count(/cu.mm)

S – CRP

T – Platelet count (/ cu.mm)

U - Absolute Neutrophil Count (/cu.mm)

V – Blood Culture

W – Vitamin D Levels (ng/mL)

X – Early Onset Sepsis

S.No	UHID	Maternal Age (Years)	Baby Gender	Maternal Risk Factors	Socio-Economic Status	Sun Exposure	Vitamin D Intake	Parity	Birth Weight (Kg)	Heart Rate (BPM)	Mode Of Delivery	Respiratory Rate (CPM)	APGAR (1 Minute)	APGAR (5 Minutes)	Neonatal Reflexes	Gestational Age (Weeks)	Total Leucocyte Count (/cu.mm)	CRP	Platelet Count (/cu.mm)	Absolute Neutrophil Count (/cu.mm)	Blood Culture	Vitamin D Levels (ng/mL)	Early Onset Sepsis
1	840381	23	Female	PROM	Lower	Present	Not Taken	Primipara	2450	148	Vaginal	46	7	9	Present	38	9600	Positive	152000	1400	Negative	21.4	Positive
2	842622	28	Female	PROM	Lower Middle	Absent	Taken	Multipara	3458	148	LSCS	48	7	9	Present	39	24000	Positive	262000	14600	Negative	17	Positive
3	843410	19	Male	PROM	Lower Middle	Absent	Taken	Primipara	3250	159	Vaginal	46	8	9	Present	38	26520	Negative	128000	15200	Negative	26.2	Negative
4	833799	21	Male	Foul Smelling Liquor	Upper Lower	Absent	Not Taken	Multipara	3245	156	LSCS	47	8	9	Present	37	22000	Positive	134000	16000	Negative	17.8	Positive
5	834114	23	Male	PROM	Lower Middle	Present	Taken	Multipara	2650	128	LSCS	52	8	8	Present	39	20000	Negative	128000	12400	Negative	30	Negative
6	834210	26	Male	UTI	Lower Middle	Present	Not Taken	Primipara	3800	133	Vaginal	44	8	9	Present	40	21000	Negative	168000	13200	Negative	34	Negative
7	834268	20	Male	Foul Smelling Liquor	Upper Middle	Present	Not Taken	Multipara	2980	165	Vaginal	58	8	8	Present	42	23000	Negative	234000	14200	Negative	32	Negative
8	834966	24	Female	PROM	Upper Middle	Absent	Not Taken	Multipara	3200	148	LSCS	52	7	9	Present	41	21000	Negative	162000	1450	Negative	22	Negative
9	835000	28	Female	PROM	Lower Middle	Present	Not Taken	Multipara	2650	152	LSCS	46	8	9	Present	38	26000	Negative	167000	13200	Negative	24.8	Negative
10	837893	32	Female	UTI	Upper Lower	Present	Taken	Multipara	2450	148	Vaginal	43	7	9	Present	39	18000	Negative	234800	14800	Positive	36	Negative
11	835056	20	Female	PROM	Upper Middle	Absent	Taken	Primipara	2320	162	Vaccum	46	8	9	Present	42	22000	Negative	134000	14200	Negative	14	Negative
12	835064	32	Male	Fever	Upper Lower	Present	Not Taken	Primipara	2420	148	LSCS	54	8	8	Present	38	16000	Negative	345000	7800	Negative	16	Negative
13	835372	27	Male	PROM	Lower Middle	Absent	Taken	Multipara	2350	122	LSCS	62	8	9	Present	39	19000	Negative	67000	11200	Negative	22	Negative
14	843862	29	Male	PROM	Upper Middle	Present	Not Taken	Multipara	3250	128	Vaginal	66	8	9	Present	38	22000	Negative	236800	10480	Negative	18	Negative
15	843862	22	Male	PROM	Upper Middle	Present	Taken	Primipara	2200	152	Vaginal	66	8	9	Present	39	24000	Negative	326000	16420	Negative	18	Negative
16	868982	24	Female	PROM	Lower Middle	Absent	Not Taken	Primipara	2150	148	LSCS	48	8	9	Present	38	32000	Positive	128000	18000	Positive	16	Positive
17	872371	28	Female	Foul Smelling Liquor	Upper Middle	Present	Taken	Multipara	3250	146	LSCS	55	7	9	Present	42	22000	Positive	326000	16200	Negative	16	Positive
18	872161	24	Female	UTI	Lower Middle	Absent	Taken	Primipara	2030	148	Vaginal	54	8	9	Present	37	26000	Positive	124000	8920	Negative	17	Positive
19	872488	26	Male	Foul Smelling Liquor	Upper Middle	Present	Taken	Multipara	3420	152	Vaginal	48	8	9	Present	39	28000	Positive	282000	16240	Negative	19	Positive
20	871979	32	Female	PROM	Lower	Absent	Not Taken	Multipara	3100	148	Vaccum	60	8	9	Present	38	23000	Positive	428300	14230	Negative	20	Positive
21	866053	28	Female	PROM	Upper Lower	Present	Taken	Multipara	2100	152	Vaginal	54	8	9	Present	40	38000	Positive	382000	30200	Positive	18	Positive
22	849495	24	Female	Perinatal Asphyxia	Upper Lower	Present	Taken	Primipara	2890	148	Vaccum	58	7	9	Poor	38	18000	Positive	443200	12430	Positive	24	Positive
23	871349	28	Female	PROM	Upper Lower	Absent	Taken	Multipara	2340	148	Vaginal	46	8	9	Present	38	24000	Positive	38000	18240	Negative	19	Positive
24	869437	19	Female	PROM	Lower Middle	Present	Not Taken	Primipara	3420	148	LSCS	52	8	9	Present	39	22000	Positive	432600	12860	Negative	34	Positive
25	843855	22	Female	Fever	Upper Middle	Absent	Taken	Primipara	1900	136	Vaginal	46	8	9	Present	38	28000	Positive	342000	12400	Positive	18	Positive
26	795545	23	Male	PROM	Lower Middle	Absent	Not Taken	Multipara	2340	142	LSCS	54	8	9	Present	40	26000	Positive	134000	1300	Positive	14	Positive
27	849250	28	Male	PROM	Lower Middle	Absent	Taken	Multipara	3460	138	LSCS	58	8	9	Present	39	32000	Positive	342000	18200	Negative	22	Positive
28	843520	30	Female	Foul Smelling Liquor	Upper Middle	Present	Not Taken	Multipara	3460	142	LSCS	64	8	9	Present	42	26000	Positive	52000	16000	Negative	28	Positive
29	843991	32	Female	PROM	Upper Lower	Present	Taken	Multipara	2100	138	Vaginal	48	8	9	Present	39	34000	Positive	426000	12860	Negative	26	Positive
30	846571	27	Female	PROM	Upper Lower	Absent	Not Taken	Multipara	3200	128	Vaginal	56	8	9	Present	38	22000	Positive	358000	15680	Negative	24	Positive
31	847858	28	Male	PROM	Lower Middle	Absent	Not Taken	Multipara	2320	145	LSCS	58	8	9	Present	40	22000	Positive	274000	8600	Positive	16	Positive
32	840309	31	Male	PROM	Upper Middle	Absent	Taken	Primipara	2100	146	Vaginal	48	8	9	Present	39	17892	Positive	64000	11260	Negative	18	Positive
33	840781	21	Female	PROM	Lower Middle	Absent	Not Taken	Primipara	2540	132	LSCS	45	8	9	Present	41	3850	Positive	298000	12320	Negative	22	Positive
34	844569	28	Male	PROM	Upper Lower	Absent	Taken	Multipara	3400	142	LSCS	48	8	9	Present	39	23842	Positive	198000	14300	Negative	21	Positive
35	834210	24	Female	Fever	Lower Middle	Present	Not Taken	Multipara	1800	146	LSCS	44	8	9	Present	38	42421	Negative	248000	30100	Negative	16	Negative
36	813807	21	Female	PROM	Lower Middle	Present	Taken	Primipara	2100	142	LSCS	54	8	9	Present	41	38000	Negative	172000	18000	Negative	14	Negative
37	827612	26	Male	PROM	Upper Lower	Absent	Not Taken	Multipara	3450	146	LSCS	54	8	9	Present	38	23482	Negative	48000	14200	Negative	26	Negative
38	900295	20	Female	Foul Smelling Liquor	Upper Lower	Present	Taken	Primipara	2140	144	Vaginal	42	8	9	Present	42	12890	Positive	248000	4300	Positive	18	Positive
39	901328	27	Male	PROM	Upper Middle	Absent	Not Taken	Multipara	2100	148	LSCS	46	8	9	Present	38	6382	Negative	568000	2010	Negative	24	Negative
40	900651	25	Female	Fever	Lower Middle	Absent	Taken	Multipara	2340	152	LSCS	50	7	9	Present	38	4289	Positive	342800	1860	Negative	16	Positive
41	899347	28	Male	Perinatal Asphyxia	Lower Middle	Absent	Not Taken	Primipara	3400	148	LSCS	38	8	9	Present	42	11942	Negative	284000	62320	Negative	18	Negative
42	899010	23	Male	Fever	Lower	Present	Taken	Primipara	2800	152	LSCS	38	8	9	Present	38	28000	Positive	326000	16800	Positive	18	Positive
43	900584	29	Female	UTI	Upper Middle	Present	Not Taken	Multipara	2670	138	Vaginal	42	8	9	Present	39	32000	Positive	178000	18200	Negative	28	Positive
44	898974	30	Female	Fever	Lower Middle	Absent	Not Taken	Multipara	2600	142	Vaginal	48	8	9	Present	38	32542	Positive	238000	22340	Negative	16	Positive
45	898811	22	Male	Foul Smelling Liquor	Upper Middle	Absent	Not Taken	Primipara	3200	132	LSCS	42	8	9	Present	39	3248	Positive	168000	1250	Negative	24	Positive

S.No	UHID	Maternal Age (Years)	Baby Gender	Maternal Risk Factors	Socio-Economic Status	Sun Exposure	Vitamin D Intake	Parity	Birth Weight (Kg)	Heart Rate (BPM)	Mode Of Delivery	Respiratory Rate (CPM)	APGAR (1 Minute)	APGAR (5 Minutes)	Neonatal Reflexes	Gestational Age (Weeks)	Total Leucocyte Count (/cu.mm)	CRP	Platelet Count (/cu.mm)	Absolute Neutrophil Count (/cu.mm)	Blood Culture	Vitamin D Levels (ng/mL)	Early Onset Sepsis
46	898137	21	Female	Obstructed Labour	Upper Middle	Present	Not Taken	Primipara	3270	152	Vaccum	46	8	9	Present	39	42980	Positive	128000	32000	Negative	26	Positive
47	899014	29	Male	Fever	Upper Lower	Absent	Not Taken	Multipara	2100	148	LSCS	48	8	9	Present	42	23000	Positive	84000	16840	Positive	14	Positive
48	897829	29	Female	Foul Smelling Liquor	Upper Middle	Absent	Taken	Primipara	2130	132	LSCS	42	8	9	Present	40	4800	Negative	128000	4560	Negative	16	Negative
49	899021	24	Female	PROM	Upper Middle	Present	Not Taken	Multipara	2100	138	LSCS	48	8	9	Present	39	12890	Negative	268000	8672	Negative	18	Negative
50	895279	19	Female	Fever	Lower Middle	Present	Not Taken	Primipara	3420	142	LSCS	46	8	9	Present	40	26934	Positive	168000	12460	Negative	26	Positive
51	896865	26	Male	PROM	Lower	Present	Not Taken	Multipara	3800	148	Vaginal	44	8	9	Present	41	22382	Positive	48000	16820	Negative	24	Positive
52	897440	20	Female	Obstructed Labour	Upper Middle	Present	Taken	Primipara	2300	146	Vaccum	42	8	9	Present	38	18912	Negative	348000	8620	Negative	18	Negative
53	894367	23	Male	Perinatal Asphyxia	Lower Middle	Absent	Not Taken	Multipara	1890	138	LSCS	48	8	9	Present	39	23264	Negative	234000	15620	Negative	18	Negative
54	898296	27	Female	Fever	Upper Lower	Present	Not Taken	Multipara	1900	142	LSCS	46	8	9	Present	39	24231	Positive	472000	18200	Positive	18	Positive
55	891972	28	Female	Fever	Lower Middle	Present	Taken	Primipara	3500	160	LSCS	38	8	9	Present	38	17621	Negative	32000	8292	Negative	42	Negative
56	892404	27	Female	Obstructed Labour	Upper Lower	Present	Taken	Primipara	2180	132	Vaginal	34	8	9	Present	38	12432	Negative	426800	9246	Negative	18	Negative
57	892877	26	Female	Fever	Upper Lower	Absent	Not Taken	Multipara	2500	142	Vaginal	44	8	9	Present	40	12821	Negative	64000	4520	Negative	23	Negative
58	894032	28	Male	UTI	Upper Lower	Present	Not Taken	Multipara	2860	128	LSCS	52	8	9	Present	41	32145	Positive	342800	4520	Positive	18	Positive
59	888407	29	Female	Foul Smelling Liquor	Upper Middle	Absent	Not Taken	Multipara	3200	132	LSCS	56	8	9	Present	40	3975	Positive	231820	26430	Positive	22	Positive
60	888555	30	Male	PROM	Lower	Absent	Not Taken	Multipara	1890	152	Vaginal	54	8	9	Present	39	23656	Positive	234600	15420	Negative	14	Positive
61	889781	22	Female	PROM	Lower Middle	Present	Taken	Primipara	3340	146	LSCS	32	8	9	Present	38	12346	Negative	436820	8200	Negative	36	Negative
62	891783	28	Male	Fever	Upper Middle	Absent	Taken	Multipara	3450	128	Vaginal	43	8	9	Present	39	13000	Negative	48000	6800	Negative	24	Negative
63	891453	30	Male	Obstructed Labour	Upper Middle	Absent	Not Taken	Multipara	3420	132	Vaccum	46	8	9	Present	38	26450	Positive	268000	12460	Positive	13	Positive
64	881306	21	Female	Fever	Lower Middle	Absent	Taken	Primipara	2600	142	LSCS	44	8	9	Present	41	22000	Negative	175000	16450	Negative	26	Negative
65	884906	21	Female	PROM	Upper Middle	Absent	Not Taken	Primipara	2900	128	Vaginal	45	8	9	Present	38	8440	Positive	432800	3280	Negative	26	Positive
66	884001	28	Male	PROM	Lower Middle	Present	Not Taken	Multipara	3100	142	Vaginal	46	8	9	Present	39	28480	Positive	168000	18200	Negative	22	Positive
67	885999	27	Female	Obstructed Labour	Lower	Present	Not Taken	Multipara	3200	128	LSCS	46	5	6	Present	41	14160	Negative	234080	7800	Negative	28	Negative
68	886961	22	Female	PROM	Lower Middle	Absent	Taken	Primipara	2470	142	Vaginal	44	8	9	Present	41	12290	Negative	48000	6200	Negative	22	Negative
69	888095	24	Male	PROM	Upper Middle	Absent	Taken	Primipara	2790	128	Vaginal	46	8	9	Present	40	16960	Negative	483000	5200	Negative	26	Negative
70	879943	29	Male	PROM	Upper Middle	Present	Not Taken	Multipara	2450	142	LSCS	48	6	9	Present	39	24760	Negative	24000	16280	Negative	24	Negative
71	881987	28	Female	Fever	Lower Middle	Absent	Not Taken	Multipara	1910	160	LSCS	44	8	9	Present	38	3450	Positive	236800	1320	Negative	16	Positive
72	880196	20	Male	Fever	Upper Middle	Absent	Taken	Primipara	2280	128	LSCS	42	8	9	Present	41	32000	Positive	684000	21460	Negative	13	Positive
73	884218	21	Male	Foul Smelling Liquor	Upper Middle	Absent	Not Taken	Primipara	3200	148	LSCS	44	8	9	Present	38	23100	Negative	364000	18000	Negative	30	Negative
74	884616	29	Female	UTI	Upper Middle	Present	Not Taken	Multipara	2450	128	Vaginal	52	8	9	Present	41	22000	Negative	72000	12400	Negative	26	Negative
75	875722	30	Female	PROM	Upper Middle	Absent	Not Taken	Multipara	2420	122	Vaginal	42	8	9	Present	38	4500	Positive	168000	2100	Negative	18	Positive
76	875465	27	Male	PROM	Upper Lower	Present	Not Taken	Multipara	2340	126	LSCS	44	8	9	Present	41	3200	Positive	234000	1920	Positive	16	Positive
77	876979	21	Male	Perinatal Asphyxia	Lower Middle	Absent	Taken	Primipara	3350	153	LSCS	46	8	9	Present	38	32000	Negative	138000	18450	Negative	26	Negative
78	877412	30	Male	Foul Smelling Liquor	Upper Middle	Present	Taken	Multipara	3500	142	Vaginal	44	8	9	Present	39	42000	Positive	98000	28430	Negative	22	Positive
79	877441	30	Male	PROM	Upper Middle	Absent	Not Taken	Multipara	3200	146	Vaginal	42	8	9	Present	41	43000	Positive	154000	30400	Negative	14	Positive
80	877441	22	Female	PROM	Upper Middle	Present	Taken	Primipara	3280	122	LSCS	44	9	9	Present	38	26000	Negative	268000	15400	Negative	26	Negative
81	875919	21	Male	PROM	Lower Middle	Absent	Taken	Primipara	2600	132	Vaginal	46	8	9	Present	39	3450	Positive	342000	1920	Negative	16	Positive
82	874643	29	Male	Foul Smelling Liquor	Upper Middle	Present	Not Taken	Multipara	3450	146	LSCS	42	8	9	Present	41	33000	Negative	23000	24640	Negative	22	Negative
83	873859	28	Female	PROM	Upper Middle	Absent	Not Taken	Multipara	3249	142	Vaginal	48	8	9	Present	40	32000	Positive	264000	22000	Negative	24	Positive
84	873661	29	Male	PROM	Lower Middle	Present	Taken	Primipara	2100	144	LSCS	43	8	9	Present	39	23000	Positive	128000	14200	Negative	18	Positive
85	931566	26	Female	PROM	Upper Middle	Present	Taken	Multipara	3460	138	Vaginal	46	8	9	Present	38	18000	Negative	168000	10290	Negative	36	Negative
86	931803	24	Female	Foul Smelling Liquor	Upper Middle	Present	Not Taken	Multipara	2800	152	LSCS	54	8	9	Present	42	12000	Positive	264000	8750	Positive	22	Positive
87	932046	23	Male	Foul Smelling Liquor	Lower Middle	Absent	Taken	Primipara	1980	148	Vaginal	48	8	9	Present	37	16400	Negative	365000	9780	Negative	20	Negative
88	932036	22	Female	Foul Smelling Liquor	Upper Middle	Absent	Taken	Primipara	2050	145	Vaginal	54	8	9	Present	38	4200	Positive	167000	1680	Negative	18	Positive
89	932353	22	Male	PROM	Lower Middle	Present	Not Taken	Multipara	2150	148	Vaginal	47	8	9	Present	40	12680	Positive	187000	8760	Negative	16	Positive
90	931536	28	Female	PROM	Upper Middle	Absent	Not Taken	Multipara	2670	143	LSCS	46	8	9	Present	42	28000	Positive	184000	18670	Negative	15	Positive

S.No	UHID	Maternal Age (Years)	Baby Gender	Maternal Risk Factors	Socio-Economic Status	Sun Exposure	Vitamin D Intake	Parity	Birth Weight (Kg)	Heart Rate (BPM)	Mode Of Delivery	Respiratory Rate (CPM)	APGAR (1 Minute)	APGAR (5 Minutes)	Neonatal Reflexes	Gestational Age (Weeks)	Total Leucocyte Count (/cu.mm)	CRP	Platelet Count (/cu.mm)	Absolute Neutrophil Count (/cu.mm)	Blood Culture	Vitamin D Levels (ng/mL)	Early Onset Sepsis
91	931187	32	Male	Foul Smelling Liquor	Lower Middle	Absent	Taken	Multipara	2500	160	Vaginal	48	8	9	Present	41	32000	Positive	128000	23560	Negative	22	Positive
92	931296	32	Male	Foul Smelling Liquor	Lower Middle	Present	Not Taken	Primipara	2980	142	Vaginal	54	8	9	Present	40	16000	Negative	185000	12340	Negative	32	Negative
93	931296	23	Female	Obstructed Labour	Upper Middle	Absent	Not Taken	Multipara	2430	152	LSCS	48	8	9	Present	41	13000	Negative	234000	7890	Negative	22	Negative
94	931187	23	Female	Foul Smelling Liquor	Lower Middle	Absent	Not Taken	Primipara	2100	154	Vaginal	44	8	9	Present	38	14520	Negative	228000	11230	Positive	14	Negative
95	930829	28	Male	PROM	Lower Middle	Absent	Not Taken	Multipara	2780	148	Vaginal	54	8	9	Present	40	28000	Positive	382000	22348	Negative	14	Positive
96	931331	26	Female	Foul Smelling Liquor	Lower Middle	Present	Taken	Primipara	2800	144	Vaginal	53	8	9	Present	38	16280	Negative	284000	11230	Negative	26	Negative
97	931543	25	Male	PROM	Lower Middle	Present	Not Taken	Multipara	2450	154	Vaginal	56	8	9	Present	38	15240	Negative	384000	9870	Negative	16	Negative
98	929577	20	Male	Foul Smelling Liquor	Lower Middle	Present	Taken	Multipara	3400	148	Vaginal	40	8	9	Present	38	10000	Positive	284000	6870	Negative	19	Positive
99	930435	32	Female	Foul Smelling Liquor	Lower Middle	Present	Not Taken	Multipara	3480	144	LSCS	46	8	9	Present	40	12540	Negative	382000	7680	Negative	22	Negative
100	930686	24	Male	Foul Smelling Liquor	Lower Middle	Present	Taken	Multipara	3390	148	LSCS	50	8	9	Present	39	5420	Positive	284000	1420	Negative	18	Positive
101	930512	28	Male	Foul Smelling Liquor	Lower Middle	Absent	Taken	Multipara	4100	152	Vaginal	46	8	9	Present	38	18000	Negative	284000	16570	Negative	30	Negative
102	928223	29	Female	Perinatal Asphyxia	Lower Middle	Absent	Not Taken	Multipara	3450	154	Vaginal	44	8	9	Present	40	19240	Negative	187000	17650	Negative	26	Negative
103	928289	21	Female	Obstructed Labour	Lower Middle	Absent	Not Taken	Multipara	2880	148	LSCS	44	8	9	Present	41	21000	Negative	178000	17650	Negative	22	Negative
104	928293	34	Female	Foul Smelling Liquor	Lower Middle	Absent	Taken	Primipara	2450	156	Vaginal	48	8	9	Present	38	19000	Negative	164000	16508	Negative	24	Negative
105	928774	23	Male	Foul Smelling Liquor	Upper Middle	Absent	Not Taken	Multipara	2670	148	LSCS	44	8	9	Present	38	17530	Negative	264000	12348	Positive	16	Negative
106	928223	24	Male	Foul Smelling Liquor	Lower Middle	Absent	Not Taken	Primipara	2080	143	Vaginal	42	8	9	Present	40	18630	Negative	275000	12480	Positive	14	Negative
107	927090	28	Female	PROM	Lower Middle	Absent	Not Taken	Multipara	1890	150	Vaginal	48	8	9	Present	38	28000	Positive	125000	22340	Negative	18	Positive

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