DOCOSAHEXANOIC ACID SUPPLEMENTATION IN PRETERM NEONATES ADMITTED IN NICU AND ITS EFFECT ON INFLAMMATORY MARKERS AT DAY 10 -AN OPEN LABELLED RANDOMIZED CONTROL TRIAL

BY

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DISSERTATION SUBMITTED TO

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TAMAKA, KOLAR, KARNATAKA

In partial fulfilment of the requirement or the degree of

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IN
PAEDIATRICS

Under The Guidance Of

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LIST OF ABBREVIATIONS

PPROM	preterm premature rupture of membranes
PRM	Premature rupture of membranes
PTB	Preterm birth
PR	progesterone receptor
CRF	corticotropin-releasing factor
TLR	Toll-like receptors
DAMS	Damage associated molecular patterns
PAMS	pathogen associated molecular patterns
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
TNF	Tumor necrosis factor
IL	Interleukin
A	Alpha
B	Beta
RDS	respiratory distress syndrome
Γ	Gamma
DHA	Docosahexaenoic acid
PUFA	polyunsaturated fatty acids
BPD	Broncho pulmonary dysplasia
ARA	arachidonic acid
LCPUFA	long chain polyunsaturated fatty acid
ALA	α-linolenic acid
LA	Linoleic acid
GA	Gestational age

NICU	Neonatal intensive care unit
NEC	Necrotizing enterocolitis
LOS	Late onset sepsis
USA	Unites states
ROC	Receiver operating characteristic
EPA	Eicosapentaenoic acid
ROP	Retinopathy of prematurity
CRP	C Reactive Protein
CLD.	Chronic lung disease
ELGAN	Extremely Low Gestational Age Newborn Study
PMA	Post menstrual age
VEGF	Vascular endothelial growth factor
PPAR-γ	Peroxisome proliferator activated receptor γ
LCPUFA	Long chain polyunsaturated fatty acid
LBW	Low birth weight
IGF-1	Insulin-like growth factor-1

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DOCOSAHEXANOIC ACID SUPPLEMENTATION IN PRETERM NEONATES ADMITTED IN NICU AND ITS EFFECT ON INFLAMMATORY MARKERS AT DAY 10 -AN OPEN LABELLED RANDOMIZED CONTROL TRIAL

ABSTRACT:

Introduction:

With an undeveloped immune-regulatory system, preterm neonates are more susceptible to developing chronic inflammation. This sensitivity raise the likelihood that they may develop inflammation. In the immediate life, there is an urgent need for effective measures in the prevention of 'SEPSIS, NEC, BPD, and ROP' including dietary approaches. The purpose of this research is to find whether or not supplementation with DHA has the ability to modify immune responses and decrease inflammation in pre-term newborns who have been hospitalized to NICU

Methods:

In order to carry out this experiment, a randomized controlled trial with open labels was used. Fifty infants were divided into 2 groups by random assignment by a computerized randomized controlled trial (RCT): one group received DHA and the other group acted as control. Newborns between 32 & 34 weeks gestational age were considered for the study, Levels of C-reactive protein, interleukin-6 & procalcitonin were measured on the tenth day of life.

Results:

25 neonates in DHA Group and 24 neonates in control group have finished study. A statistically noteworthy variance was detected between the 2 groups for procalcitonin & IL-6.

Mean Procalcitonin values is 0.27 + 0.152 in DHA given group, whereas in control group , the Mean Procalcitonin is 0.72+0.930, p value between two groups is0.029, less than 0.05, which is statistically significant. In DHA group IL-6 values are 2.47+ 0.552 whereas in Control group IL-6 values are 3.40+1.80, p value between two groups is 0.019, less than 0.05, which is statistically significant. A statistically noteworthy variance between DHA group and control group for abdominal distension and ROP is also noted. In DHA supplementation group, abdominal distension is seen in 1 patient (4%) and in control group abdominal distension is seen in 8 patients (33.3%) and P value is 0.011, which is statistically noteworthy. Presence of ROP are seen in 2 patients, In group 2 control group presence of ROP are seen in 2 patients. p value is 0.043 indicating they were significant statistically.

Conclusion:

The study suggests that DHA supplementation may improve clinical conditions such as abdominal distension and may possibly reduce the incidence of inflammation as evidenced by documentation of inflammatory markers (CRP, procalcitonin, IL-6). The observations of this research imply that supplementing of oral DHA may help in preventing retinopathy of prematurity, however to what extent DHA help in preventing ROP needs further study with larger sample size.

Key words: Enteral Dha supplementation, preterm neonates, Inflammatory markers, Procalcitonin, IL-6

INTRODUCTION

INTRODUCTION :

The World Health Organization characterizes preterm labor as the onset of labor prior to completion of 37 weeks of gestation, in pregnancy beyond 20 weeks of gestation.[1] Preterm birth, or birth prior to 37 weeks of gestation, affects 5%-7% of live births in the highly developed countries & upto 25% in the context of underdeveloped countries. Preterm birth rates are a serious public health concern because there is evidence that they have been increasing constantly in several nations over the past few years.[2]

Preterm birth risk factors include a range of factors, including personal choices, environmental exposures, medical complications, infertility treatments, biological variables, and genetic predispositions. Preterm infants are at a increased risk of experiencing a varied range of health and developmental challenges compared to neonates delivered at full term. Complications of this condition include acute respiratory, gastrointestinal, immunologic, central nervous system, hearing, and vision issues. Additionally, there may be long-term mental, vision, auditory, interactive , movement, development problems.[3]

Preterm newborns are more vulnerable to sepsis due to their immature immune systems. Premature infants often get sepsis without normal symptoms like fever. [4] Preterm newborns have an underdeveloped immune system, which increases the risk of chronic inflammation. Imbalance in the modulation of inflammatory responses is a key factor in the causation of serious neonatal diseases like BPD, NEC, and sepsis. [5]

Inflammation is a crucial factor in the progression of BPD, NEC, and ROP. Preterm neonates with sepsis or Nectrotizing enterocolitis have classical "inflammatory phenotypes," which are the 2nd most prevalent cause of mortality in preterm neonates, behind respiratory failure. Insufficient resolution of acute inflammatory conditions, especially in those who have survived sepsis or NEC, may lead to the development of severe illness[6]. Timely identification

of neonatal infections and associated disorders, including NEC, is crucial for minimizing the sickness and death rate in newborns.[4]

Necrotizing enterocolitis (NEC) is the most common and serious gastrointestinal catastrophe that occurs in preterm neonates in the Intensive Care Unit (NICU). This is a serious gastrointestinal disorder that leads to sepsis, intestinal perforation, and high rates of illness and death. The probability of NEC is negatively correlated with gestational age and birth weight[2-4]. Up to 15% of all babies treated in the NICU are premature neonates with low birth weight.[7]

Multiple studies have shown an 'upregulation in the production of inflammatory cytokines' like TNF, interleukin (IL)-1β, and IL-6, in both plasma and tissues of individuals affected with NEC .[8]

DHA; 22:6 n-3 is the predominant fatty-acid found in brain and essential for the growth of new nerve cells and the development of their projections. Docosahexaenoic acid is transferred from the maternal side to baby throughout pregnancy, with a special emphasis in third trimester. Preterm newborns lack the in uterus accumulation of DHA, which contributes to increased likelihood of delay in development in comparison to full-term babies.[9]

Long-chain poly-unsaturated fatty acids (LCPUFA), namely DHA are necessary for achieving optimum health and promoting neuro-development. Moreover, there is a growing body of research suggesting that Omega-3 (n-3) LCPUFA might decrease the occurrence or intensity of main inflammatory ailments and associated conditions in premature infants by controlling several aspects of the immune & anti-inflammatory response. The anti-

inflammatory activity of docosahexaenoic acid (DHA) is shown by its ability to inhibit the release of "interleukin-1β (IL-1β) and interleukin-6 (IL-6)".[10]

A longitudinal study examining the cytokine profiles in the blood of preterm newborns revealed that children who were subsequently diagnosed with bronchopulmonary dysplasia (BPD) had raised amounts of granulocyte colony stimulating factor(G-CSF), Interleukin-6, Interleukin-8 during the initial weeks of their lives.[11]

Research has shown that inflammation is a significant factor in both the normal and abnormal growth of blood vessels in the retina. [12,13,14]Research has provided evidence to support the theory that inflammation in newborns plays a important part in the development and advancement of retinopathy of prematurity (ROP). [14]

Preterm newborns have a diverse immune regulatory system in comparison to both term newborns and adults. The immune defense of preterm infants primarily depends on non-specific innate immunity. T cell responses particularly T helper cells that regulate inflammation, play a crucial role in this defense mechanism. Consequently, there is an excessive production of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor (TNF)-a, as well as other inflammation-related proteins including C-reactive protein (CRP), intercellular cellular adhesion molecule (ICAM)-1, erythropoietin, and ferritin. Serum and plasma are used as proxy measures to determine systemic inflammation in premature newborns, namely those born before 28 weeks of gestation, as described in several papers from the multicenter (ELGAN) group. [15,16,17]

Therefore, there is a need to study supplementation of enteral DHA in preterm neonates and to look how they effect on inflammatory markers. Aim of present study is to assess and compare the inflammatory markers in pre-term infants who receive DHA supplementation .

OBJECTIVES

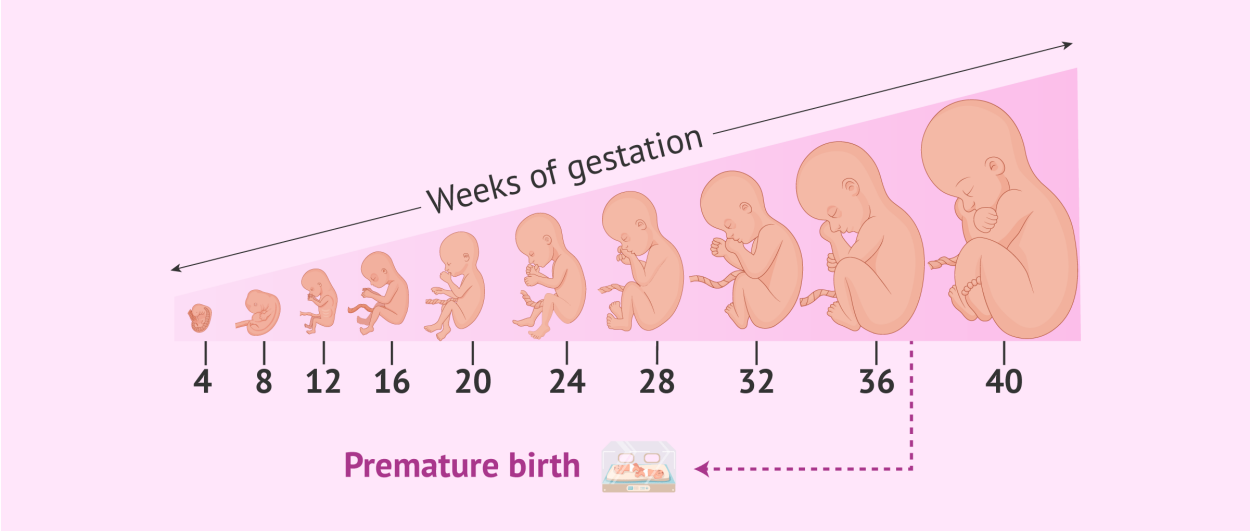
OBJECTIVES

1. To measure the inflammatory markers at day 10 of admission in babies with DHA supplementation
2. To measure the inflammatory markers at day 10 of admission in babies without supplementation of DHA
3. To compare the level of inflammatory markers between two groups
4. To compare the defined clinical outcomes i.e (sepsis, necrotising enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity)

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Preterm labor is the term used to describe the phenomenon of a woman giving birth between the ages of "20 0/7 weeks and 36 6/7 weeks of gestation.The Centers for Disease Control and Prevention and American College of Obstetricians" have determined that it may be further subdivided into two categories: early preterm and late preterm. The word "early preterm" refers to a baby who is delivered within 32 weeks & 33 weeks 6 days, whereas the term "late preterm" refers to baby who is delivered within 34 weeks & 36 weeks 6 days. Preterm delivery may result in newborn death, in addition to raising the risk of infections in early life and neurodevelopmental, cardiometabolic, and inflammatory illnesses in later life for babies who survive the birth process.[18]



Gestational weeks and premature baby

Gestational age at birth, along with birthweight, is considered a reference standard for predicting preterm infant outcomes and prognosis. More specifically, extremely early preterm birth occurs before 32 weeks of gestation, early preterm birth occurs between 32 0/7 and 33 6/7 weeks, and late preterm birth occurs between 34 0/7 and 36 6/7 weeks. Preterm delivery is defined as birth that occurs before 37 weeks of gestation. Although immediate neonatal

outcomes are typically regarded as satisfactory, this group had a significant impact on infant mortality in the post-neonatal period (up to one year) due to hypoxia, infection, and sudden infant death syndrome.[19]

Etiology of preterm labour and preterm births:

Pre-term labor can occur due to various causes like stress, infection, abruption of placenta, placenta previa, substance abuse, smoking, inadequate prenatal and mother age lesser than 18 or older than 40, low body mass index, poor nutrition, fetal anomaly, fetal growth restriction, oligohydramnios, polyhydramnios, vaginal bleeding, premature preterm rupture of membranes (PPROM), and environmental factors. [18]

Idiopathic preterm births (PTBs) and other human pregnancy complications have been linked to inflammation. It is believed that PTB begins in the early stages of pregnancy, prior to placental formation. Like preeclampsia, PTB results from a problem with the deep placenta. [18]

Inadequate immune adaptation during conception, along with the inability to build immune tolerance or reduce excessive inflammation, may contribute to preterm birth (PTB) since these processes are involved in the procedures that maintain a successful pregnancy throughout gestation.[18]

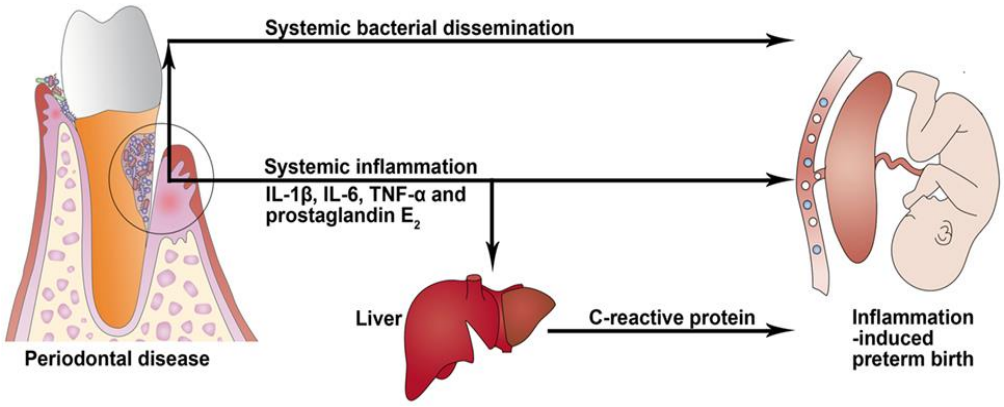
The inflammatory load and the development of PTB later in pregnancy may be exacerbated by maternal sickness, endocrine dysfunction, microbiota arrangement, or metabolic dysregulation.[18]

It is believed that immunological illnesses, infection/inflammation, overdistended uterus , vascular sickness, and intrauterine growth restriction are among the many potential causes of spontaneous preterm births, in contrast to iatrogenic preterm births most often related to

preeclampsia or restricted intrauterine growth. Additionally, racial disparity, small length of cervix, poly-hydramnios, multiple gestations, poor nutritional status in mother, periodontal conditions, and uteroplacental infarction and hemorrhage are risk factors for PTB.[20]

Causes for preterm labour

Research has linked preterm birth (PTB) to various health issues, such as "periodontitis, pneumonia, cholecystitis, pyelonephritis, pancreas inflammation sepsis, and vaginal tract inflammatory states like bacteria-related vaginosis, deciduitis, chorioamnionitis, and intra-amniotic diseases". This happens because inflammation activates the immune system, which thereby increase the formation of 'inflammatory cytokines, elastases & matrix metallo-proteinases . It also results in the functional removal of progesterone, that is crucial for the continuation of pregnancy.[20]



Periodontitis and preterm birth

Respiratory distress follows preterm birth as the most prevalent consequence. Nonetheless, sepsis, intraventricular hemorrhage, and necrotizing enterocolitis need to be taken into account. A higher risk of neonatal white matter injury is linked to early gestational age at membrane rupture in PPROM with intrauterine inflammation, and both conditions can affect neurodevelopment. Following premature preterm PRM, there is a 1-2% chance of prenatal fetal death due to infection and umbilical cord accidents.[18] Remarkably, inflammation has a major role in initiating labor at term physiologically as well. Therefore, it appears that the start of inflammation is a common factor in both term & preterm labor.

Preterm Labour :

A woman goes into labor when her decidua and membranes become activated, her uterus contracts for an extended period of time, and there are changes in her cervical anatomy. Term labor is the product of a normal physiological process, in contrast to preterm labor, which is the outcome of a pathological process. Some procedures lead to premature labor quickly, while others take weeks. [21]

Pregnancies that proceed typically arise from the well-coordinated processes of periconception, implantation, decidualization, and placentation. The receptive endometrium

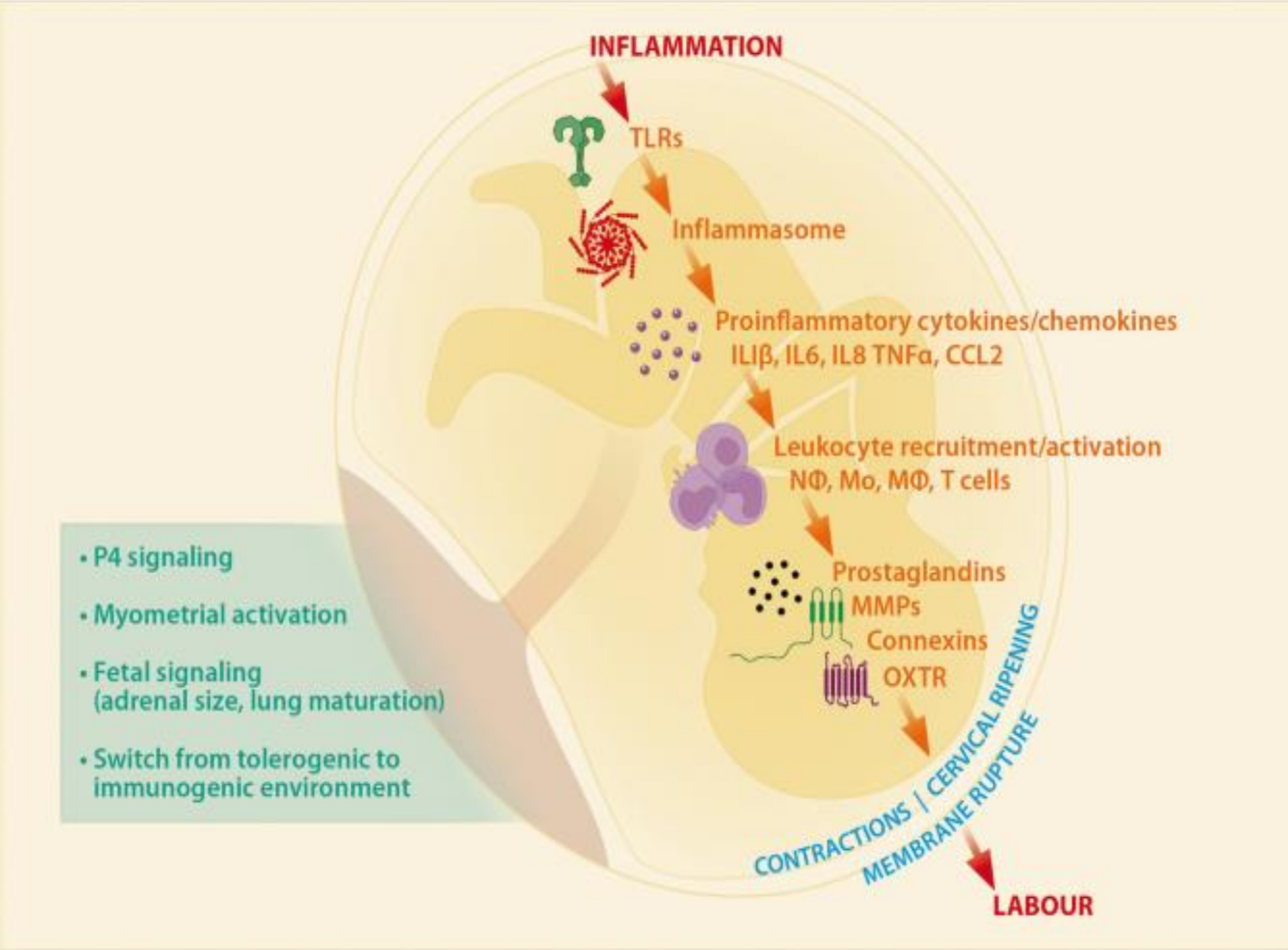
and decidual quiescence are established by hormone signaling, specifically progesterone (P4); maternal immunological tolerance reduces the likelihood of embryonic rejection & promotes spiral artery remodeling and as well as placentation. As the process of giving birth begins, the local immune ecosystem shifts from 'tolerogenic to activating state' , the decidual quiescence is replaced by myometrial activation & P4 signaling is turned off. Age, ethnic origin, genetics, socioeconomic status, and mother and father lifestyle riskfactors (like stress & food) are among the many elements that impact the overall outcome of a pregnancy, as well as the risk for preterm birth. [22]

The fundamental mechanism of both term and preterm labor is same, according to several studies on preterm birth; the only variation is the age of gestation at which labor starts. It is believed that these diseases follow a same path. The pathogenic mechanisms that cause preterm labor activate at least one component of this common pathway. These components include the following: an increase in prostaglandin and production of protease in the genital tract; a decrease in progesterone receptor (PR) isoform expression in the cervix, decidua, and myometrium; and changes in hormone concentrations, such as cortisol and corticotropin-releasing factor (CRF).[22]

There is evidence that maternal and foetal stress contribute to preterm birth. It suggests that corticotropin-releasing hormone (CRH) mediates stress-induced premature deliveries. Hormone CRH is a peptide of 41 amino acids that is produced by cells in the brain, placenta, chorionic, amniotic, and decidual areas during pregnancy. Elevated levels of CRH cause an increase in cortisol in the mother and the baby in response to stress experienced by either party during pregnancy.[22]

Several different classes of diaminoacetic acids (DAMPs) and prostaglandin E (PAMPs) activate toll-like receptors (TLRs) on immune & endothelial cells at the feto -

maternal junction during pregnancy. Intracellular signaling processes set in motion by activated Toll-like receptors (TLRs) lead to the release of chemokines and cytokines that promote inflammation. The decidua, placenta, and amniotic cavity are inundated with pro-inflammatory leukocytes, monocytes, also neutrophils, and T cells as a result of this.[22]



Current understanding of the inflammatory mechanisms involved in parturition.

When macrophages are activated, NF-κb controls the production of genes , involved in contractility of the uterus and cervical ripening. Additionally, it modulates the expression of pro-inflammatory cytokines such as TNFα, IL1β, IL6, and IL8. Uterine contractile ability & ripening of cervix are the two physiological processes that lead to membrane rupture, which ultimately leads to the beginning of labor. Myometrium mucle

activation, fetal-signalling, and a change in maternal immune phenotypes from resistance to inflammation are all factors that lead to onset of major inflammatory course. Withdrawal of P4 signaling is another factor that plays a role.[22].

The fetal brain provides a signal that induces the CRH to be produced, which in turn prompts the fetal adrenal glands to create more cortisol and engage the parturition pathway. This process continues until the fetal brain delivers the signal again. The inflow of cells which leads to inflammation into the stroma of cervix causes ,production of prostaglandins & cytokines, in turn stimulating the ripening of the cervical tissue. The collagen and glycosaminoglycan characteristics that are responsible for the formation of cervical tissue are influenced by these altered structures. On the other hand, estrogen encourages the breakdown of collagen, whereas progesterone does the opposite. Because of this, progesterone is helpful to halt or delay the process of ripening. These hormones are responsible to regulate the formation of gap junctions as well as the overexpression of connexin 43 proteins, which are proteins that assists in the process of parturition.[23]

The detection of fetal fibronectin in cervicovaginal secretions is utilized for the purpose of measuring the disintegration of the extracellular matrix, which is a component of the process of parturition. When it is discovered between twenty two & thirty seven weeks of GA, it implies that the decidual & chorionic connection has been disrupted, and it also indicates that there is an increased chance of entering labor prematurely. [23]

In the context of premature labor, fetal inflammatory response syndrome, often known as FIRS, is a significant pathogenic occurrence. Symptoms include inflammation throughout the body and an increase in the level of interleukin-6 in the fetal plasma.[21]

Pre-term delivery or rupture of the membranes with or without chorio-amnionitis (also known as "first inflammatory hit"), is the outcome of a process of inflammation at feto-maternal junction, which accounts for around half of all the preterm deliveries. This process leads to preterm labor or membrane rupture. Newborns who are born prematurely have exceedingly delicate body surfaces and organ systems that have not yet formed. They are subjected to a dramatically changed antigen exposure after birth, which may include microorganisms that are peculiar to the hospital, artificial equipment, drugs, food antigens, hypoxia or hyperoxia (also known as a "second inflammatory hit"). [6.]

This is of utmost importance for severely premature children who were born before 28 weeks of gestation since they have not yet finished the essential third-trimester adaptation mechanisms that are necessary to tolerate maternal and self-antigens. The complex co-regulation of immunological defense systems and immunosuppression (tolerance) that allows for the creation of a microbiome is often interrupted, which results in a disruption of the microbiome rather than a healthy adaptation to life beyond pregnancy. As a consequence of this, preterm neonates are more likely to develop sepsis, in addition to a variety of other potentially dangerous disorders that may contribute in the development or continuation of persistent inflammation (SI). Due to the fact that SI is regarded as a pivotal factor in the development of mortality and morbidity in preterm babies, this is a problem that is always present for physicians who interact with individuals who were born prematurely. [6]

Physiology and anatomy of preterm births [24] :

Because there are insufficient glycogen, protein, and fat reserves which normally increase in the third trimester of pregnancy, premature babies are at a greater risk of experiencing adverse developmental outcomes. In the event that glycogen is exhausted, lipolysis which results in the production of glycerol or ketone bodies, plays a crucial role in supporting the

metabolic requirements of pre-mature infants. However, premature newborns have restricted lipolysis and ketogenesis due to fat loss in adipose tissue.

The respiratory system:[25,26] Respiratory system changes significantly throughout intrauterine development. During the pseudoglandular stage (16 weeks of gestation), the airways form completely. During the canalicular stage (weeks 16-24), conductive structures grow in size, while the saccular stage (weeks 24-36) sees the development of pre-acinar airways, bronchioles, and acini. Throughout the saccular pulmonary development stage, which generally occurs about 28 weeks of gestation, the alveoli start to form. Around 35 weeks gestation, the production of pulmonary surfactant reaches mature levels. The surface-tension in alveoli is reduced by surfactant, which enables alveoli to maintain their inflated state. In preterm neonates, RDS is a common illness that may be caused by a lack of pulmonary surfactant or a failure in the pulmonary surfactant system.

85% of babies who survive delivery before 34 weeks of gestation are affected by prematurity apnea, and the likelihood of developing this condition rises with each week of gestation that is lost. An immature central respiratory control system (such as lower sensitivity to CO2 and hypoxia) and an increased protective reaction to laryngeal stimulation are the causes of a cessation of breathing that lasts for more than fifteen to twenty seconds. Due to this, the inspiratory activation of the breathing muscles is disrupted, which ultimately results in the closure of the upper airway.

Immune response:[27] The fundamental function of the liver is hematopoiesis, which occurs between weeks 6 and 22 of gestation. Premature children have an undeveloped complement system, which is further aggravated by such a condition. Intracellular bacteria resulting in uterine infections (intrapartum and postpartum) also induce innate immune responses in both the fetus and the neonate, and premature newborns are more vulnerable to these pathogens.

Premature newborns have temporarily impaired regulatory T cell function, which can cause immune response dysregulation or overactivation .

Adrenal function: [28] Premature newborns respond incompletely to stress. Preterm newborns experience transitory adrenocortical insufficiency in the first two weeks of life, leading to a reduced response primarily at the adrenal gland. Prenatal conditions, including maternal glucocorticoid medication, might negatively impact the baby's adrenal response.

Renal function: [29] Beginning about the ninth week of pregnancy, nephron development reaches its highest point during the third trimester, and it reaches adult levels around the 36-weeks gestation.. It is possible for premature babies to undergo decreased or abnormal nephrogenesis after birth, and it is also possible that they do not generate as many nephrons as their full-term counterparts.

In comparison, kids born after 35 weeks of gestation have an efficient renal plasma flow of roughly 45 mL/min/1.73 m2, whereas babies born at term have an efficacious renal plasma flow of 83 mL/min/1.73 m2. Extremely premature infants have an efficacious renal plasma circulation of approximately 20 mL/min/1.73 m2. The growth of the external cortical area is supported by an increase in blood flow that occurs throughout time and leads to a greater flow to that region.

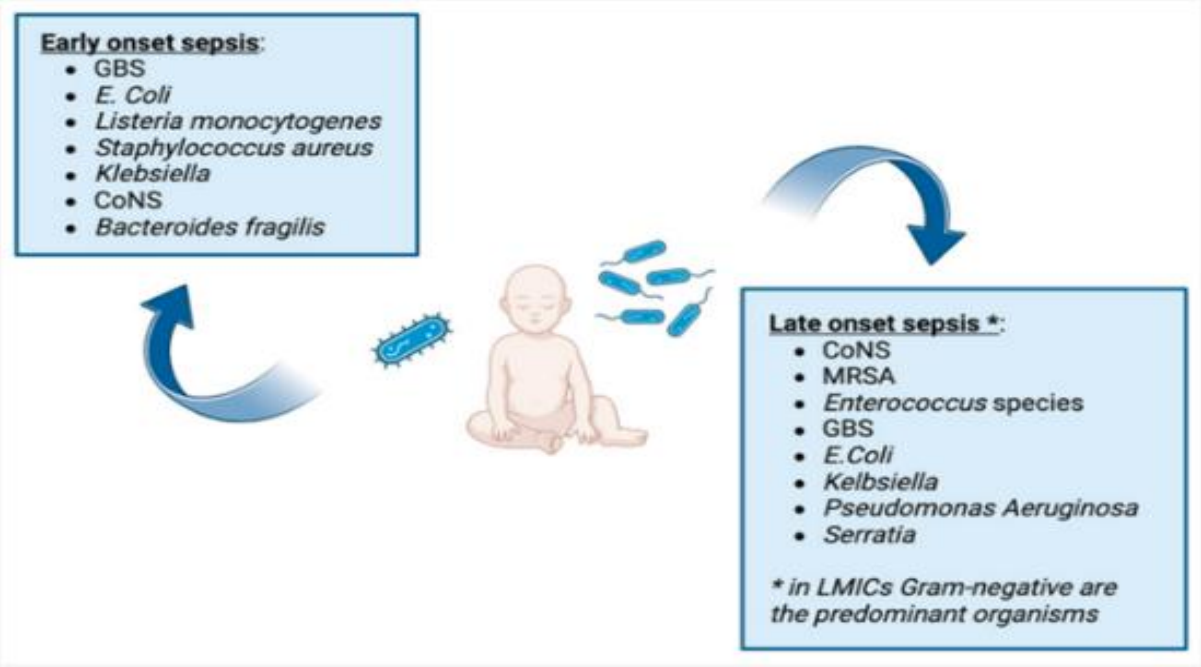
Hepatic function: Preterm newborns with immature liver function may have hypoglycemia, hyperbilirubinemia, cholestasis, hemorrhage, and poor medication metabolism.

Neonatal sepsis : [30,31,32]

Both early and late onset are considered to be different types of neonatal sepsis. When a pathogen is passed from mother to neonate in a vertical manner, a condition known as early onset sepsis (EOS) begins to manifest. At the time of birth & during the initial three days of

neonatal life. Late-onset sepsis, often known as LOS, is a condition manifesting itself post 72 hours after delivery and is primarily obtained horizontally from surrounding environment of the newborn. On the other hand, it may also arise as a result of a delayed presentation of illnesses that were acquired vertically from the mother.[32]

The condition known as early-onset neonatal sepsis (EOS) results in two to three percent of all fatalities that occur in term neonates and twenty to thirty percent of deaths that occur in preterm newborns. Although it is uncommon, it poses a considerable risk of disastrous effects. Although the bacterial etiology of EOS has evolved , Streptococcus B continues to be most prevalent infection in term neonates. On other hand, Escherichia coli is the bacterium that is most often seen in preterm neonates. EOS is twice as likely to occur in newborns who are 34-36 weeks old as it is in those who are delivered at term.[30]



Major bacterial species associated with neonatal sepsis

Infants that were born at a younger gestational age are more prone to be infected, regardless of the route of transmission that may have occurred. A increased risk of having sepsis is

associated with neonates that were born very prematurely and had a VLBW of fewer than 1500 grams. This is in comparison to term babies. Neonatal risk factors include preterm, status of very low birth weight , and congenital abnormalities. Neonates at risk for these conditions may need invasive medical equipment, delay in feeding, drugs and advanced treatment in the NICU. Some drugs, such as "antibiotics, histamine receptor antagonists, and proton pump inhibitors, may affect the microbiota of a neonate and increase their susceptibility to pathogens". Delayed enteral feedings are another factor that might have this effect.[31]

According to the findings of a retrospective cohort research, the risk of sepsis is increased by 2% for every 1% of neonates living in a unit census who are under 32 weeks old.Escherichia.coli is the leading cause of illness and fatality among EOS newborns, despite the fact that GBS is becoming more widespread among the general population.

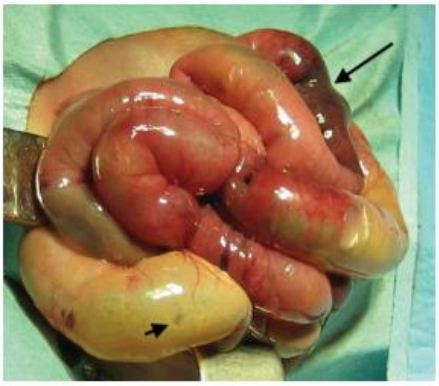
Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus species, gram-negative bacteria (including Haemophilus influenzae and Enterobacter species), and Listeria monocytogenes are examples of pathogens that make up a smaller percentage of the overall population. Polymicrobial illnesses are quite uncommon.[31, 32]

Late-onset sepsis arises from gram positive bacteria the majority of the time; however, gram-negative bacteria, fungi, and viruses may also play a role in the development of this condition. LOS caused by fungi affects very low birth weight neonates, with incidence ranging from 5% to 28% depending on the facility.[31,32]

Necrotizing enterocolitis (NEC) : [33] Preterm newborns have higher morbidity and mortality rates due to undeveloped physiology and neonatal problems. Necrotizing enterocolitis (NEC) is a severe gastrointestinal condition that causes morbidity and mortality in premature newborns. Necrotizing enterocolitis, often known as NEC, is the most prevalent of the life-

endangering illness that affect the gastrointestinal tract (GIT) in neonates & preterm babies. One of the defining characteristics of NEC is the presence of hemorrhagic & necrotizing inflammation along the whole surface of intestine. [34]

One of the most important factors in the pathophysiology of the illness is the movement of bacteria that produce gas from lumen of gastrointestinal tract (GIT) to intestinal wall. There is a possibility that NEC will be localized or distributed across the GIT . First clinical manifestations of NEC are often unique & vague. When initially beginning to differentiate between NEC and food intolerance, which is common in preterm newborns, as well as other gastrointestinal diseases and sepsis, it may be difficult to establish a clear distinction between the two.[35]

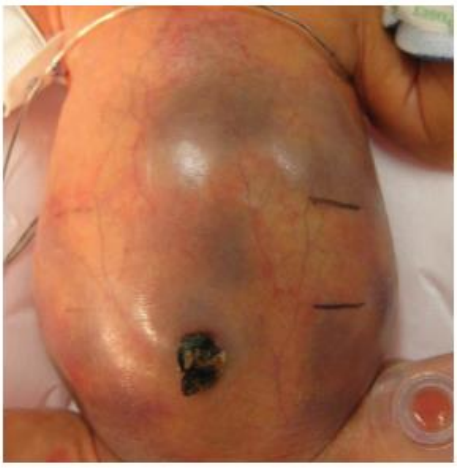


Necrosis of the intestines in a premature newborn with involvement of the whole gastrointestinal tract & signs of necrosis , perforation (long arrow), and air pockets found inside the intestinal wall as a consequence of gas-producing bacteria (short arrow).

Most preterm infants experience NEC as an acute illness. Nursing staff are generally the first to observe alterations in a child's clinical status, making them crucial for early identification of NEC. Inflammatory indicators such as IL-6 and IL-8, as well as

procalcitonin (PCT) and CRP, increase over time and can be associated with various bacterial infections.[35]

Abdominal X-ray remains the preferred modality for optical imaging of NEC. Interpreting these data in immature infants can be tricky. Contrast agents and enemas are not recommended for patients with NEC due to the risk of perforation.[34]



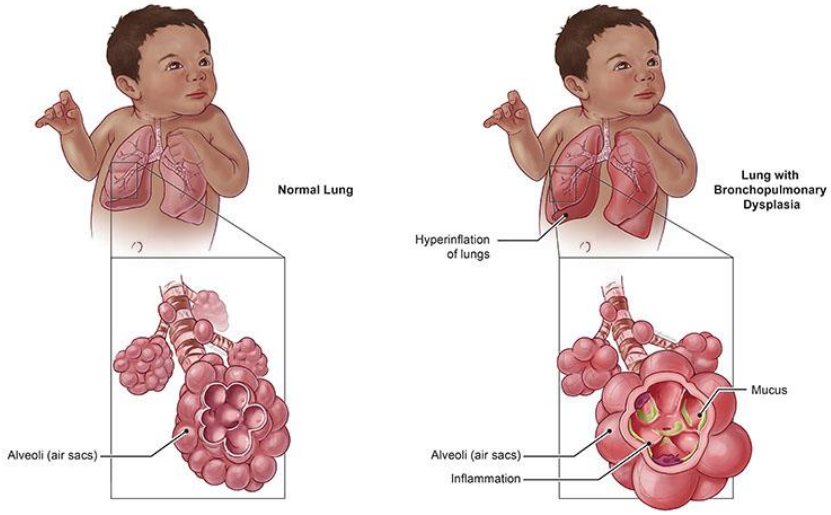
Abdominal wall erythema with livid discoloration as late clinical signs in a Premature baby on day 17 of life with NEC.[34]

Premature newborns are more susceptible to acquire this condition because to GIT immaturity. Ischemia likely plays a secondary role in the progression of NEC caused by inflammatory processes. Inflammation in the mucosa can cause pathogenic bacteria to invade and release cytokines such TNF-α and IL-1, IL-6, and IL-8.[34]

In the majority of preterm newborns, NEC manifests itself as an acute sickness. Newborns who are born preterm and have a gestational age of less than 26 week often develop NEC around the 23rd day of their lives, but babies who have agestational age of more than 31 week typically get unwell during the second week of their lives. Around twenty-five percent of infants will have NEC after the thirty-first day of their lives. [34]

It is possible for a complete blood count to detect thrombocytopenia and leukopenias that occurs throughout stages of inflammation due to deprivation of platelets and granulocytes. Nonspecific inflammatory measurements such as procalcitonin (PCT), C-reactive protein (CRP), and inflammatory markers IL-8 and IL-6 all rise with time. These inflammatory markers are consistent with a broad variety of bacterial infections. In the case of metabolic acidosis brought on by fluid displacement in intestine or due to sepsis with capillary leak syndrome, blood gas analysis (BGA) may distinguish between the two conditions. When dealing with young newborns, it might be difficult to interpret this facts. Due to possibility of perforation, contrast agents and enemas are not suggested for individuals who have (NEC). When assessing it, USG of abdomen is a helpful tool that should be used in addition to typical radiologic symptoms. [34]

Broncho-pulmonary Dysplasia:[36,37] Inflammation, disturbance of architecture, fibrosis, and developmental delay of the baby lung are symptoms that are frequently associated with (BPD). A 'new' BPD is developing as a result of the survival of children born at earlier gestational age throughout their neonatal period.The majority of children that develop this condition are, without a doubt, premature babies. When compared to ventilated babies, premature neonates that were able to survive without the need for additional mechanical ventilatory support had normal alveolar numbers and a lower incidence of morphologic airway abnormalities.



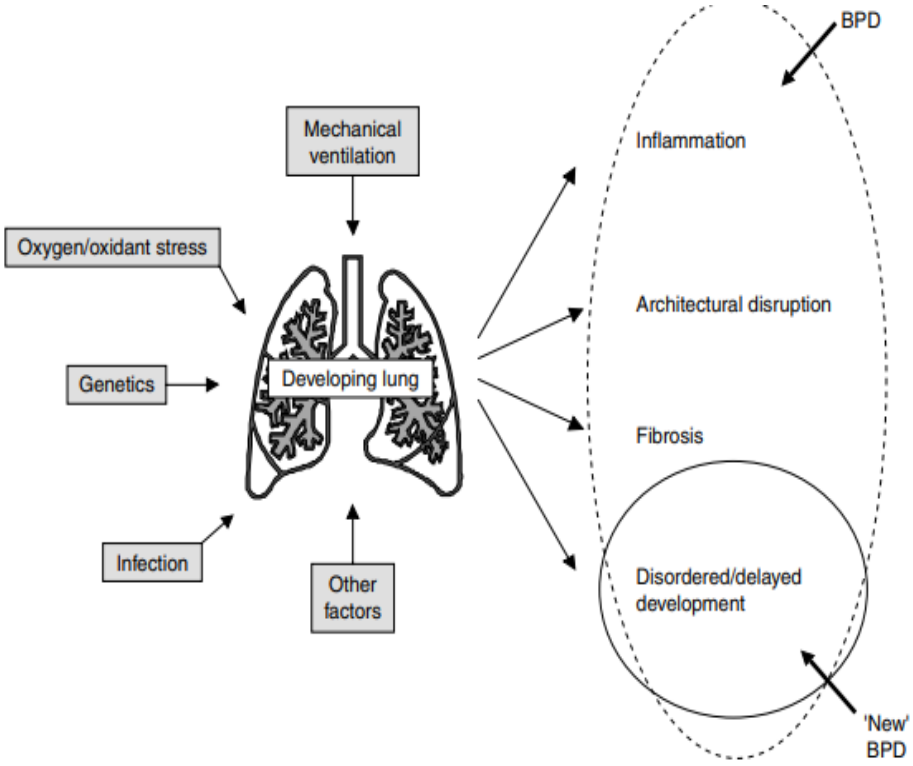
Bronchopulmonary dysplasia of preterm babies

The pathology of BPD has developed throughout the course of time, which has led some writers to differentiate between "old" and "new" BPD. In addition to the loss of alveolar septa and the ultimate development of fibrosis, there was a significant amount of inflammation, edema, fibroproliferation, and hypercellularity that existed. Muscular hyperplasia was also found surrounding the bronchi and bronchioles, in addition to an increased number of goblet cells, submucosal gland hypertrophy, an excessive amount of mucus production, and mucosal squamous metaplasia. In spite of the fact that the division of the pulmonary airways is almost finished and the acinar borders have been established by the beginning of the third trimester, the distal saccules of lung, have not yet differentiated into alveoli.

This airway disorder is the leading cause of prolonged hospitalization of newborns and mortality in premature babies. Infants who have BPD may also have an increased chance of developing prematurity-related complications, like bouts of oxygen desaturation, apnea, or stomach reflux because of their premature birth. The additional work of breathing that is put

on infants with BPD often results in poor development because of the higher metabolic demands that are imposed on them.

Poor neurodevelopmental outcomes are associated with premature birth, which is a risk factor. Although there have been research that have shown that this disorder does not have an independent influence on this risk, other studies have shown that it is connected to worse neurodevelopmental outcomes from the age of three to over fifteen years old. Even when other variables are addressed, this influence continues to be felt, and it seems to be present in babies who were born during the surfactant period. There is a 'dose effect' that seems to be present, as the need for oxygen support at 36 weeks of post- menstrual age ,predicts a more negative result than the demand for oxygen at 28 days of age.



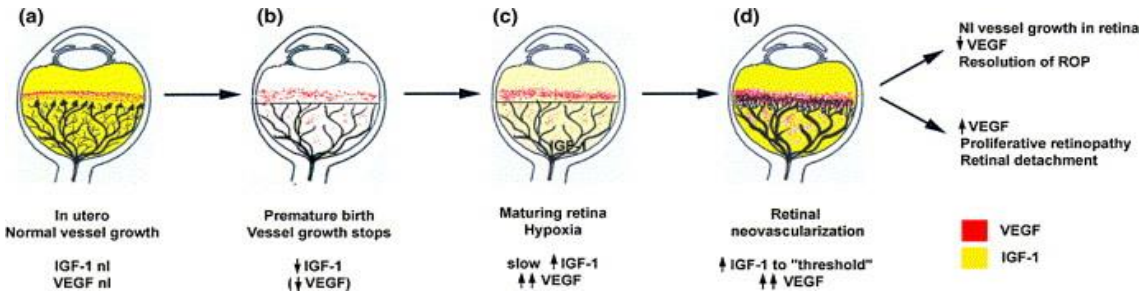
Pathogenesis of bronchopulmonary dysplasia (BPD).

There has been a significant amount of research conducted on preterm neonates to investigate the influence that “proinflammatory mediators, such as cytokines, have on recruiting

inflammatory cells to the lung. The lungs Both increased levels of proinflammatory cytokines (particularly TNFα, IL-1β, IL-6, or IL-8) in amniotic fluid and elevated levels of IL-6 in cord blood have been associated with the later development of BPD. Individuals who were born prematurely and had elevated amounts of TNFα, IL-1β, IL-6, IL-8, and monocyte chemo attractant protein-1" in their airway fluid were at a greater risk of having (BPD) in the future. Leukotrienes, thromboxanes, and complement components are some of the other noncytokine proinflammatory chemicals that are found in increased concentrations in newborns who develop this respiratory disorder during the first seven to ten days of their lives.

The cannalicular stage of lung development has recently been completed by an ext-preterm who was born between 24 and 28 weeks of gestation. This newborn is currently in the saccular stage of lung development.Not yet to take place. The 'new' BPD is characterized by the fact that injuries that occur during this time period are likely to impede development.

Retinopathy of prematurity (ROP) It is a condition , that affects premature newborns who are receiving oxygen treatment. It is characterized by the growth of their retinal capillaries and vascular vessels. The illness cause retinal vascular and capillary growth, also known as retinopathy of prematurity . It is a syndrome affecting preterm neonates who are receiving oxygen treatment. While retina which is still in the uterus, is subjected to physiological hypoxia. The development of new blood vessels in the retina is facilitated by elevated amounts of VEGF The process of normal vascular development may be broken down into two distinct phases: vasculogenesis, which takes place between the 14th and 21st weeks, and angiogenesis, which starts at 22weeks & continues till retina is completely vascularized at the end of pregnancy. As the medial and lateral parts of retina mature at 32 and 40 weeks, premature neonates have insufficient vascularization of these areas. This is because the nasal region develops sooner than the temporal region.[38]



Pathophysiology of retinopathy

DHA :

DHA is among the most plentiful "LCPUFAs in the brain, playing a crucial role in neurotransmission and neurogenesis. Early preterm children with low birth weights (<1500 g) benefited the most from DHA supplementation, as they missed the majority of the third trimester and had the highest fetal DHA accretion rates. [39]

The long-chain polyunsaturated fatty acid known as docosahexaenoic acid (DHA) is a member of the n-3 (or omega-3) family of monounsaturated acid compounds. Both red blood cell phospholipid (RBC-PL) DHA as a percentage of total membrane fatty acids and human milk DHA as a percentage of total fats are the two most used methods for determining the presence of DHA in the body. Pregnant women who consume more DHA offer more DHA to their fetus, and postpartum milk DHA levels are higher. DHA biosynthesis from α-linolenic acid is reduced under some situations, such as caloric deprivation, protein deficiency, and corticosteroids that inhibit δ6-desaturase and hence DHA synthesis.[40]

Mother milk contains substances which had anti-inflammatory effect on babies, that can decrease the chances of death and inflammation related morbidity in premature infants. DHA, a long-chain omega-3 PUFA found in human milk, is anti-inflammatory and antioxidant. DHA is a key component of phospho-lipid membrane's lipid raft, where it regulates expression of cytokines and reduce signaling, influencing PG synthesis and associated

metabolites. DHA metabolites can decrease stimulating anti-inflammatory transcription factors, including PPAR-γ. Oral supplementation of DHA lowers chance of severe retinopathy in preterm newborns, while whole blood DHA concentrations predict CLD and LOS.[40]

Premature newborns have higher chances of inflammatory illnesses such BPD and NEC, which DHA's anti-inflammatory characteristics may help to alleviate.[39]

Homeostasis in inflammation is often difficult to achieve in preterm children, which raises the risk of sepsis and, paradoxically, has the effect of inflicting pathological damage to critical tissues. "IL-6, IL-1β, and TNF-α" are examples of proinflammatory cytokines that are found in the amniotic fluid. These cytokines significantly increase the likelihood of postnatal brain and lung damage. A Notable raise in the levels of cytokines IL-6, IL-10, and TNF-α is seen in preterm babies who have been diagnosed with disseminated coagulopathy. In the 48-hour period, the ratio of IL-10 to TNF-α experiences a significant decrease, whereas the ratio of IL-6 to IL-10 remains unchanged. There is a significant increase in amounts of pro-inflammatory cytokines comprising 'IL-1, IL-6, IL-8, and TNF-α' in plasma & broncho-alveolar lavage in preterm neonates who are diagnosed with chronic lung illness.[41]

There is a significant raise in the quantity of proinflammatory cytokines, including IL-1, IL-6, IL-8, and TNF-α, in plasma and bronchoalveolar lavage in preterm neonates who are diagnosed with chronic lung illness. The presence of higher levels of IL-8 expression in newborns with a very low birth weight is indicative of a significant risk of BPD. Additionally, DHA is responsible for the synthesis of a potent anti-inflammatory compound known as N-acyl ethanolamine. This compound has been shown to reduce the production of IL-6 in adipocytes and monocyte chemotactic protein- 1, hence improving metabolic health. It is possible that the hydroxyl radical scavenging ability that has been observed to be

improved in rat fetuses that have been treated with DHA would mitigate the effects of oxidative stress on the developing brain.[41]

Through the use of a series of lipases, the liver is the primary organ that is responsible for receiving triglycerides from dietary fat. The liver then extracts the nonesterified fatty acid, which is then saturated and extended in the endoplasmic reticulum to produce its longer chain and more unsaturated materials. These compounds include arachidonic acid (ARA) (C20:4n-6) and docosahexaenoic acid (DHA) (C22:6n-3). Not only can these long-chain polyunsaturated fatty acids (LCPUFA) produce a variety of prostaglandins, but DHA metabolites also produce resolvins, which are also capable of contributing to the reduction of inflammation". Additionally, DHA is the most dominant fatty acid in retinal rods and cones, as well as the cerebral cortex, and it has a significant impact on the function of these structures.[41]

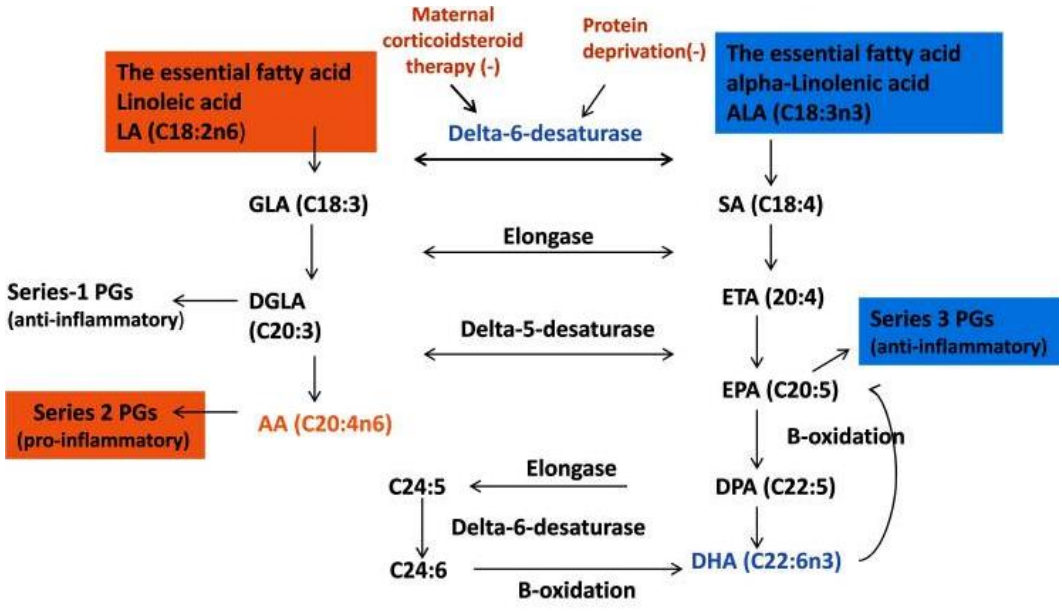


Figure : The pathway of the biosynthesis of DHA

Docosahexaenoic acid, is a kind of longer chain PUFA that plays a part in the intellectual & vision development of infants, in addition to their immune system function.

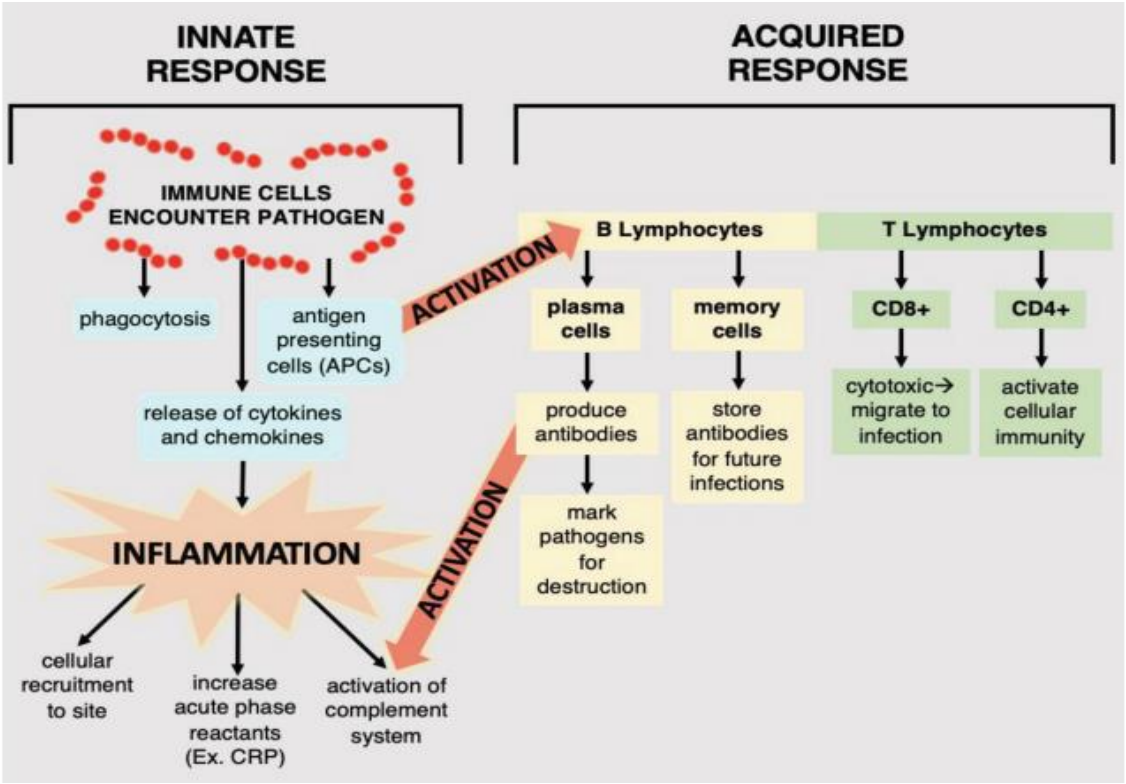
Despite the fact that DHA is essential for all children, it is of utmost significance for premature infants who were born early in the third trimester or earlier before that. As a whole, it is anticipated that the accumulation of fetal DHA will amount to 10 grams, with the bulk of this happening during the third trimester. By transmitting DHA more often than other fatty acids like LA and ALA, the placenta is able to facilitate the accumulation of docosahexaenoic acid (DHA). During the third trimester of pregnancy, the intrauterine accretion rate of DHA is around 43 mg/kg/day, which is betweeno 42-67 mg/day.[39]

In a post-hoc analysis of their KUDOS study, Shireman et al. found that a daily DHA intake of 600 mg led to a reduction in the time of hospitalization for the newborn. As a result, requiring mothers to take DHA on a daily basis might potentially contribute to cost savings for the healthcare system.[39]

There are a number of factors that may lead to a deficiency in DHA in premature babies. These factors include a failure to gather DHA in utero during the third trimester, a problem in converting precursor fatty acids to DHA in large amounts, and an inadequate intake of DHA after birth. Infants who are born at the earliest possible gestational age have the highest likelihood of having a shortage in DHA. The intake of omega-6 and omega-3 fatty acids from all sources was investigated in this longitudinal research of babies under the age of 28 weeks. It was established by the authors that the total amount of DHA that babies got after six weeks was only 36.6% of what they would have received if they had been developing inside of their mothers". Infants born with an extremely LBW who are given intravenous lipids for an extended period of time see a significant decrease in their levels of DHA.[39]

NEONATAL IMMUNE RESPONSE:

Newborn immunity includes both innate as well as acquired immunity. Newborn innate immunity relies on phagocytes and the complement cascade to combat infection.The innate system governs self-tolerance and works with acquired immune systems to create memory responses to previously encountered antigens. Acquired immunity is a slow but more of a targeted immune response triggered by lymphocytes & maternally acquired antibodies. Neonatal immune deficits affect both systems, making them more susceptible to infection.[42]



Neonatal immune system

Due to the fact that the innate immune system of a neonate is not yet fully developed, it is more vulnerable to sepsis than the immune system of an adult. The development of the skin and its ability to operate as a barrier become progressively immature as the gestational age declines. In addition, the use of intrusive equipment such as central vein catheters and tubes utilised in intubation, on a regular basis might result in a breach of

the physical barrier. The ability of neutrophils to migrate and phagocytose is decreased in newborns, and the amount of neutrophils in the body becomes less numerous. Monocytes are shown to be present in greater numbers as the gestational age decreases; nevertheless, their recruitment and chemotaxis are hindered, which results in a diminished inflammatory response despite the increasing availability of monocytes. These antigen-presenting skills of neonatal monocytes are already compromised, and they become much more diminished if the infant is born prematurely.[42]

Exposure is necessary for the acquired immune system to function well. Neonatal immune systems develop cellular memory to respond to infections experienced outside the womb. Because of the sterility of the uterine environment, neonates do not have past exposure to establish a memory response. As a result, they lack acquired immunity. The neonate's immune response to maternal antigens is reflected in its anti-inflammatory pathway, reduced cytotoxicity of CD8+ cells, and preference for suppressor cells. While useful in pregnancy, these anti inflammatory properties make newborn more susceptible to infection.[42]

All neonates have less IgG levels, which are amplified in the preterm infant. Transplacental IgG acquisition starts in second trimester & peaks in last weeks of gestation. Neonates born before this shift are at a higher risk of infection.[42]

In response to bacterial infection & tissue damage, the liver generates CRP, which is a protein that is produced during the acute phase. Before immunoglobulins are produced, CRP is produced during the development of the fetus. The levels of CRP in older children who have bacterial and fungal infections increase, but the levels remain low when they have viral illnesses. In both preterm and term neonates, the presence of CRP levels alone may be indicative of bacterial infection. Despite the fact that reference values for serum CRP have

been established for infants, there is a lack of information available on other immunological and inflammatory markers.[4].

The purpose of the study conducted by Wendel K and colleagues [43] was to determine the impact that supplementation with "ARA and DHA had on the systemic inflammation of very preterm newborns and to identify the clinical parameters that are linked with early inflammation.Based on the results of a randomized clinical trial (the ImNuT study), a secondary analysis was performed. From the second day of life until 36 weeks postmenstruation, infants with a gestational age (GA) of less than 29 weeks were randomly allocated to receive either a daily enteral supplement comprising ARA 100 mg/kg and DHA 50 mg/kg (ARA:DHA group) or MCT oil (control group). The ARA:DHA group received the supplement, while the control group received MCT oil. They assessed ARA, DHA, and four proinflammatory cytokines (IL-1β, IL-6, IL-8, and TNF-α) in serial dried blood samples from birth to day 28. These samples were collected from the mother's blood.The ARA: DHA group had considerably less amount of IL-6 than the control group from day 3 to day 28. The mean difference in AUC log10 (95% CI)" was 0.16 (0.03-0.30) picogram/millilitre ($p = 0.018$), which indicates that statistically noteworthy difference was present. Levels of cytokines & amounts of ARA or DHA in the blood were not shown to be associated with one another. Throughout the first four weeks of life, there was a connection between a lower GA and greater levels of all cytokines. This correlation worked independently.

Researchers Fadl DK et al [44] explored the potential immunomodulatory impact of supplementing preterm neonates in the NICU with docosahexaenoic acid (DHA). Additionally, they evaluated the effect of DHA supplementation on prevention or decrease of the incidence of necrotizing entero-colitis. In this prospective RCT, 67 newborns with a GA of 32 weeks or less & birth weight of 1500 grams or less were randomly alloted to either the

DHA or control groups. The investigation was conducted in order to determine the association between the two variables.

Through the use of modified Bell's staging criteria, NEC was identified and staged in an objective manner. IL-1β measured twice: first at the beginning of therapy and again ten days later. Mortality and duration of stay in the NICU were also monitored. Research was carried out with thirty babies from each of the groups. When comparing the two groups in terms of the diagnosis & NEC staging , there was a difference that was statistically significant. A much greater percentage of change in amount of IL-1β was seen in the DHA group compared to the control group. Correlation that was shown to be statistically significant was found between changes in IL 1 β and the detection of NEC. In comparison to the control group, the DHA group saw a significantly shorter duration of stay in the ICU. In spite of the fact that the mortality rate (percentage) in the control group was higher than in the DHA group, there was no statistically significant difference between the two groups. The researchers came to the conclusion that the observations of the study reveal that oral supplementation of DHA can decrease the incidence of neonatal encephalopathy in preterm infants by modulating the production of regulatory cytokines.

For the purpose of determining whether or not ,DHA supplementation in prematurely born children increases the attention at 18 months of corrected age, Hewawasam E. et al. [45] conducted research. Beginning in the earlier days of birth and continuing until 36 weeks PMA, infants were randomly randomized to get either an oral emulsion containing higher-dose of DHA (60 mg/kg/ day) or no DHA at all (soya oil served as control). There were three activities that were included in the attention evaluation. Each of these tasks required the kid to concentrate on a toy, regardless of whether there was competition or a distractor for them. The most important result was that the youngster was able to concentrate on a toy for longer periods of time without being distracted by other things. Seventy-three of

the one hundred and twenty babies who were eligible to take part in the study were present for the main outcome.Between the groups, there was no discernible difference in the delay of distractibility . At the age of 18 months, the administration of oral DHA did not result in an improvement in attention span in prematurely born babies.

It was predicted by Valentine CJ and colleagues [46] that providing DHA supplements to moms who breastfeed very preterm babies would result in a reduction in the inflammatory signs associated with the newborn. There were a total of 27 mother-infant pairs who were registered at birth, and the women were given either 200 or 1000 milligrams of DHA each day. The milk &plasma samples were analyzed to detect the fatty acids and inflammatory markers it contained. There was a correlation between the amounts of RBC DHA and the reduction in inflammation that was seen in both the mother's and the baby's plasma. Due to the fact that maternal DHA supplementation has been shown to diminish inflammatory markers in infants, it may be inferred that DHA that is delivered via breastmilk has the capacity to reduce inflammation in infants.

As opposed to the 200 mg of DHA that is often included in prenatal supplements, Carlson SE and colleagues [47] postulated that a daily dose of 1000 mg of DHA would be desirable.This superiority study was done at three medical facilities in the USA. It was randomized, multicenter, double-blind, and adaptively designed. Women who were pregnant with a single child and were between 12 and 20 weeks along in their pregnancy were eligible. Randomization was developed using SAS® in blocks of four, according to the site. Before thirty days had passed after the last delivery, the persons in charge of managing the trial were uninformed of the therapy. Extreme pretreatment was the key result, evaluated according to dosage and enrollment DHA status (low/high). Using the intention-to-treat method, Bayesian posterior probabilities (pp) were computed for the predicted outcomes of effectiveness and safety.

With the aim of determining the status of LCPUFAs in severe preeclampsia and premature birth, Irwinda et al. [48] conducted a research. There were 104 pregnant women who participated in a cross-sectional research. These women were divided into three groups: those with normal pregnancy, those with severe preeclampsia, and those who had preterm delivery. The use of gas chromatography/mass spectrometry allowed for the determination of the proportion and concentration of total LCPUFA, omega-3, alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), omega-6, linoleic acid (LA), and arachidonic acid (AA) in the blood. Different types of analysis, including ROC, bi & multivariate were carried out. When compared to the control group, those with severe preeclampsia had the highest total PUFA concentration and the lowest DHA percentage. Additionally, they had a sustantially greater Omega-6 to Omega-3 ratio and a lower omega-3 index. When compared with controls, deliveries which happened preterm was associated with significant reductions in omega-3 concentrations as well as significant reductions in omega-6 derivatives

Between November 2022 and March 2023, Aziz MA et al [49] did a study ,where they investigated the levels of DHA and EPA in a total of 44 pre-term and 44 term infants who were born in a tertiary hospital in the province of West Java in Indonesia. In this research, a total of 88 patients were recruited from a tertiary hospital located in West Java Province, Indonesia. Among these patients, 44 were born preterm (with a gestational week of less than 37) and 44 were born term (with a gestational week of 37 or more). In the period beginning in November 2022 and ending in March 2023, an observational and cross-sectional research was conducted. With the intention of evaluating the amounts of DHA and EPA in the mother, an enzyme-linked immunosorbent assay test was used. In order to do statistical analysis on the results, IBM SPSS 24.0 was used.In patients who were born prematurely, the average levels of DHA and EPA in the mother were significantly lower than those in patients

who were born at term. On the other hand, it was discovered that patients who had preterm deliveries had considerably lower levels of maternal DHA and EPA. It was shown that pregnant women who adhered to dietary requirements and consumed an adequate amount of omega-3 LCPUFA in the early stages of their pregnancy had a decreased chance of having their babies born prematurely.

An investigation was conducted by Jisun So and colleagues [50] to evaluate the effects of EPA and DHA supplementation on the inflammatory response of monocytes and the PUFA SPM lipidome. Following a baseline phase that lasted for four weeks, nine men and twelve postmenopausal women (reaching the age range of fifty to seventy-five) who were experiencing chronic inflammation were randomly allocated to two 10-week periods of treatment with three grams of EPA and DHA per day, followed by a 10-week washout period.There were distinct differences in the effects that both omega-3 fatty acids had on the inflammatory response of monocytes, with DHA having a more extensive effect in decreasing the levels of pro-inflammatory cytokines. These varied effects may have been mediated by several groups of PUFA derivatives, which suggests that SPM and related intermediates possess immunomodulatory capabilities.

A method of supplementing with DHA was devised by Baack ML [51] and their collegues in order to get over these many obstacles. This investigation was designed to evaluate the feasibility, acceptability, and effectiveness of daily oral DHA supplementation of around (50 mg/day) in addition to traditional food for premature neonates (24-34 weeks GA) starting in their 1st week after birth. Study was done in a controlled, randomized, and double-blind manner. When preterm babies were administered DHA (n = 31) or a placebo (n = 29), blood FA levels were determined at the beginning of the study, after all feedings were finished, and when the time for release drew near. For the purpose of comparison, term mates (n = 30) were investigated. infants born prematurely have lower amounts of DHA at the beginning of

their lives.babies that were given DHA exhibited a gradual increase in the amount of circulating DHA over the course of time (from 3.33 to 4.09 weight percent or 2.88 to 3.55 mole percent, $p < 0.0001$). On the other hand, babies who were given a placebo (and were receiving traditional neonatal feeding) did not exhibit any increase (from 3.35 to 3.32 weight percent or 2.91 to 2.87 mole percent). At discharge, preterm infants exhibited lesser DHA levels in the blood than their term counterparts , despite the fact that they received a higher amount of DHA supplementation. As far as unfavorable occurrences were concerned, there were no differences between the groups. Ensuring that preterm neonates get daily enteral DHA supplementation is not only possible but also helps to prevent deficiencies.

An investigation conducted by Eruk kung et al, on newborns admitted between September 2015 -19 reviewed retrospectively revealed Serum IL-6, can be beneficial in detecting sepsis in newborns and cut off values were established at Day 1, Day 2-7, After Day 7 were 80, 40, 30pg/ml respectively [52]

MATERIALS & METHODS

MATERIALS AND METHODS:

Source of data: All clinically stable early preterm neonates (32- 34 weeks) delivered at RL Jalappa hospital during the period of study and consented to be a part of the study.

Study design: An Open labelled Randomised control trial

Study period: 1 year(September 2022 to December 2023)

Inclusion Criteria:

- Early preterm neonates (32-34 weeks) delivered at RL Jalappa Hospital whose parents had consented to be a part in the study.

- Clincally stable neonates to begin enteral feeding

Exclusion Criteria:

-Neonates with congenital anomalies

-Neonates born to Mothers with PPROM history

-Neonates with contraindication for enteral feeding

-Neonates with maternal use of omega-3 supplements

Sample size calculation:

Sample size was derived from the percentage difference in change of IL 1 b levels between the DHA group, and the control groups. it was found that % change in IL- 1b levels in DHA group was 73. 3% and 26% in the control group respectively from the study by **Dina Khaled abou el Fadl et al**.[44] Using these values in the below mentioned formula

$$N = \frac{2 (Z_{\alpha/2} + Z_{\beta})^2 P (1-P)}{(p_1 - p_2)^2}$$

Where,

"$Z_{\alpha/2=} Z_{0.05/2}=Z_{0.025}$ = 1.96 at type 1 error of 5%

$Z_{\beta}=Z_{0.20}$= 1.28= At 80% power

$p_1 - p_2$= Difference in proportion in the two different groups = 46.6%

P= Pooled prevalence = [Proportion in DHA group (p_1) + Proportion in control Group (p_2)]/2 = [73.3 + 26.7]/2 = 50"

$N = \frac{2 \times 50 \times 50 (1.96 + 0.84)^2}{46.6 \times 46.6} =$ 19 in each group

Considering Non response rate of 10%, 19 + 1.9 = 20.9 ≈ **21 subjects** will be included in each group.

Minimum number to be taken in our study is 21.But we are considering 25 from each group.

Instead of IL-1b, Il- 6 is considered in our study.

METHODOLOGY:

Study conducted in "R.L Jalappa hospital and Research Centre, affiliated to Sri Devaraj Urs Medical College, a constituent of Sri Devaraj Urs Academy of Higher Education and Research".

Babies recruited are randomly allocated by computerised RCT into blocks containing equal number of DHA group or control group and followed up for 10days.

This study started after parents have given their consent. Based on the inclusion criteria all the neonates enrolled in the study.

Information obtained included - Gestational age at birth, mode of birth, gender, weight, length and head circumference of the new born.

WEIGHT- A scale that uses a holder or pan for calculating weight used. The digitally validated tray can measure in increments of at least 10g, making it suitable for use with infants.

LENGTH- Infantometer from Harpendens used to determine the length . It has a flat wooden base and two standing planks vertically at the two ends balancing the base. On the

one end plank is securely made to rest on the flat board which is called the head piece. The other end of the instrument, which is a movable vertical plank to find the length of the infants (foot piece). The length of the baby will be read directly on a calibrated reading strip in the middle of the board.

HEAD CIRCUMFERENCE - is the highest measurement of the head taken with a measuring instrument placed across the occiput, which is situated behind the ears, and the supraorbital ridge, which are positioned in front of the head**.** It is measured using a non stretchable measuring tape.

Postnatal weight loss (%) will be calculated using

formula: (birth weight - minimum weight) / birth weight × 100%

Growth parameters at birth

Weight gain /loss at day 10 of discharge measured .

DHA group received 100mg/day(1ML) of AQUA OMEGA DHA DROPS(NUTRIGOLD OMEGA3 BRAND) administered by oral route along with standard feeding for neonates.

1ML OF AQUA OMEGA DROPS CONTAIN:

DHA- 100MG EPA 50MG TOTAL OMEGA 3 - 200MG.

Control group received only the standard neonatal feeding.

Complications like

-**Neonatal sepsis,** In babies less than 28 days old, a condition known as neonatal sepsis may develop when an infection spreads to their circulation.

- **Necrotising enterocolitis** : It commonly affects the patients of lower birth weight and is a condition where the intestinal tissue becomes inflamed and thereafter dies and peels off. Common in infants who are born prematurely or those who are already in poor health.

NEC is a condition in which the intestine of a newborn is inflamed, and this mostly occurs in premature babies within the first 2-3 weeks after birth.

- Bronchopulmonary dysplasia It is a type of chronic lung disease that happens in pre term neonates who receive supplemental oxygen and mechanical ventilation.

- Retinopathy of prematurity noted.

ROP is an eye disorder that happens because of the development of abnormally of blood vessels in the retina of premature babies.

ROP commonly occurs in infants born prematurely, before the 31st week of pregnancy and those with a birth weight of approximately (1,250 grams) or less. However, ROP in most cases is self-limited and does not cause any harm to the baby. This is because advanced ROP as earlier noted can lead to the complete loss of vision or even blindness.

Inflammatory markers like:

C Reactive Protein (CRP),

Procalcitonin measured by **Vitros ECI**

Interleukin- 6 (IL-6) measured on Day 10 of admission estimated by **AGAPPE i CHROMA**

Statistical analysis:

Data entered in MS excel and analyzed using SPSS 22 version software. Qualitative data presented in the form of Proportions and pie diagrams, bar charts used to represent graphically. Quantitative data presented as mean, standard deviation. Student's t test was the test of significance for quantitative data and chi-square test is test of significance for qualitative data. P value <0.05 considered as statistically significant.Medians were compared between study groups using Mann Whitney u test.

RESULTS

RESULTS

The present study is Randomized control trial consists a total of 49 babies allocated into 2 groups. Group 1 is DHA supplementation group and group 2 is control group.

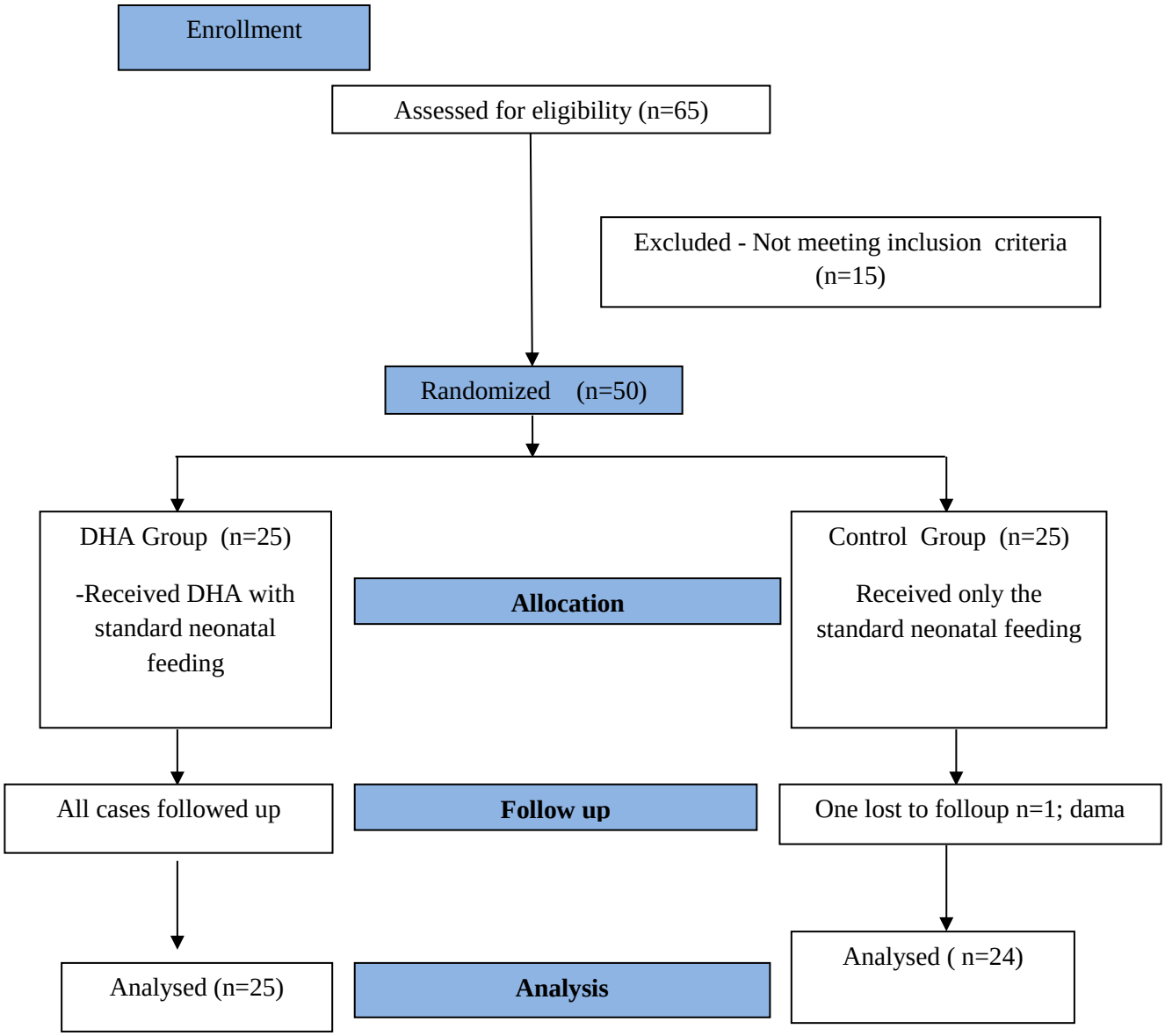
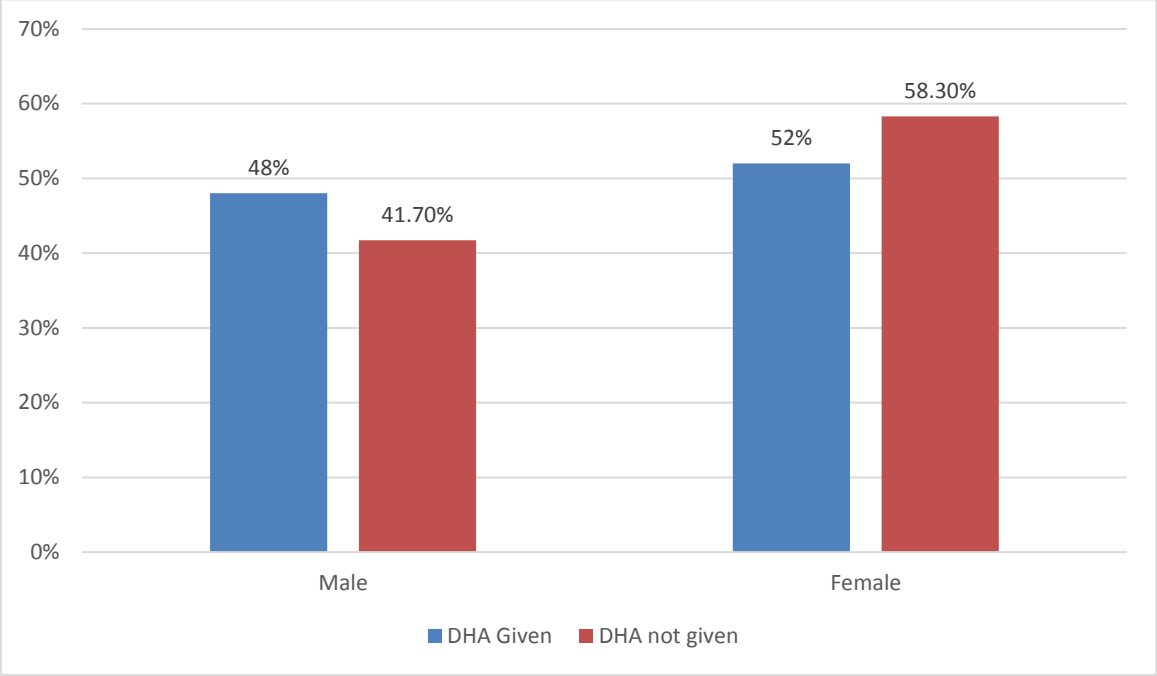


Table 1: Gender distribution among 2 groups

Sex	DHA given		Total
	yes	No	
Female	13(52.0)	14(58.3)	27(55.1)
Male	12(48.0)	10(41.7)	22(44.9)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Figure 1 : Gender distribution among 2 groups



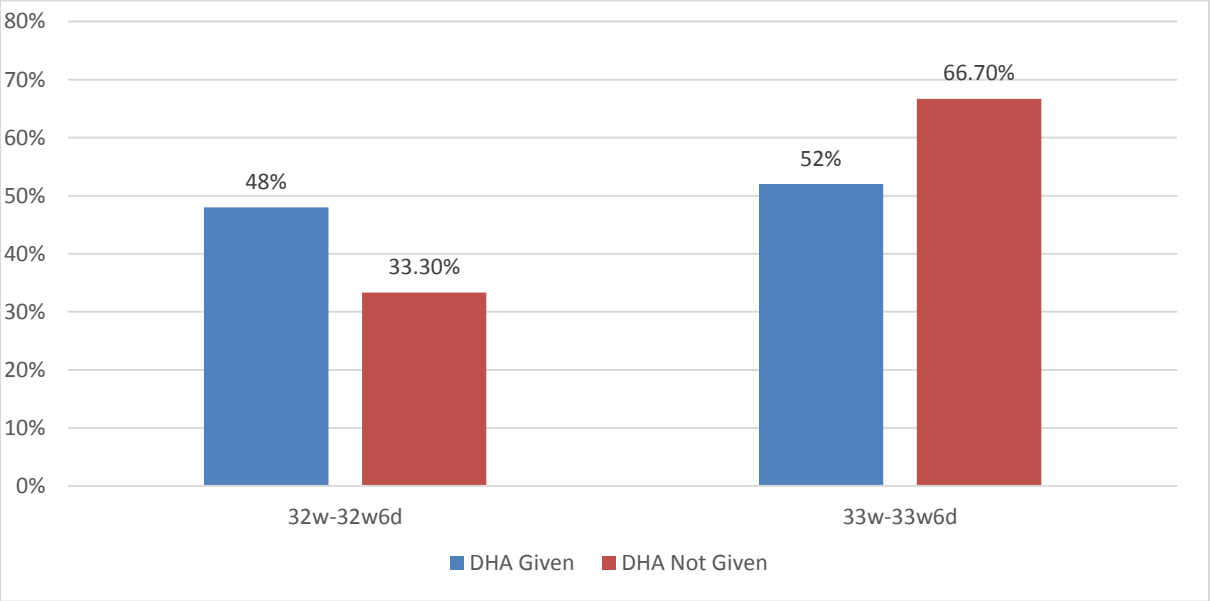
In the present study, the patients under DHA supplemented group has 13 female (52%) and 12 male (48%), the patients under control group has 14 female (58.3%) and 10 male (41.7%)

.

Table 2: Gestational age distribution Among 2 groups.

Gestational age	DHA given		Total
	yes	No	
32w to 32w6days	12(48.0)	8 (33.3)	20(40.8)
33w to 33w6days	13(52.0)	16(66.7)	29(59.2
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 2: Gestational age distribution Among 2 groups.



In the present study, patients under DHA supplemented group has gestational age of 32 weeks in 12 patients (48%) and gestational age of 33 weeks in 13 patients (52%). Patients undercontrol group has gestational age of 32 weeks in 8 patients (33.3%) and gestational age of 33 weeks in 29 patients (59.2%).

Table 3: Weight distribution in study population (n=49)

Weight	Number	Percentage
<1.5 kg	12	24.4%
1.5 to 2kg	33	67.3%
>2 kg	4	8.1%

Fig 3: Weight distribution Among 2 groups.

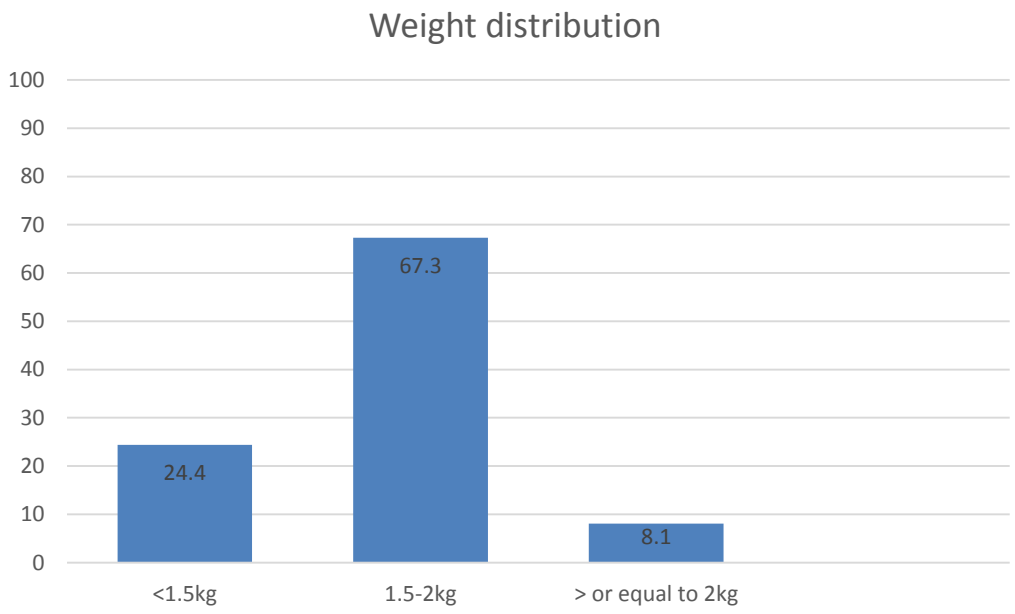
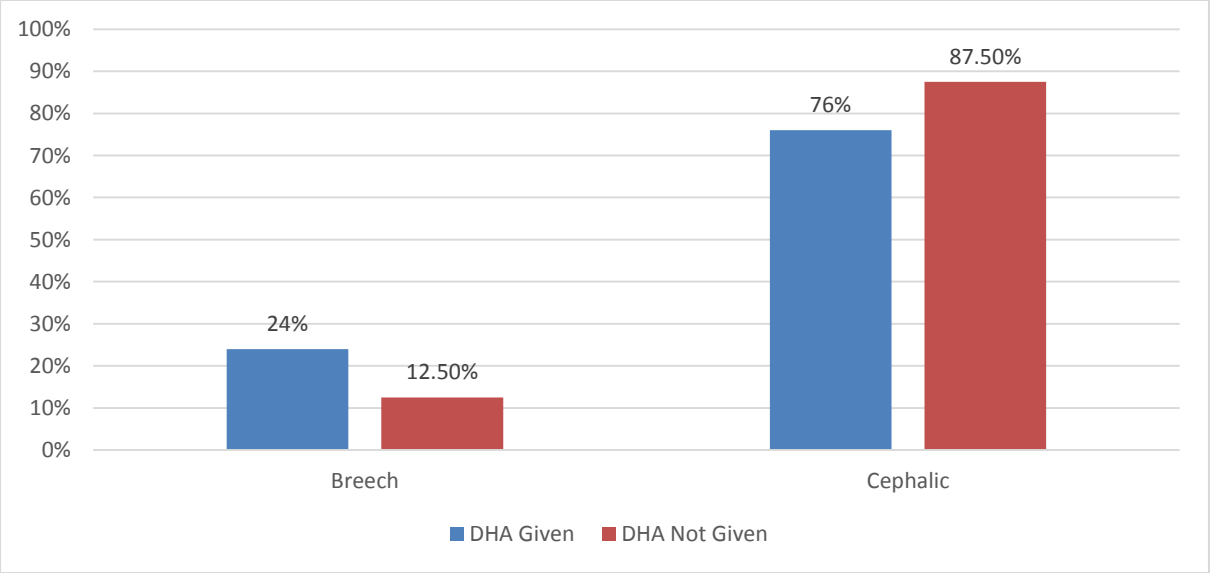


Table 3 and Fig 3 ; Depict distribution of study population according to weight. In the present study ,12 (52%) neonates were <1.5kg and 33 (67.3%) neonates were between 1.5-2kg , 4 (8.1%) neonates were equal to or greater than 2kg .

Table 4: Distribution based on presentation of neonate in 2 groups.

Presentation	DHA given		Total
	Yes	no	
Breech	6(24.0)	3(12.5)	9(18.4)
Cephalic	19(76.0)	21(87.5)	40(81.6)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 4: Distribution based on presentation of neonate in 2 groups.



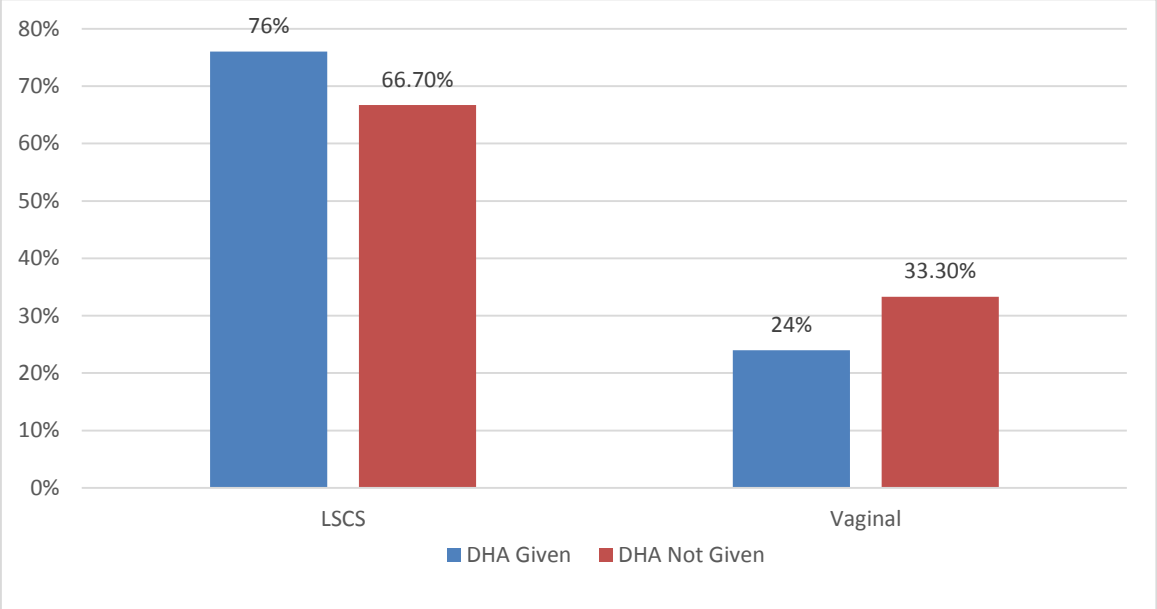
In the present study, patients under DHA supplementation has breach presentation in 6 patients (24%) and cephalic presentation in 19 patients (76 %) , Patients under control group has breach presentation in 3 patients (12.5%) and cephalic presentation in 21 patients (87.5 %).

Table 5: Distribution of mode of delivery between 2 groups

Mode of delivery	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	yes	no			
LSCS	19(76.0)	16(66.7)	35(71.4)	0.523 (0.470)	1.583 (0.454, 5.527)
Vaginal	6(24.0)	8(33.3)	14(28.6)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Statistical test used: Chi Square test: *p value<0.05 is considered statistically significant

Fig 5 :Distribution of mode of delivery between 2 groups



In the present study, patients under DHA supplemented group has LSCS delivery in 19 patients (76%) and vaginal delivery in 6 patients (24 %). Patients under control group has LSCS delivery in 16 patients (66.7%) and vaginal delivery in 8 patients (33.3 %).

Table 6:Distribution based on weight for gestational age(n=49)

Gestational classification	Number	Percentage
SGA	13	26.5%
AGA	36	73.4%
LGA	0	0

Fig 6:Distribution based on weight for gestational age

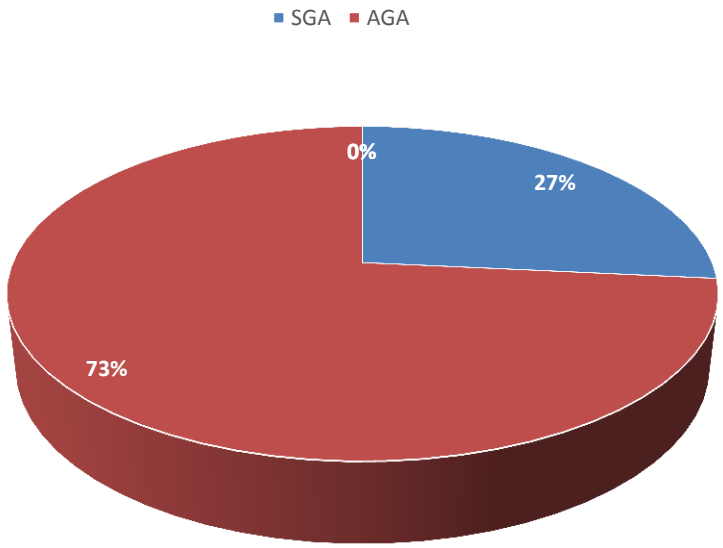
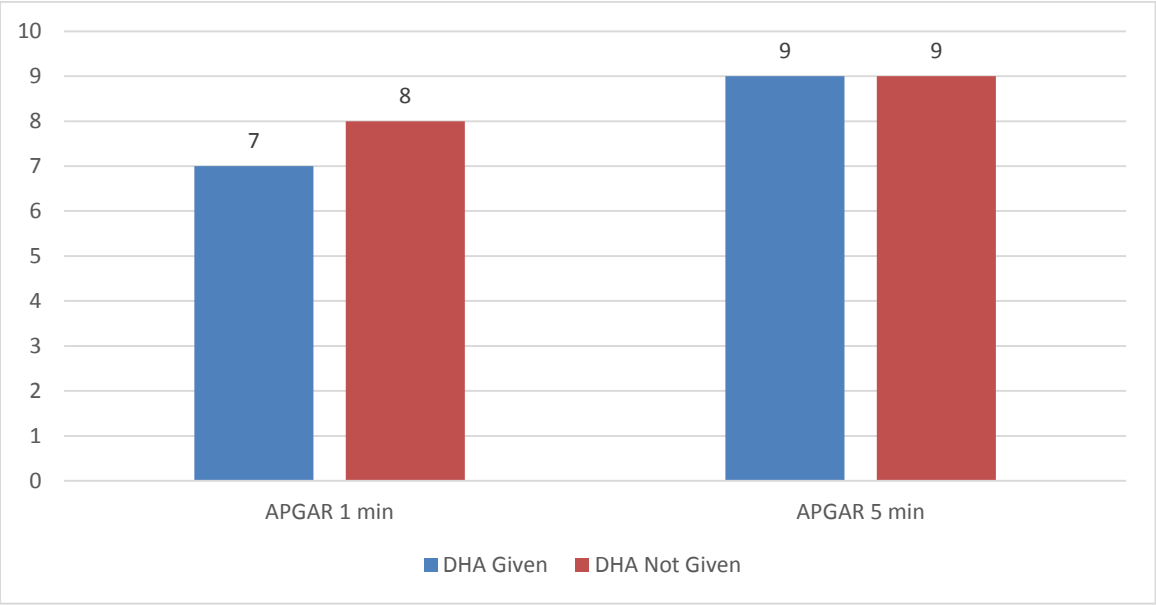


Table 6 and Figure 6 depict distribution of study population according to weight for gestational age. In the present study ,13(26.5%) neonates were SGA, 36(73.4%) were AGA

Table 7 : Distribution of APGAR score between 2 groups.

APGAR score	DHA given	
	Yes (n=25)	No (n=24)
1 min	7 (7,8)	8 (7,8)
5 min	9 (8,9)	9 (8,9)

Fig 7 : Distribution of APGAR score between 2 groups.

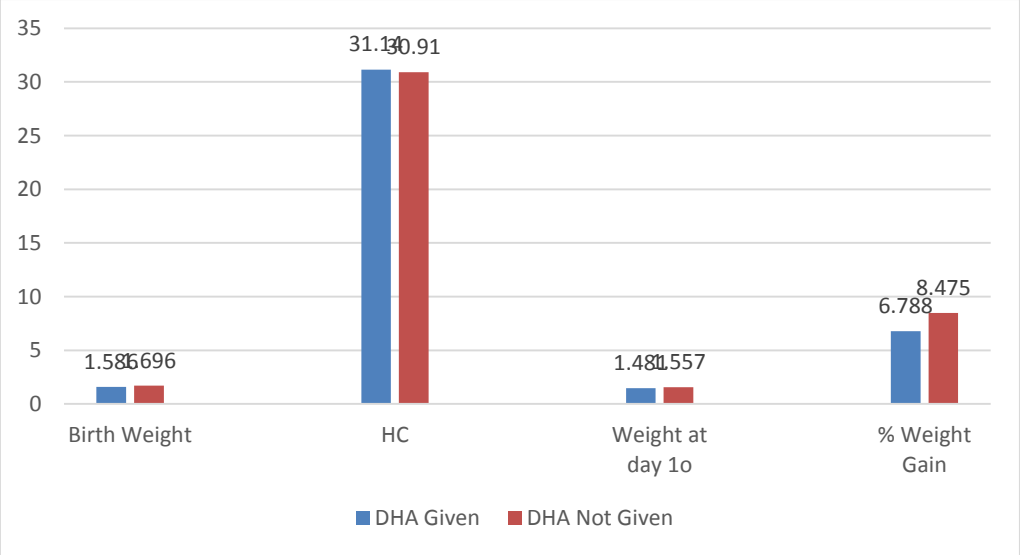


In the present study, patients under DHA supplemented group showed a APGAR score of 7 with lower and upper quartile of 7,8 at 1 minute & at 5 minutes APGAR score showed of 9 with upper and lower quartiles being 8,9 . Patients under control group showed a APGAR score of 8 with lower and upper quartile of 7,8 at 1 minute and at 5 minutes APGAR score showed of 9 with upper and lower quartiles being 8,9.

Table 8: Distribution of Birthweight, HC, Weight at day 10, % Weight gain, among 2 groups.

	DHA given	
	Yes (n=25)	**No (n=24)**
Birth weight	1.586 ± 0.313	1.696 ± 0.211
HC	31.14 ± 1.461	30.917 ± 0.637
Weight at day 10	1.481 ± 0.293	1.557 ± 0.199
% weight loss	6.788 ± 3.625	8.475 ± 3.927

Fig 8: Distribution of Birthweight, HC, Weight at day 10, % Weight gain, among 2 groups.

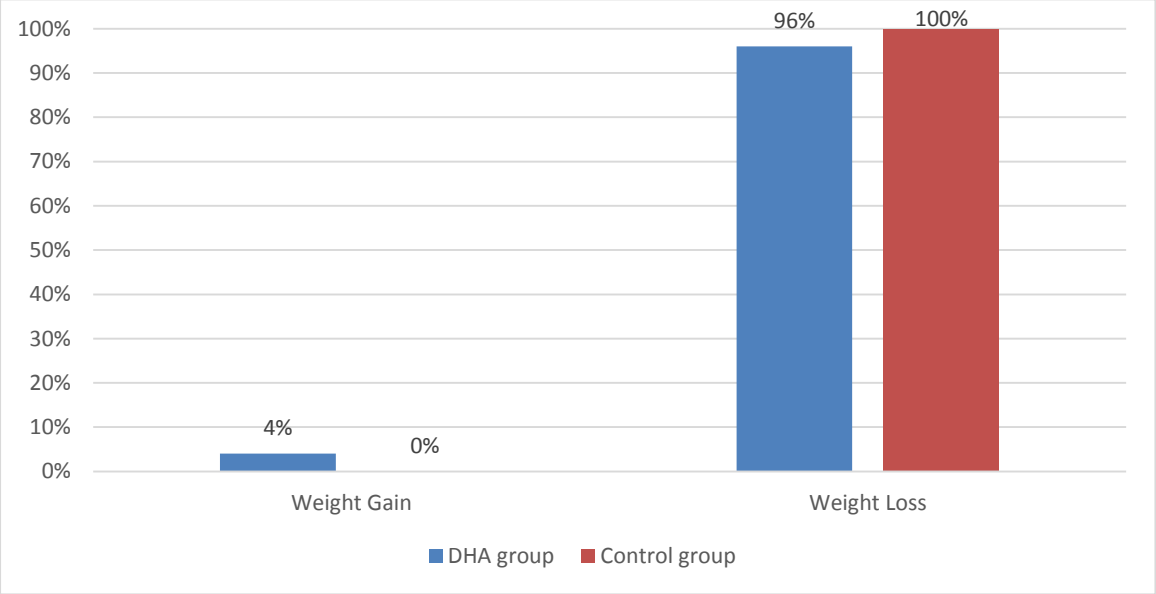


In the present study, in DHA supplemented group birth weight is 1.586 ± 0.313, HC is 31.14 ± 1.461, Weight at day 10 is 1.481 ± 0.293, % weight gain is 6.788 ± 3.625, whereas in control group birth weight is 1.696 ± 0.211, HC is 30.917 ± 0.637, Weight at day 10 is 1.557 ± 0.199, % weight loss is 8.475 ± 3.927.

Table 9: Presence of weight gain / loss among 2 groups

Weight	DHA given		Total
	yes	no	
Gain	1(4.0)	0	1(2.0)
Loss	24(96.0)	24(100.0)	48(98.0)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 9 : **Presence of weight gain / loss among 2 groups**



In the present study, in DHA supplemented group weight gain is seen in 1 patient (4%) whereas weight loss is seen in 24 patients (96 %). In control group, weight gain is not seen and weight loss is seen in 24 patients (100%)

Table 10: Distribution based on the Morbidity Pattern (n=49)

Morbidity Pattern	Number	Percentage
Neonatal respiratory distress	36	73.4%
Abdominal distension	9	18.3%
Vomitings	9	18.3%
Blood in Stools	0	0%
Hypoglycemia	0	0%
Hyperbilirubinemia	22	44.8%

Fig 10: Distribution based on the Morbidity Pattern

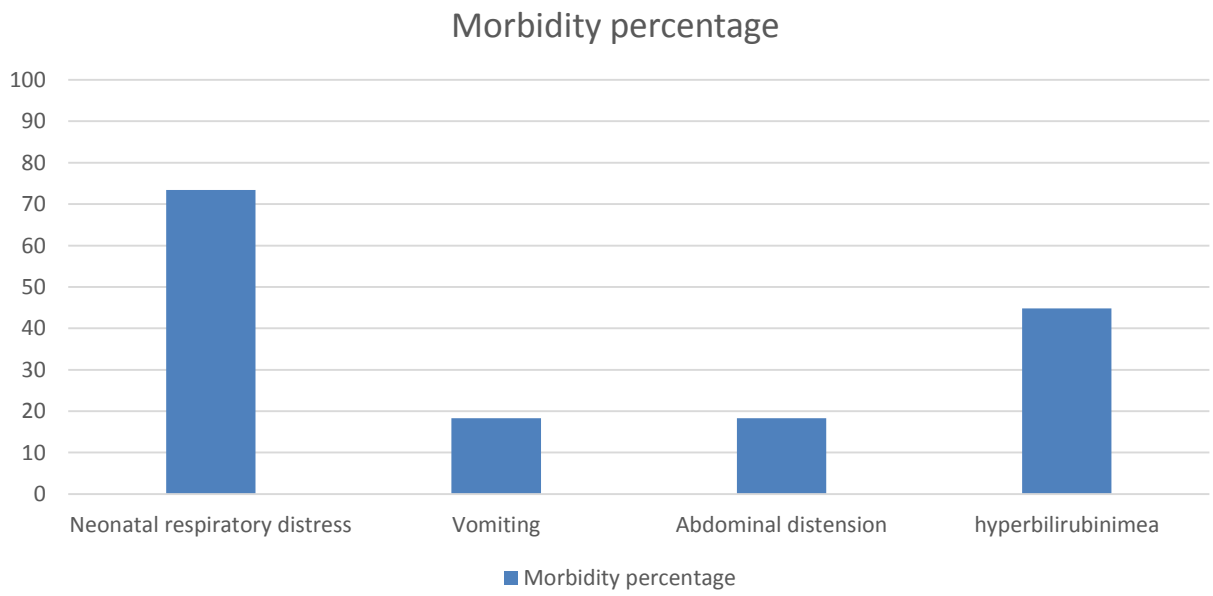
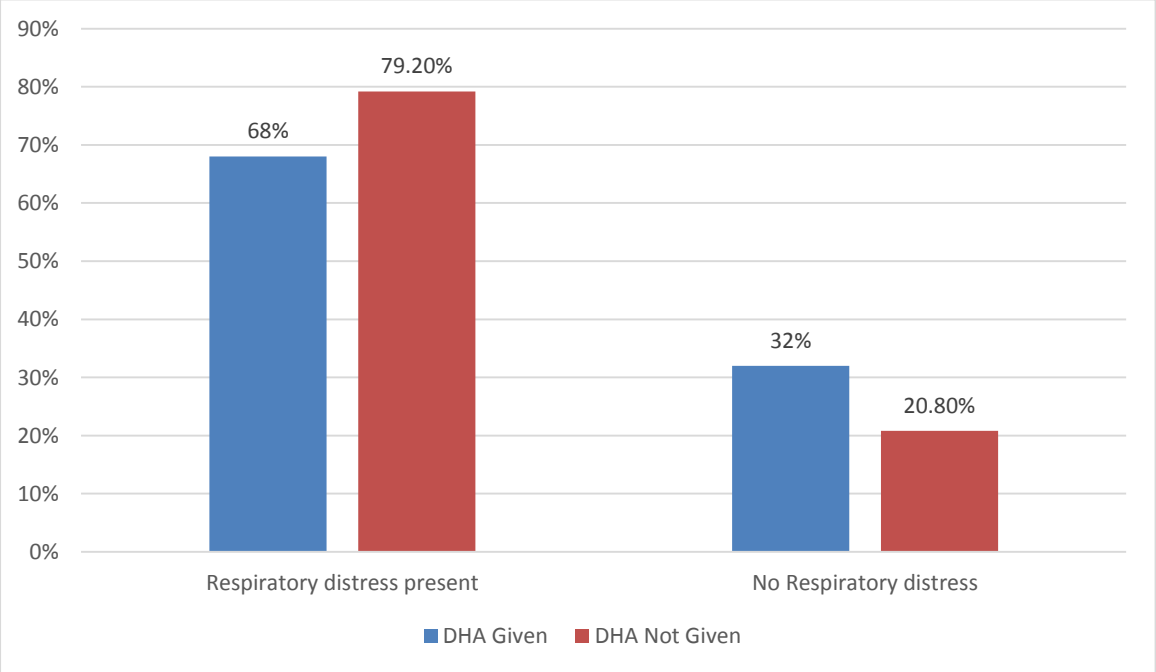


Table 11: Presence of respiratory distress in 2 groups

Respiratory distress	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	Yes	no			
Yes	17(68.0)	19(79.2)	36(73.5)	0.783 (0.376)	0.559 (0.153,2.041)
No	8(32.0)	5(20.8)	13(26.5)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Statistical test used: Chi Square test
*p value <0.05 is considered statistically significant

Fig 11: Presence of respiratory distress in 2 groups



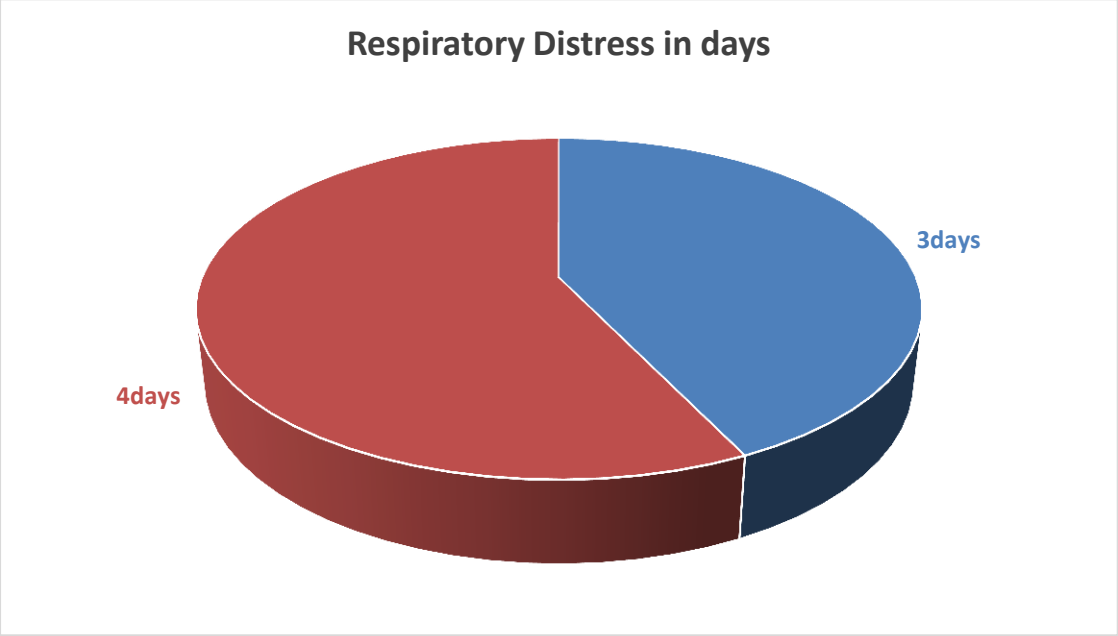
In the present study, in DHA supplemented group, respiratory distress is seen in 17 patients (68%) and no respiratory distress in 8 patients (32%). In control group, respiratory distress is seen in 19 patients (79.2%) and no distress in 5 patients (20.8%). P value is 0.376 indicating no statistical significant difference.

Table 12: Presence of Respiratory distress (in days) changes among 2 groups.

	DHA given		Test statistic	p value
	Yes (n=25)	No (n=24)		
Respiratory distress (in days)	3(3,5)	4(2.5, 5.5)	16.0	0.974

Statistical test used: Mann Whitney U test
*p value <0.05 is considered statistically significant

Fig 12: Presence of Respiratory distress (in days) changes among 2 groups.



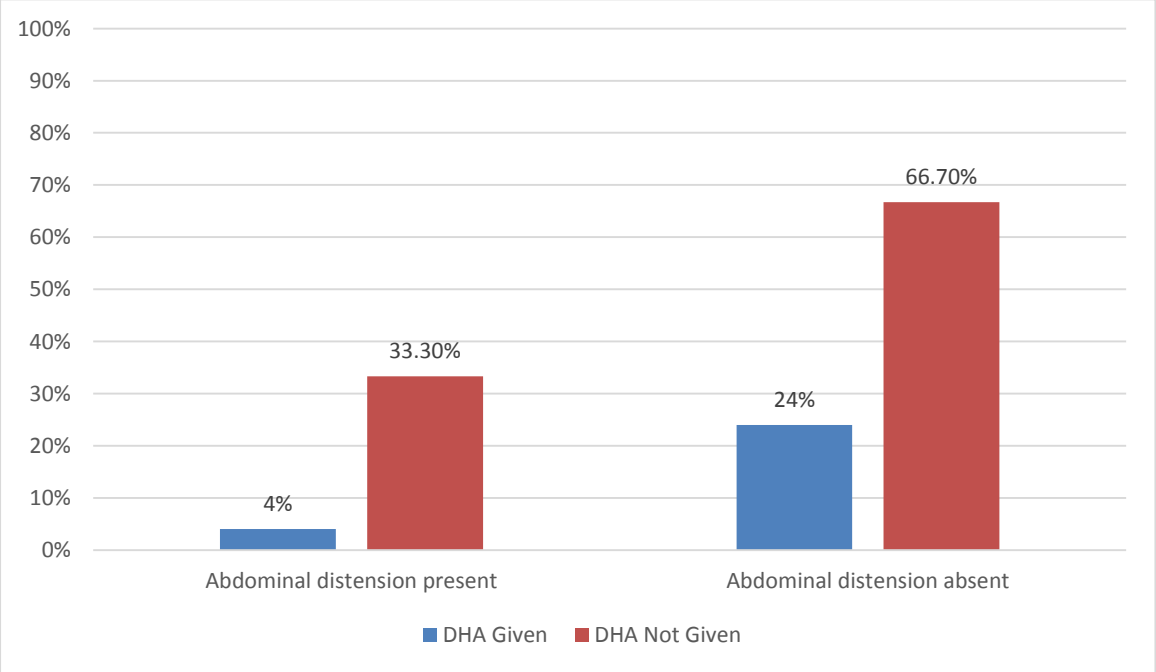
In the present study, in DHA supplemented group, Respiratory distress is seen for 3 days with min and max of 3 and 5 days whereas in control group, Respiratory distress seen for 4 days with min and max of 2.5 and 5.5 days. p value of 0.974 indicating statistically it is not significant.

Table 13: Presence of abdominal distension in 2 groups

Abdominal distension	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	Yes	no			
Yes	1(4.0)	8(33.3)	9(18.4)	7.027 **(0.011*)**	0.083 (0.009, 0.732)
No	24(96.0)	16(66.7)	40(81.6)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Statistical test used: Fishers exact test
*p value <0.05 is considered statistically significant

Fig 13: **Presence of abdominal distension in 2 groups**



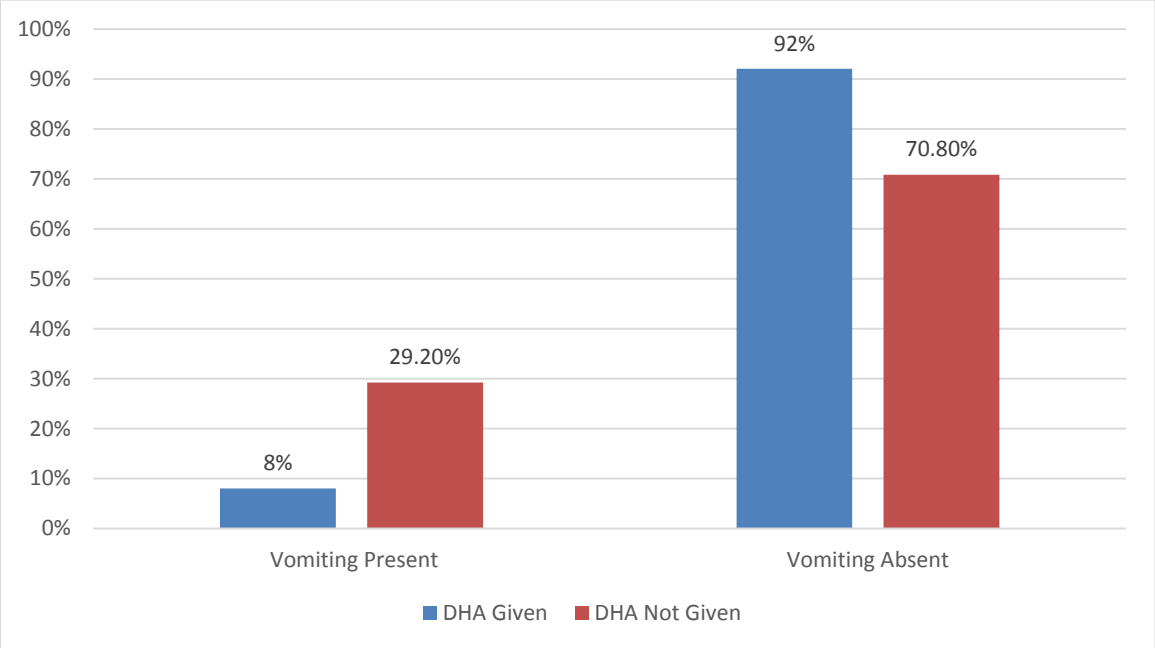
In the present study, in DHA supplemented group, abdominal distension is seen in 1 patient (4%) and is absent in 24 patients (96%) .In control group ,abdominal distension is seen in 8 patients (33.3%) and absent in 16 patients (66.7%). P value is 0.011 suggesting a statistically significant difference.

Table 14: Presence of vomiting among 2 groups

Vomiting	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	yes	no			
Yes	2(8.0)	7(29.2)	9(18.4)	3.659 (0.074)	0.211 (0.039,1.147)
No	23(92.0)	17(70.8)	40(81.6)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Statistical test used: Fishers exact test
*p value <0.05 is considered statistically significant

Fig 14: Presence of vomiting among 2 groups



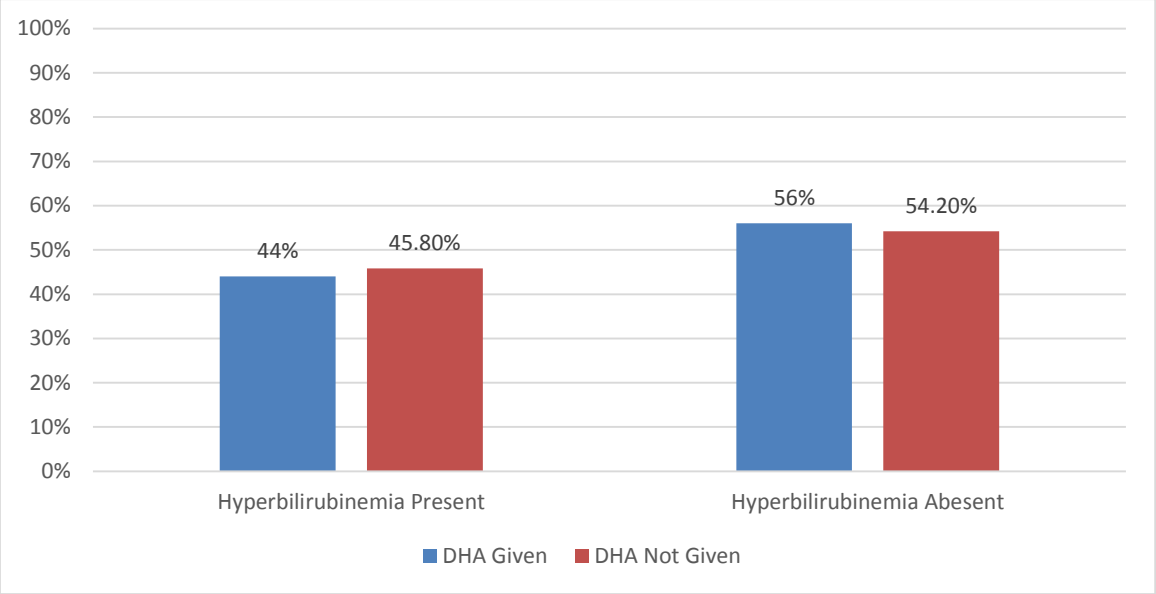
In the present study, in DHA supplemented group ,vomiting is seen in 2 patients (8%), absent in 23 patients (92%). In control group vomiting is seen in 7 patients (29.2%) and absent in 17 patients (70.8%).p value of 3.659 indicating statistically not significant.

Table 15: Presence of Hyperbilirubinemia among 2 groups.

Hyperbilirubinemia	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	yes	no			
Yes	11(44.0)	11(45.8)	22(44.9)	0.017 (0.897)	0.929 (0.301, 2.864)
No	14(56.0)	13(54.2)	27(55.1)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Statistical test used: Fishers exact test
*p value <0.05 is considered statistically significant

Fig 15: Presence of Hyperbilirubinemia among 2 groups.

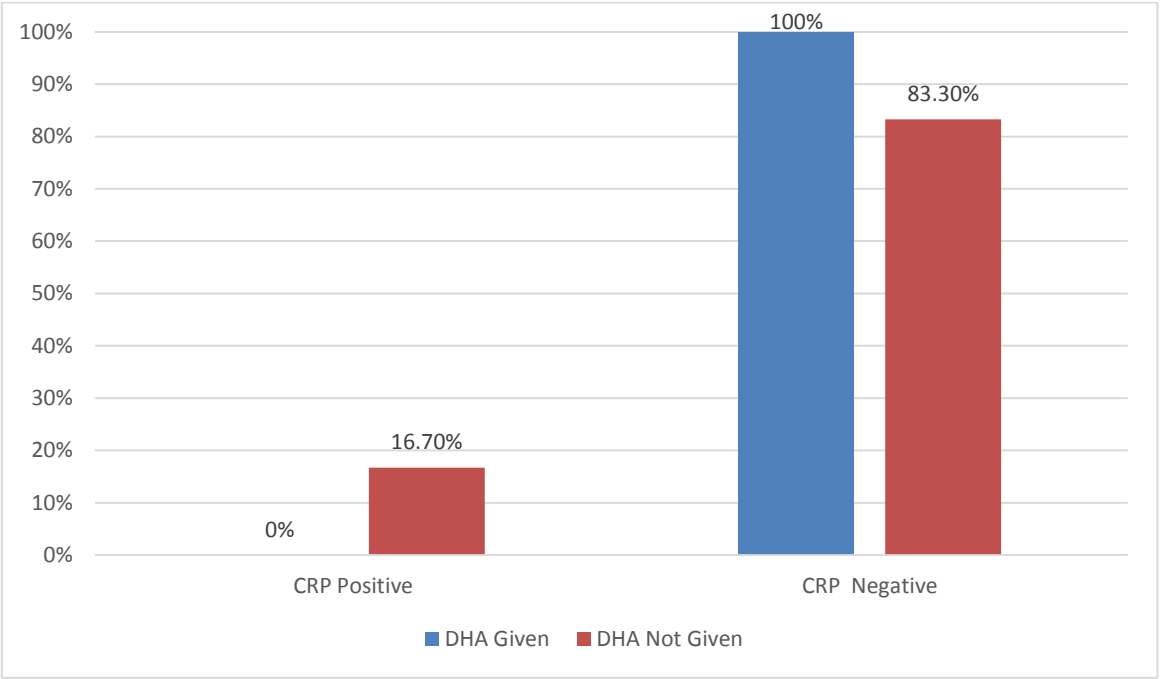


In the present study, in DHA supplemented group , Hyperbilirubinemia are seen in 11 patients (44%), absent in 14 patients (56%). In control group Hyperbilirubinemia are seen in 11 patients (45.8%) and absent in 13 patients (54.2%).p value of 0.017 indicating statistically not noteworthy.

Table 16: CRP among 2 groups.

CRP	DHA given		Total
	yes	no	
Positive	0	4(16.7)	4(8.2)
Negative	25(100.0)	20(83.3)	45(91.8)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 16: CRP among 2 groups.



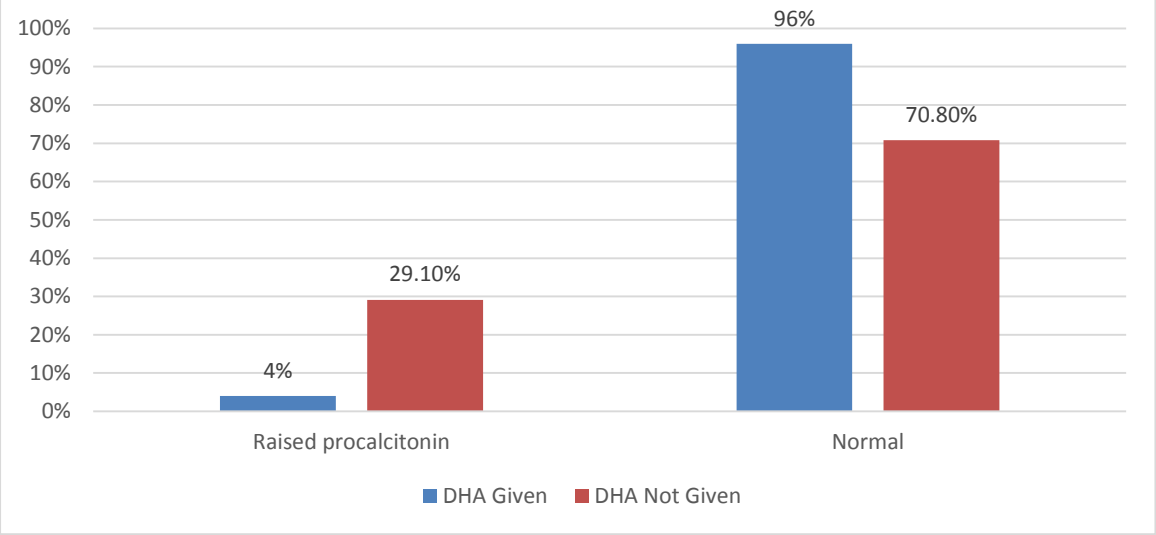
In the present study, in DHA supplementation group , CRP negative in all 25 patients (100%). In control group positive CRP are seen in 4 patients (16.7 %) and CRP negative seen in 20 patients (83.3 %).

Table 17: Procalcitonin values among 2 groups.

Statistical test used: Fishers exact test *p value<0.05 is considered statistically significant

Procalcitonin on Day 10	DHA given		Total	Test statistic	p value
	yes	no			
Raised (>0.50ng/ml)	1(4)	7(29.1)	8(16.3)	5.677	0.017*
Normal	24(96)	17(70.8)	41(83.6)		
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**		

Fig 17: Procalcitonin values among 2 groups



After 3 days of life ,S.Procalcitonin, normal range is till 0.50ng/ml according to BRAHMS PCT Assay studies.

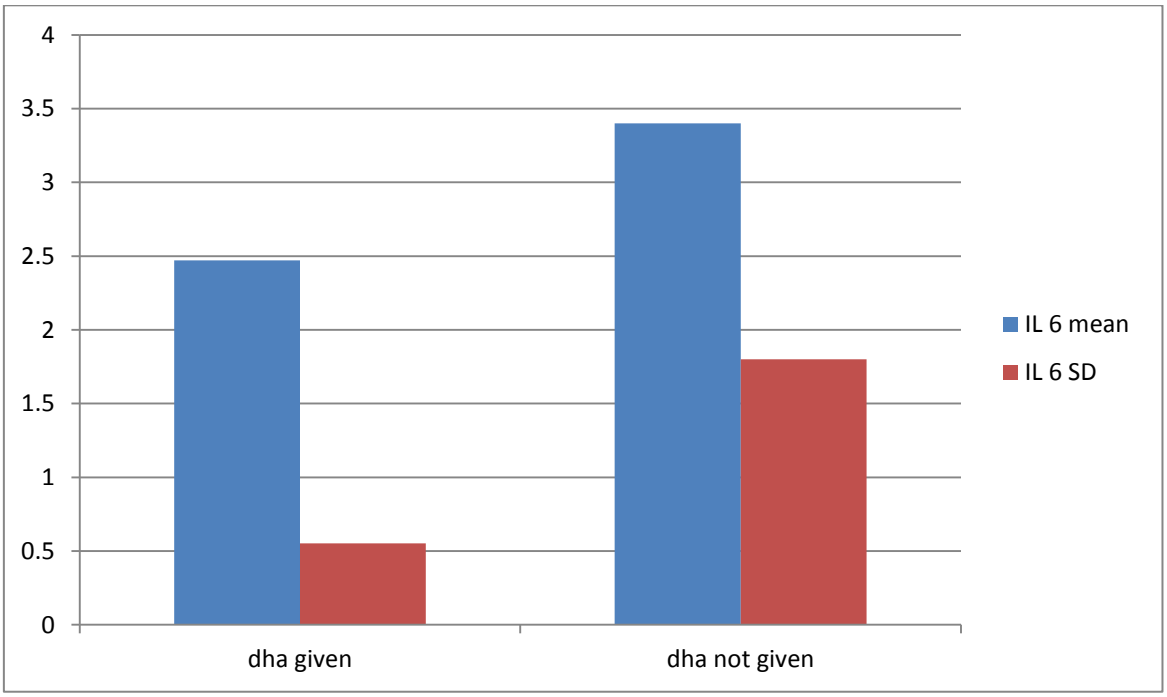
-Here, In DHA group, 1 case were having procalcitonin above normal range, In control group, 7 cases have procalcitonin level beyond normal range, p value is < 0.05 which tells us they were statistically significant.

Table 18: Mean procalcitonin values among 2 groups.

† Mann Whitney U test *p value <0.05 is considered statistically significant

	DHA given		Test statistic	P value
	Yes(n=25)	No(n=24)		
Procalcitonin	0.27 ± 0.152	0.72±0.930	2.388†	**0.029***

Fig 18: Mean procalcitonin values among 2 groups.

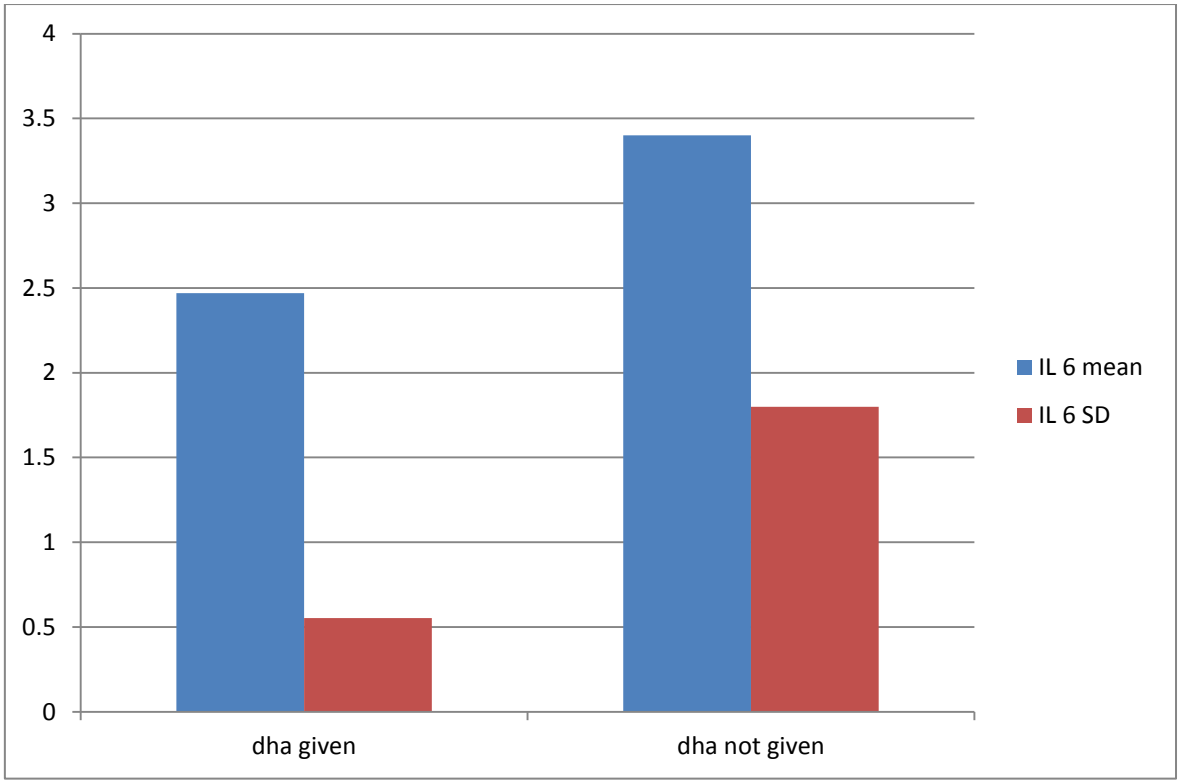


Procalcitonin is 0.27 ± 0.152 in DHA given group,whereas in (group 2) control group Procalcitonin is 0.72±0.930. P value is 0.029 ,which indicates a statistically significant difference among 2 groups.

Table 19: Il-6 values among 2 groups.

	DHA given		Test statistic	P value
	Yes(n=25)	No(n=24)		
IL 6	2.47+ 0.552	3.40±1.80	2.420	**0.019***

Fig 19 : IL-6 values among 2 groups.



After day 7 of life , cutoff values for S.Interleukin 6 is 30pg/ml.

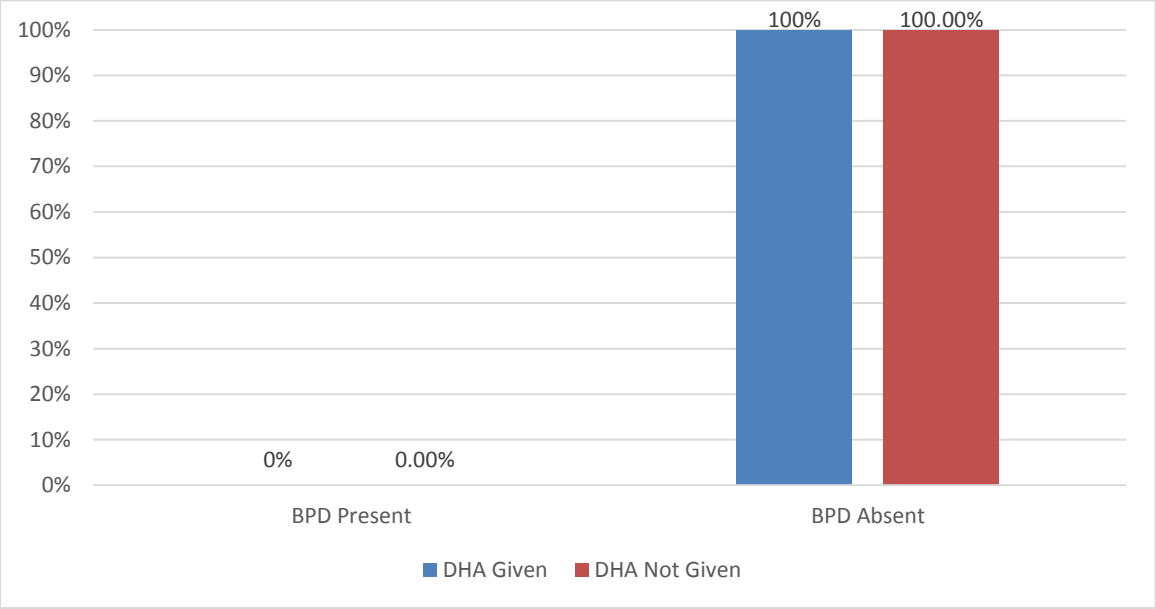
In this study , All participants in both groups have IL-6 levels less than the cutoff .

In DHA group IL-6 values are 2.47+ 0.552 whereas in Control group IL-6 values are 3.40±1.80 , p value between two groups is less than 0.05, which is statistically noteworthy

Table 20: Presence of Culture proven Sepsis among 2 groups.

Sepsis	DHA given		Total
	yes	no	
Yes	0	1(4.2)	1(2.0)
No	25(100.0)	23(95.8)	48(98.0)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 20: Presence of Culture proven Sepsis among 2 groups.

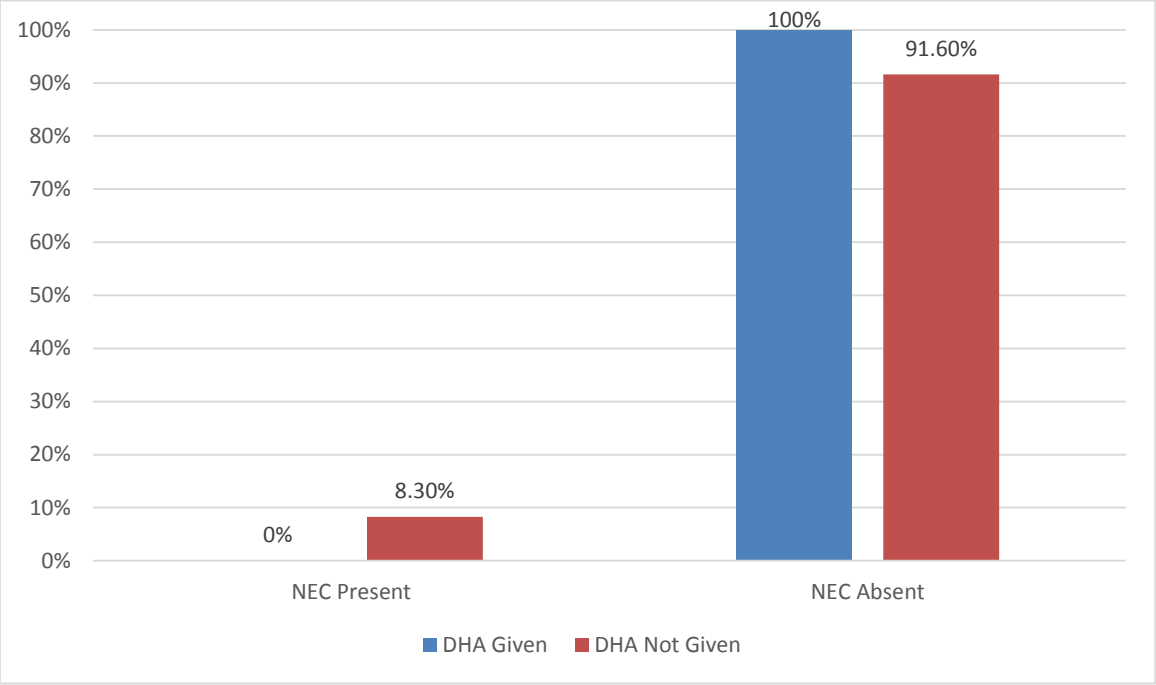


In the present study, in DHA supplemented group , Sepsis was absent in all 25 patients (100%). In group 2 control group ,Sepsis seen in 1 patients(4.2 %) and absent in 23 patients (95.8 %).

Table 21: Presence of NEC among 2 groups.

NEC	DHA given		Total
	yes	no	
Yes	0	2(8.3)	1(2.0)
No	25(100.0)	22(91.6)	48(98.0)
Total	**25(100.0)**	**24(100.0)**	**49(100.0)**

Fig 21: Presence of NEC among 2 groups.



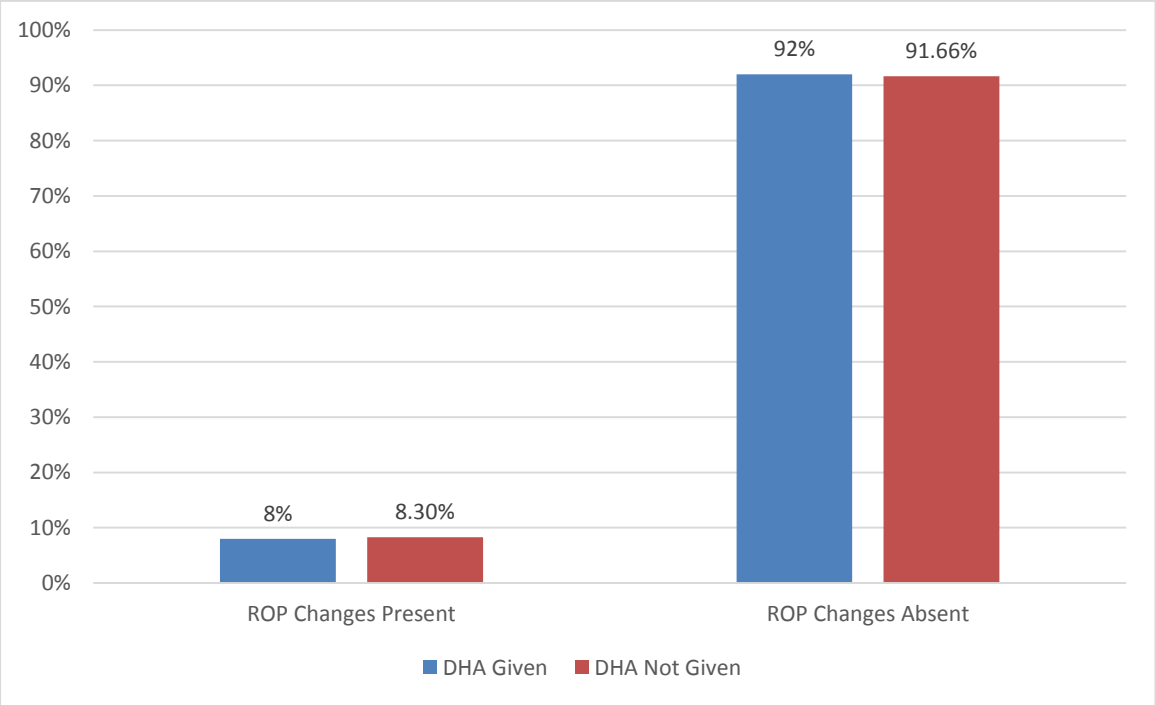
In the present study, in DHA supplementation group , NEC was absent in all 25 patients (100%). In group 2 control group NEC seen in 2 patients (8.3 %) and not seen in 23 patients (91.6 %).

Table 22: Presence of ROP changes among 2 groups.

ROP changes	DHA given		Total	Test statistic (p value)	Odds ratio (95% CI)
	Yes	No			
Yes	2(8.0%)	2(8.3%)	4	0.043* (0.966)	0.95 0.123 to 7.39
No	23(92%)	22(91.66%)	45		
Total	**25**	**24**	**49(100.0)**		

Statistical test used: Fishers exact test
*p value <0.05 is considered statistically significant

Fig 22: Presence of ROP changes among 2 groups.



In the present study, in DHA supplementation group , ROP changes are seen in 2 patients, No changes observed in 23 patients. In group 2 control group ROP changes are seen in 2 patients and no changes observed in 22 patients ; p value of 0.043 indicating statistically significant.

DISCUSSION

DISCUSSION

Preterm newborns are an at-risk population due to an immature immunosuppressive mechanism which do not dampen the immune response leading to the cytokine storm provoked by stressors of various sorts. An increased risk of inflammatory diseases, especially in the postnatal period, were associated with this. [44]

Emerging and current evidence suggests that the immune system may be impacted by early life enteral supplementation of n-3 LCPUFA, particularly DHA. Numerous studies in both humans and animals have examined the effects of n-3 LCPUFA on the immune system (Calder, 2012). 51 According to recent studies, DHA shows anti-inflammatory effects via reducing the release of IL-1β and IL-6. [53]

Babies that are born before the n-3 LCPUFA transfer from mother to fetus are at a higher risk of being prematurely inadequate and may have poor neonatal outcomes. The findings are in line with previous research that has linked high DHA levels to poor newborn outcomes in premature babies .[44]

Hence the present study was done, to measure the inflammatory markers at day 10 of admission in babies with DHA supplementation & to measure the inflammatory markers at day 10 of admission in babies without supplementation of DHA

In the present study, in table 12, DHA supplemented group, respiratory distress is seen in 68% whereas in control group, respiratory distress is seen in 79.2% patients. p value is 0.559 indicating no statistical noteworthy variance between both DHA supplementation group and control group.

In the present study, in table 12 , DHA supplemented group, Respiratory distress seen for a mean of 3 days, with min and max of 3 and 5 days . Whereas in control group ,Respiratory

distress seen for a mean of 4 days ,with min and max of 2.5 and 5.5 days. p value of 0.974 indicating statistically not significant.

The link between DHA amounts in the first month of life and persistent lung illness in preterm newborns was found by Martin et al. [54]. These infants had CLD and much reduced DHA levels, according to the current research. This research found that the risk of developing CLD almost doubled for every 1% drop in blood total fatty acid mass of DHA.

Similar to our study, in the follow-up study of the DINO experiment that compared the cognitive outcomes of preterm newborns taking DHA supplements, the authors looked at the infants' respiratory and allergy outcomes over the long term. Infants at 18 months were screened regarding the BPD history and atopic diseases in the parents, including hay fever, asthma, eczema, or food allergy. Compared to the conventional DHA group, which did not demonstrate any decrease in allergies to foods, eczema, or bronchitis[55], Manley BJ discovered that the high DHA group had a much lower number of parental reported cases of hay fever at 12 and 18 months.

In the present study, in table 13, in DHA supplemented group, abdominal distension is seen in 1 patient (4%) and absent in 24 patients (96%) . In control group abdominal distension is seen in 8 patients (33.3%) and absent in 16 patients (66.7%). P value is 0.011 indicating a statistically significant difference.

Researchers Michael S. Caplan and colleagues found that rats given PUFA supplements had decreased abdominal distension, which is consistent with our findings. The research was on the effects of PUFA supplements on inflammation of the intestinal and NEC in rats.[56]

In the present study, in table 14, in DHA supplemented group 8 % patients suffered from vomiting whereas in control group 29% patients suffered from vomitings , p value of 3.659 indicating statistically not significant.

In the present study, in table 15, in DHA supplemented group , Hyperbilirubinemia seen in 11 patients (44%), absent in 14 patients (56%). In group 2 control group Hyperbilirubinemia seen in 11 patients (45.8%) and absent in 13 patients (54.2%).p value of 0.017 indicating statistically not significant.

Docosahexaenoic acid (DHA) is a necessary component of brain development during fetal and early postnatal periods. Hyperbilirubinemia is defined by excessively high levels of bilirubin in the bloodstream, which frequently causes jaundice in neonates. In severe cases, this distress can lead to neurological impairment or kernicterus, a type of brain injury. Our initial cell-based investigations found that DHA dramatically increases the survival rate of nerve cells treated with bilirubin and reduces oxidative stress, as seen by decreased peroxide activity generated by unconjugated bilirubin (UCB). [57]

Chi YQ et al impled that DHA did a double-blind, randomized, placebo-controlled parallel study, results found that bilirubin level at 48 hours of treatment, serum neuron-specific enolase (NSE) levels, mean phototherapy duration, and abnormal rate of cranial magnetic resonance imaging (MRI) were reduced in the DHA group when compared to control group ($P < .05$) and suggested that DHA is effective as an adjuvant treatment for hyperbilirubinemia in neonates It can reduce the incidence of neonatal hyperbilirubinemia brain injury and plays a certain protective role..[57]

In table 16, In DHA supplemented group CRP is negative in all 25 patients (100%). In control group CRP positive seen in 4 patients (16.7 %) and negative in 20 patients (83.3 %).

In a research including kids having mild to severe sepsis, Mohammed Abdul Moety Al-Biltagi et al. investigated the action of omega-3 fatty acids on acute phase proteins IL-6 & when given to enteral nutrition. The supplemented group showed a decrease in mean CRP levels (P <.0001) and IL-6 levels (P <.0001) as compared to the non-supplemented group. [58]

In table 17, 'p' value of procalcitonin is 0. 019 Which means that 2 groups out of many are statistically different and in favor of procalcitonin DHA supplementation group is statistically less than the control group.

Comparable to present study, Bodil M. K. Larsen demonstarted that pretreatment of

babies with an IV infusion of lipid emulsion raised plasma EPA and reduced levels of

Leuko-triene B4, pro-calcitonin, and lymphocyte concentration following open-heart surgery .[59]

In table 19, p value of IL6 is 0.019 which indicates a statistically significant difference among 2 groups stating IL6 values of DHA supplementation group is statistically less than control group.

The current study's findings are consistent with those of Skouroliakou et al. [60], who found that contrast to lipid emulsion including soybean oil, giving preterm neonates DHA by intravenous lipid emulsion resulted in considerably reduced amounts of Interleukin 6 at the study end . The results of the research suggest that preterm infants may benefit from taking LCPUFA supplements to reduce their inflammation levels. Given the correlation between persistent inflammation and pulmonary morbidity, it is reasonable to assume that the intervention group may have benefited from reduced concentrations of IL-6 in initial four weeks after birth as a consequence of ARA and DHA's effects on respiratory outcomes.

In babies born very prematurely, Hellstrom et al. [61] found that lower levels of IL-6 were associated with higher blood levels of DHA on the first day after delivery.

Research by Wendel K et al. [43] sought to find the clinical variables associated with early inflammation in very preterm newborns & to analyze the result of ARA and DHA supplement on chronic systemic inflammation. An examination of secondary data derived from the ImNuT research, an RCT that was carried out among Irish pregnant women found that from the 2nd day of life until 36 weeks postmenstrual age (PMA), infants whose (GA) < 29 weeks were randomly assigned to get either MCT oil (control group) or an enteral supplement containing 100 mg/kg of ARA and 50 mg/kg of DHA (ARA:Randomized placebo-controlled trial of DHA rich olive oil, the DHA group). From the time of birth to the 28th day, dried blood spots were examined for "Arachadonic acid , Docosohexanoic acid & pro- inflammatory cytokines: TNF-α,Interleukin-1β, Interleukin-6 and Interleukin-8" . From day 3 to 28, ARA: DHA group had decreased IL-6 levels compared to control ,made their superiority clear.

In the present study, in Table 20 . in DHA supplemented group there is no case of culture proved sepsis; however, in control group, sepsis is found in 4.2 % indicating DHA supplementation might be beneficial to control sepsis.

According to López-Alarcón et al. (2012)[62] , in infants with proven sepsis, whether they were born prematurely or at full term, taking DHA orally for 14 days reduced IL-1β and improved the severity of the condition. Enteral injection of DHA affects inflammatory cytokines, both pro- and anti-inflammatory, according to another intervention trial .

In table 21 in the present study in DHA supplemented group ,NEC was absent in all 25 patients (100%). In control group, NEC observed in two (8.3 %) patients and absent in twenty three (91.6 %) patients.

In the same way as our work, Smith SL found out that the DHA was low and related to the increased chance of developing late-onset sepsis. In this group of preterm infants, it was also observed that lower AA and greater LA levels are significant correlates with late-onset sepsis. The authors could not identify any relationship in mean DHA levels and IVH, NEC or ROP. [64]

Supplementing baby formula for premature babies with LCPUFAs did not reduce the risk of severe negative consequences like sepsis or necrotizing intestinal inflammation, according to a meta-analysis and comprehensive review of Smithers LGA. [63]

In the present study, in table 21 , in DHA supplemented group , ROP changes seen in 2 patients, no changes seen in 23 patients. In control group ROP changes seen in 2 patients and no changes seen in 22 patients. p value of 0.043 indicating statistically significant.

Neuroprotective benefits of DHA against oxidative damage in cells of the retinal ganglion were found by Shimazawa et al. (2009). In vitro retinal photoreceptor research demonstrated DHA's protective properties against apoptosis.[64]

Rod photoreceptors and M retinal ganglion cells, which are part of the vision system, also contain a lot of DHA. In the past, studies have shown that preterm babies with low birthweights (<1500 g), who were born prematurely, had the highest rates of fetal accretion, and lost a significant portion of the third trimester reaped the most benefits from DHA supplementation..[65]

Smith et al. believe that the retina's increased metabolic requirement after birth, if not fulfilled adequately by the food supply, may result in imbalance. Decreased IGF-1, which causes inadequate weight gain after delivery, has already been linked to an higher risk of

ROP. Reduced amounts of omega 3 fatty acids, particularly DHA, could have a role. Just before birth, the placenta transports a large amount of nutritional elements, including DHA, from the maternal side to the newborn. After birth, DHA is obtained exogenously from the diet. Poor maternal nutrition may cause a DHA deficiency, which may be responsible for ROP-like alterations in the newborn. [39]

Additionally, they imply that consuming DHA supplements might aid in the prevention of ROP. One of the key risk factor for developing ROP is having a low body weight. According to Sanghi et al , severe ROP affects significantly larger and heavier infants in India than in the West.[39]

SUMMARY

SUMMARY:

The study investigated the morbidity patterns and effect of DHA supplementation on inflammatory markers, effect on preterm complications in early preterm neonates .It encompassed 49 neonates, categorizing them into DHA group and Control group. The current investigation was conducted at the "RL Jalappa Research Centre and Hospital". The parents' consent was obtained.

Babies recruited are randomly allocated by computerized RCT into DHA group or control group and followed up for 10days.

Here is the detailed summary of study findings:

Neonatal Characteristics:

-In both DHA and Control group, females outnumbered males

- Both groups had more number of babies between 33 to 33w 6days and were in cephalic presentation,

-Delivery by Cesarean sections outnumbered vaginal deliveries in both the groups.

Morbidities:

-Respiratory distress is seen with a mean of 3 days in DHA group and mean of 4 days in control group.

- DHA group had significantly less number of babies having abdominal distention (4%)when

compared to control group(33.3%)

- In both the groups , no significant difference is observed between DHA and control group for vomitings & Hyperbilirubinemia

Inflammatory markers:

-In DHA group, CRP negative in all 25 patients (100%). In Control group, CRP positive in 4 patients (16.7 %) and CRP negative in 20 patients (83.3 %).

- Statistically significant difference between Mean Procalcitonin values in DHA group and Control group was observed with a Mean of 0.27 ± 0.152 in DHA group, whereas 0.72±0.930 in control group.

- Though all participants in both groups have IL-6 levels less than the cutoff for Day 10 which is 30pg/ml .A statistically significant difference is observed between mean IL-6 values in DHA vs control group, with Mean of 2.47± 0.552 in DHA group & a mean of 3.40±1.80 seen in control group.

Complications:

-In both the groups no patient had BPD.

-In DHA group, No Culture proven sepsis seen; In control group, 1 patient had culture proven sepsis (4.2 %) and negative in 23 patients (95.8 %).

-In DHA group, ROP changes are seen in 2 patients (8.0%) In control group ROP changes are seen in 2 patients (8.3%) .

The study's findings contribute to the evolving branch of neonatology by emphasizing the importance of decreasing inflammation there by reducing neonatal co-morbidities. They underscore the need for management strategies that address inflammation especially in preterm neonates.

Additional research is needed to elucidate the role of effect of Dha supplementation on preterm neoantes and inflammation

Very few studies are done to assess the role of dha on inflmmatory markers. This study provided foundation for understanding of the effect of dha supplementation on preterm inflammatory markers.

LIMITATIONS

LIMITATIONS:

1. Small sample size
2. Base line inflammatory markers after birth were not considered.
3. The DHA supplement which we have used contains EPA 50MG , and OMEGA 3 - 200MG , therefore we cannot consider all the benefits are exclusively due to DHA
4. Sepsis outbreak in ICU which had caused late onset sepsis in few babies is not considered.
5. Prenatal steroidal coverage to mother is not considered which might give bias while considering respiratory distress and associated inflammation.
6. Both groups have equal number of patients having ROP, due to its small size, it shown significant statistically.
7. Economically its not feasible to do for all babies , as tests and supplement are both expensive

CONCLUSION

CONCLUSION :

The present conclusions are made from the study

1. 1.The study suggests that DHA supplementation may improve clinical conditions such as abdominal distension and possibly reduce the incidence of inflammation as evidenced by documentation of inflammatory markers viz CRP, procalcitonin, IL-6.

2. Our study popose DHA supplementation may help in preventing retinopathy of prematurity. However ,to what extent needs multicentric and larger sample size studies

3. Findings of this study reveal the beneficial role of DHA supplementation in prevention of inflammation in premature neonates .Further research to be done in larger and more diverse population to validate these findings and to understand mechanisms through which DHA exerts its effects on inflammatory pathways.

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ANNEXURE

PATIENT INFORMATION SHEET

Principal investigator: Dr M.SAITEJA /Dr. KNV. PRASAD

I Dr. SAITEJA.M , Post graduate student in Department at Sri Devraj Urs Medical College, will be conducting a study titled.**DOCOSAHEXANOIC ACID SUPPLEMENTATION IN PRETERM NEONATES ADMITTED IN NICU AND ITS EFFECT ON INFLAMMATORY MARKERS AT DAY 10 -AN OPEN LABELLED RANDOMIZED CONTROL TRIAL** "for my dissertation under the guidance of Dr. KNV PRASAD Professor of Department of Paediatrics. The participants of this study i.e. include neonates among which in each group of neonates will be supplementing with DHA with enteral feeds admitted in NEONATAL INTENSIVE CARE UNIT at RL JALLAPA hospital and blood sample will be collected on Day 10 of life .You will not be paid any financial compensation for the participation of your child in this research project.All investigations cost will be beared by me.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 this 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-

INFORMED CONSENT FORM

Date:

I, Mr/Mrs _____ ,have been explained in my own vernacular language that my child will be included in the **DOCOSAHEXANOIC ACID SUPPLEMENTATION IN PRETERM NEONATES ADMITTED IN NICU AND ITS EFFECT ON INFLAMMATORY MARKERS AT DAY 10 -AN OPEN LABELLED RANDOMIZED CONTROL TRIAL ,**hereby I give my valid written informed consent without any force or prejudice for recording the observations of haematological and clinical 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.

_____ _____

(Signature & Name of Pt. Attendant) (Signature/Thumb impression &

Name of Patient/Guardian)

(Relation with patient)

Witness:

_____

(Signature & Name of Research person/doctor)

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಎಂ. ಸಾಯಿತೇಜ / ಡಾ. ಕೆ.ಎನ್.ವಿ. ಪ್ರಸಾದ್

ನಾನು ಡಾ. ಸಾಯಿತೇಜ.ಎಂ ಅವರು ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜಿನ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿಯಾಗಿದ್ದು, ಎನ್ಐಸಿಯುಗೆ ದಾಖಲಾಗಿರುವ ಪ್ರಸವಪೂರ್ವ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಡೊಕೊಸಾಹೆಕ್ಸೆನೊಯಿಕ್ ಆಸಿಡ್ ಪೂರೈಕೆಯ ಕುರಿತು ಅಧ್ಯಯನ ನಡೆಸುತ್ತಿದ್ದಾರೆ ಮತ್ತು 10 ದಿನಗಳ ನಂತರ ಉರಿಯೂತದ ಮಾರ್ಕರ್ ಮೇಲೆ ಅದರ ಪರಿಣಾಮ. ಡಾ.ಕೆ.ಎನ್.ವಿ.ಪ್ರಸಾದ್ ಅವರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಕ್ಕಳ ವಿಭಾಗದ ಪ್ರೊ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಿದವರು ಆರ್ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆಯ ನವಜಾತ ಶಿಶುಗಳ ತೀವ್ರ ನಿಗಾ ಘಟಕಕ್ಕೆ ದಾಖಲಾದ ನವಜಾತ ಶಿಶುಗಳನ್ನು ಒಳಗೊಂಡಿದ್ದು, ಅವರಿಗೆ ಎಂಟರಲ್ ಫೀಡ್ಗಳೊಂದಿಗೆ DHA ನೀಡಲಾಯಿತು ಮತ್ತು ಜೀವನದ 10 ನೇ ದಿನದಂದು ರಕ್ತದ ಮಾದರಿಯನ್ನು ಸಂಗ್ರಹಿಸಲಾಗುತ್ತದೆ. ನಿಮ್ಮ ಮಗುವಿನ ಭಾಗವಹಿಸುವಿಕೆಗಾಗಿ ನಿಮಗೆ ಆರ್ಥಿಕವಾಗಿ ಪರಿಹಾರವನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ. ಈ ಸಂಶೋಧನಾ ಯೋಜನೆ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಈ ಸಂಸ್ಥೆಯಿಂದ ಸಂಶೋಧನಾ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ. ಎಲ್ಲಾ ತನಿಖೆಯ ವೆಚ್ಚವನ್ನು ನಾನು ಭರಿಸುತ್ತೇನೆ.ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಮಗುವಿನ ಭಾಗವಹಿಸುವಿಕೆಗೆ ಒಪ್ಪಿಗೆ ನೀಡಲು ನೀವು ಸ್ವತಂತ್ರರಾಗಿದ್ದೀರಿ. ಯಾವುದೇ ಕಾರಣವನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಮಗುವನ್ನು ಅಧ್ಯಯನದಿಂದ ಹಿಂಪಡೆಯಬಹುದು. ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ನಿರಾಕರಣೆಯು ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ನಿಮ್ಮ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಕಾಳಜಿಯನ್ನು ಪೂರ್ವಾಗ್ರಹ ಮಾಡುವುದಿಲ್ಲ.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ _____, ಎನ್‌ಐಸಿಯುನಲ್ಲಿ ದಾಖಲಾದ ಪ್ರಸವಪೂರ್ವ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಡೊಕೊಸಾಹೆಕ್ಸಾನೊಯಿಕ್ ಆಸಿಡ್ ಸಪ್ಲಿಮೆಂಟೇಶನ್‌ನಲ್ಲಿ ನನ್ನ ಮಗುವನ್ನು ಸೇರಿಸಲಾಗುವುದು ಎಂದು ನನ್ನದೇ ಆದ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ್ದೇನೆ ಮತ್ತು ಅದರ ಪರಿಣಾಮವು ಅದರ ಪರಿಣಾಮ - ಸಂಸ್ಥೆಗಳು ಹೆಮಟೊಲಾಜಿಕಲ್ ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ನಿಯತಾಂಕಗಳ ಅವಲೋಕನಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನನ್ನ ಮಾನ್ಯವಾದ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯನ್ನು ನೀಡಿ. ಒಳಗೊಂಡಿರುವ ಸ್ವಭಾವ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ, ನನ್ನ ತೃಪ್ತಿ. ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ನನ್ನ ಮಗುವನ್ನು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಂತೆ ಅನುಮತಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಇತ್ಯಾದಿಗಳನ್ನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳಿಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಶೈಕ್ಷಣಿಕ ಮತ್ತು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ, ಇತ್ಯಾದಿಗಳನ್ನು ವೀಡಿಯೊ ಗ್ರಾಫ್ ಅಥವಾ ಛಾಯಾಚಿತ್ರ ಮಾಡಬಹುದು. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಜವಾಬ್ದಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ.

(ಸಹಿ ಮತ್ತು ಪಂ. ಪರಿಚಾರಕರ ಹೆಸರು) (ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತು &

ರೋಗಿಯ/ರಕ್ಷಕನ ಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

ಸಾಕ್ಷಿ:

(ಸಂಶೋಧನಾ ವ್ಯಕ್ತಿ/ವೈದ್ಯರ ಸಹಿ ಮತ್ತು ಹೆಸರು)

DOCOSAHEXANOIC ACID SUPPLEMENTATION IN PRETERM NEONATES ADMITTED IN NICU AND ITS EFFECT ON INFLAMMATORY MARKERS AT DAY-10 -AN OPEN LABELLED RANDOMIZED CONTROL TRIAL

PROFORMA

DATE:

SLNO:

UHID:

NAME OF THE MOTHER:

NAME OF THE FATHER:

ADDRESS:

GESTATIONAL AGE:

PRESENTATION

MODE OF DELIVERY

IF LSCS, INDICATION OF LSCS:

DATE OF BIRTH:

TIME OF BIRTH:

SEX OF THE BABY

WEIGHT OF THE BABY AT BIRTH:

HEAD CIRCUMFERENCE:

APGAR SCORE:

PROVISIONAL DIAGNOSIS FOR ADMISSION:

WEIGHT OF THE BABY ON DAY 10:

WEIGHT GAIN OR LOSS %:

DAY ON WHICH FEEDS WERE STARTED:

DHA SUPPLEMENTATION GIVEN:

DATE	YES	NO
Day 1		
Day 2		
Day 3		
Day 4		
Day 5		
Day 6		
Day 7		
Day 8		
Day 9		
Day 10		

Day	1	2	3	4	5	6	7	8	9	10
Respiratory distress										
Abdominal distension										
Vomitings										
Blood in stools										
Hypoglycemia										
Hyperbilirubinemia										
Activity										

INFLAMMATORY MARKERS (ON DAY10)	LEVEL
CRP	
PROCALCITONIN	
IL-6	

COMPLICATIONS		
BRONCHOPULMONARY DYSPLASIA		
NECROTIZING ENTEROCOLITIS		
SEPSIS		
RETINOPATHY OF PREMATURITY		

MASTER CHART

SL NO	UHID	MOTHERS NAME	FATHERS NAME	ADDRESS	GESTATIONAL AGE	PRESENTATION	MODE OF DELIVERY	DOB	TOB	SEX	WEIGHT FOR GESTATIONAL AGE	WEIGHT AT BIRTH	HC	APGAR	WT ON DAY 10	WT GAIN OR LOSS %	FEEDS STARTED ON	DHA GIVEN	RESP DISTRESS	ABDOMINAL DISTENSION	VOMITINGS	BLOOD IN STOOLS	HYPOGLYCEMIA	HYPERBILIRUBINEMIA	ACTIVITY	CRP	PROCALCITONIN	IL-6	BPD	NEC	SEPSIS	ROP CHANGES
1	208411	SUNANDA	E SRINIVAS	VEMGAL,KOLAR KARNATAKA	32W 1D	CEPHALIC	LSCS	10.03.23	4.36AM	FEMALE	AGA	1.98KG	31CM	1-7/10 5-8/10	1.90KG	4% LOSS	17HRS OF LIFE	NO	TILL DAY 6	-	-	-	-	-	NORMAL	NEGATIVE	0.58ng/ml	2pg/ml	-	-	-	NO
2	222630	DIVYA	NAGARAJA R	SHELTIMADA MANGALA KOLAR,KARNATAKA	32W6DAYS	CEPHALIC	VAGINAL	16.04.23	3.15AM	FEMALE	SGA	1.16KG	28.5CM	1-7/10 5-8/10	1.20KG	3% GAIN	31HRS OF LIFE	YES	TILL DAY 2	-	-	-	-	-	NORMAL	NEGATIVE	0.40ng/ml	2.4pg/ml	-	-	-	NO
3	227631	THEJASWINI	MUNIRAJU	MALUR,KARNATAKA	33W2DAYS	CEPHALIC	VAGINAL	28.04.23	2.10PM	MALE	SGA	1.28KG	29CM	1-7/10 5-8/10	1.22KG	4.6% LOSS	DAY 2	YES	TILL DAY 8	-	-	-	-	-	NORMAL	NEGATIVE	0.44ng/ml	3.0pg/ml	-	-	-	NO
4	227707	MUSKAN KHANUM	JAIKAM	FEROZEPUR JHIRKA,HARYANA	33W6D	CEPHALIC	VAGINAL	29.04.23	12.40AM	MALE	AGA	1.70KG	30.5CM	1-7/10 5-8/10	1.70KG	8.2%LOSS	DAY 1	NO	TILL DAY 3	-	-	-	-	-	NORMAL	NEGATIVE	0.52ng/ml	3.2pg/ml	-	-	-	NO
5	228423	KRISHNAVENI	AMARESH	SHILLENGERE V&P,KOLAR,KARNATAKA	33W	CEPHALIC	VAGINAL	01.05.23	3.00PM	MALE	AGA	1.26KG	30CM	1-8/10 5-9/10	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	DAMA	-	-				
6	231584	SIREESHA	SHIVA	JAGAJEEVANA PALYA,SRINIVASAPURA,KARNATAKA	33W4D	CEPHALIC	VAGINAL	09.05.23	4.54PM	FEMALE	SGA	1.26KG	29.5CM	1-7/10 5-8/10	1.22KG	3% LOSS	DAY 2	YES	TILL DAY5	-	-	-	-	-	NORMAL	NEGATIVE	0.50ng/ml	2.4pg/ml	-	-	-	NO
7	231573	SOWMYA	ARUNKUMAR	KEMBODI,KOLAR,KARNATAKA	33W2D	CEPHALIC	LSCS	09.05.23	3.24PM	FEMALE	SGA	1.14KG	30CM	1-8/10 5-9/10	1.08KG	5% LOSS	DAY 1	NO	-	ON DAY 4&5	ON DAY 4	-	-	-	NORMAL	NEGATIVE	0.46ng/ml	2pg/ml	-	NEC-STAGE 1	-	NO
8	233927	KHUBRA KHANUM	IMRANKHAN	HADIGERE,ANOOR P,CHINTHAMANI,KARNATAKA	32W5D	CEPHALIC	LSCS	16.05.23	1.20AM	MALE	AGA	1.74KG	31CM	1-9/10 5-9/10	1.62KG	6.8% LOSS	DAY 1	NO	-	-	-	-	-	-	NORMAL	NEGATIVE	0.16ng/ml	3.1pg/ml	-	-	-	NO
9	233926	KHUBRA KHANUM	IMRANKHAN	HADIGERE,ANOOR P,CHINTHAMANI,KARNATAKA	32W5D	BREECH	LSCS	16.05.23	1.20AM	MALE	AGA	1.90KG	31CM	1-8/10 5-9/10	1.76KG	7.3% LOSS	DAY 1	NO	-	-	-	-	-	ON DAY 4	NORMAL	NEGATIVE	0.20ng/ml	2.4pg/ml	-	-	-	N0
10	234830	ROJA	VENGALASHELAM	BANGARPETE	32W	CEPHALIC	LSCS	17.05.23	10.10PM	MALE	AGA	1.38KG	30.5CM	1-7/10 5-8/10	1.20KG	13% LOSS	DAY 2	YES	TILL DAY 10	ON DAY 7	ON DAY 7	-	-	-	NORMAL	NEGATIVE	0.38ng/ml	4.6pg/ml	-	-	-	NO
11	236776	KAVYA	PAVAN KUMAR	SUGATURI(V&P),KOLAR,KARNATAKA	32W5D	CEPHALIC	LSCS	22.05.23	06.35PM	MALE	SGA	1.34KG	30.5CM	1-9/10 5-10/10	1.34KG	1.4%LOSS	DAY 1	YES	-	-	-	-	-	-	NORMAL	NEGATIVE	0.30ng/ml	3.2pg/ml	-	-	-	NO
12	237252	ARCHITHA.N	NAGARAJ	THIMMAPURA.V, KYRAMBALLI,KGF,KARNATAKA	32W4D	CEPHALIC	LSCS	24.05.23	12.08AM	FEMALE	AGA	2.10KG	32CM	1-8/10 5-10/10	1.88KG	10.4% LOSS	DAY 1	YES	-	-	ON DAY 1	-	-	-	NORMAL	NEGATIVE	0.18ng/ml	2.2pg/ml	-	-	-	NO
13	243868	GEETHA	SURESH KUMAR	KERASAMANGALA,MULBAGAL,KARNATAKA	33W4D	CEPHALIC	LSCS	08.06.23	12.08PM	FEMALE	AGA	1.72KG	30CM	1-8/10 5-9/10	1.50KG	12.7%LOSS	DAY1	NO	TILL DAY 6	ON DAY 2	ON DAY 1	-	-	-	NORMAL	NEGATIVE	0.36ng/ml	4pg/ml	-	-	-	NO
14	243867	GEETHA	SURESH KUMAR	KERASAMANGALA,MULBAGAL,KARNATAKA	33W4D	BREECH	LSCS	08.06.23	12.07PM	MALE	AGA	1.60KG	30CM	1-8/10 5-9/10	1.48KG	7.5% LOSS	DAY 1	YES	-	-	-	-	-	-	NORMAL	NEGATIVE	0.24ng/ml	2.2pg/ml	-	-	-	NO
15	252757	MOUNIKA	ABHILASH	BALLA V&P,MULBAGAL,KARNATAKA	33W2D	BREECH	LSCS	30.06.23	01.14AM	FEMALE	AGA	1.72KG	31CM	1-8/10 5-10/10	1.70KG	1.1%LOSS	DAY 1	YES	-	-	-	-	-	ON DAY 3&4	NORMAL	NEGATIVE	0.20ng/ml	2.6pg/ml	-	-	-	NO
16	232758	MOUNIKA	ABHILASH	BALLA V&P,MULBAGAL,KARNATAKA	33W2D	CEPHALIC	LSCS	30.06.23	01.15AM	MALE	AGA	1.86KG	32CM	1-8/10 5-9/10	1.79KG	3.7%LOSS	DAY 1	NO	TILL DAY 2	-	-	-	-	-	NORMAL	NEGATIVE	0.24ng/ml	2.8pg/ml	-	-	-	NO
17	254163	REVATHI	ARUN	KENNEDYS KARMANLINE, KGF, KARNATKA	33W	CEPHALIC	LSCS	03.07.23	11.42AM	MALE	AGA	1.80KG	32CM	1-8/10 5-9/10	1.76KG	2.2% LOSS	DAY 1	YES	-	-	-	-	-	-	NORMAL	NEGATIVE	0.20ng/ml	2pg/ml	-	-	-	NO
18	256198	ARBEEN TAJ	SHAIK SHAIEEB	KOLAR,KARNATAKA	33W	CEPHALIC	LSCS	07.07.23	08.54PM	FEMALE	AGA	1.44KG	31CM	1-8/10 5-9/10	1.32KG	8.3%LOSS	DAY 1	NO	TILL DAY 5	-	-	-	-	-	NORMAL	NEGATIVE	0.475ng/ml	2.8pg/ml	-	-	-	NO
19	258133	MUBEEN TAJ	SADDAM HUSSAIN	REHAMAD NAGAR,KOLAR,KARNATAKA	33W3D	CEPHALIC	VAGINAL	12.07.23	10.25AM	MALE	AGA	1.56KG	31CM	1-8/10 5-9/10	1.54KG	1.2%LOSS	DAY 2	NO	TILL DAY 8	ON DAY 6	ON DAY 6	-	-	ON DAY 2&3	NORMAL	NEGATIVE	0.62ng/ml	3.2pg/ml	-	-	-	MILD ROP CHANGES
20	262356	SRILATHA	BALAJI	DIBILINE OLD ORIENTAL,KGF	33W6D	CEPHALIC	LSCS	22.07.23	05.21PM	FEMALE	SGA	1.56KG	31.5CM	1-7/10 5-9/10	1.48KG	5.1%LOSS	DAY 1	NO	TILL DAY 4	-	-	-	-	-	NORMAL	NEGATIVE	0.45ng/ml	4.8pg/ml	-	-	GRAM POSITIVE BUDDING YEAST CELLS(NONON CANDIDA ALBIANS)	NO
21	264537	JHANSI P	RAJASEKHAR	GUTTALI,BANGALORE,KARNATAKA	336D	CEPHALIC	LSCS	28.07.23	11.53AM	MALE	AGA	2.40KG	33.5CM	1-8/10 5-9/10	2.22KG	7.5%LOSS	DAY 2	YES	TILL DAY 3	-	-	-	-	ON DAY 5	NORMAL	NEGATIVE	0.325ng/ml	3.1pg/ml	-	-	-	NO
22	267932	RENUKA	RAVICHANDRA	REDDYHALLI,BANGARPETE, KARNATAKA	33W6D	CEPHALIC	LSCS	06.08.23	08.40PM	FEMALE	AGA	1.88KG	32.5CM	1-7/10 5-9/10	1.74KG	7.4%LOSS	DAY 1	YES	TILL DAY 1	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.18ng/ml	2.4pg/ml	-	-	-	NO
23	272683	NITHYA	PRAVEENKUMAR	KADIRENAHALLI(V),DINAHALLI(P),MALUR,KARNATAKA	33W5D	BREECH	LSCS	18.08.23	08.48PM	MALE	AGA	1.94KG	32CM	1-9/10 5-9/10	1.80KG	7.2%LOSS	DAY 2	NO	TILL DAY 1	ON DAY 6	ON DAY 6	-	-	ON DAY 2	NORMAL	NEGATIVE	0.48ng/ml	3.2pg/ml	-	-	-	NO
24	275356	SHAHISTA	SZ.THOSIFULLA	1-35/1,MASJID STREET,NERNIPALLI,CHITTOOR,AP	33W6D	BREECH	LSCS	27.08.23	05.23PM	FEMALE	SGA	1.48KG	33.5CM	1-7/10 5-9/10	1.38KG	6.7%LOSS	DAY 2	YES	TILL DAY 8	-	-	-	-	-	NORMAL	NEGATIVE	0.24ng/ml	2.46pg/ml	-	-	-	MILD ROP CHANGES
25	275357	SHAHISTA	SZ.THOSIFULLA	1-35/1,MASJID STREET,NERNIPALLI,CHITTOOR,AP	336D	CEPHALIC	LSCS	27.08.23	05.24PM	FEMALE	AGA	1.68KG	33.5CM	1-7/10 5-9/10	1.50KG	10.71%LOSS	DAY 2	YES	TILL DAY 5	-	-	-	-	-	NORMAL	NEGATIVE	0.20ng/ml	2.0pg/ml	-	-	-	N0
26	276411	NAVITHA	VINODH KUMAR	#2B,WEVLINBLACK,CORAMANDEL,KGF	33W6D	CEPHALIC	VAGINAL	30.08.23	07.33PM	MALE	AGA	1.74KG	31.5CM	1-6/10 5-8/10	1.50KG	13.7%LOSS	DAY 1	NO	TILL DAY 1	ON DAY 7,8	ON DAY 7	-	-	-	NORMAL	1:2 POSITIVE	3.2ng/ml	6.76pg/ml	-	-	-	NO
27	287744	MANJULA	GAGAN KUMAR	TEJANAGAR,KOLAR,KARNATAKA	33W6D	CEPHALIC	VAGINAL	27.09.23	12.50PM	FEMALE	AGA	2.10KG	31.5CM	1-8/10 5-9/10	1.82KG	13.3%LOSS	DAY 1	NO	-	-	-	-	-	-	NORMAL	NEGATIVE	0.12ng/ml	2.0pg/ml	-	-	-	NO
28	289028	SHEELA KARUNYA	HARISH	NEWSTREET,DORUGAMPET ,KGF,KARNATAKA	33W4D	CEPHALIC	LSCS	30.09.23	11.52PM	MALE	AGA	2.06KG	33CM	1-7/10 5-9/10	2.02KG	1.9%LOSS	DAY 1	YES	TILL DAY 3	-	-	-	-	-	NORMAL	NEGATIVE	0.18ng/ml	2.2pg/ml	-	-	-	NO
29	289029	SHEELA KARUNYA	HARISH	NEWSTREET,DORUGAMPET ,KGF,KARNATAKA	33W4D	CEPHALIC	LSCS	30.09.23	11.52PM	MALE	AGA	1.66KG	32CM	1-8/10 5-9/10	1.58KG	4.8%LOSS	DAY 1	YES	-	-	-	-	-	ON DAY 2&3	NORMAL	NEGATIVE	0.22ng/ml	2.4pg/ml	-	-	-	NO
30	293763	ARSHIYA TAJ	AZARUDDIN	HAJI LAYOUT,KRPURAM,BANGALORE	33W3D	CEPHALIC	VAGINAL	14.10.23	05:20AM	FEMALE	SGA	1.66KG	31CM	1-8/10 5-9/10	1.66KG	1.2%LOSS	DAY 1	NO	-	-	-	-	-	-	NORMAL	NEGATIVE	0.20ng/ml	2.0pg/ml	-	-	-	NO
31	294443	ROJA	RAJESH	LAKSHMISAGARA V, HALEPALYA P,MALUR,KARNATAKA	33W2D	CEPHALIC	VAGINAL	15.10.23	02.29PM	MALE	AGA	1.78KG	31.5CM	1-5/10 5-7/10	1.66KG	6.7%LOSS	DAY 2	NO	TILL DAY 4	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.14ng/ml	2pg/ml	-	-	-	MILD ROP CHANGES
32	297396	VARSHA	CHANDRA	KUVECHAR,KARNATAKA	32W	CEPHALIC	VAGINAL	24.10.23	08.20PM	MALE	AGA	1.30KG	30.5CM	1-7/10 5-9/10	1.14KG	12.3%LOSS	DAY 2	YES	TILL DAY 3	-	-	-	-	ON DAY 3	NORMAL	NEGATIVE	0.12ng/ml	2.4pg/ml	-	-	-	NO
33	299164	SUGANDHA	HARISHKUMAR	SHASTRINAGAR,MALUR,KARNATAKA	32W	BREECH	LSCS	29.10.23	12.40PM	FEMALE	AGA	1.52KG	30.5CM	1-7/10 5-9/10	1.30KG	14.4%LOSS	DAY 2	NO	TILL DAY 2	ON DAY 5	ON DAY 5	-	-	ON DAY 2	NORMAL	1:2 POSITIVE	2.1ng/ml	7.16pg/ml	-	NEC 1A	-	NO
34	299165	SUGANDHA	HARISHKUMAR	SHASTRINAGAR,MALUR,KARNATAKA	32W	CEPHALIC	LSCS	29.10.23	12.41PM	FEMALE	AGA	1.60KG	31CM	1-7/10 5-9/10	1.39KG	13.1%LOSS	DAY 2	YES	TILL DAY 2	-	-	-	-	-	NORMAL	NEGATIVE	0.38ng/ml	2.32pg/ml	-	-	-	NO
35	309818	VYBHAVI	PARTHU	MANJUNAT FANCY STORE,GEETHAMANDIR,BANGARPETA	32W2D	CEPHALIC	VAGINAL	24.11.23	02.40AM	MALE	AGA	1.70KG	31.5CM	1-7/10 5-8/10	1.56KG	8.2%LOSS	DAY 2	YES	TILL DAY 3	-	-	-	-	ON DAY 4	NORMAL	NEGATIVE	0.24ng/ml	2.2pg/ml	-	-	-	NO
36	311702	AMREEN TAJ	FAYAZ	VATTIGAL;KAMASAMUDRA, BANGARPETE,KARNATAKA	32W1D	CEPHALIC	VAGINAL	28.11.23	06.42PM	FEMALE	AGA	1.86KG	31CM	1-8/10 5-9/10	1.60KG	13.9%LOSS	DAY 4	NO	TILL DAY 4	-	-	-		ON DAY 4 & 8	NORMAL	NEGATIVE	0.82ng/ml	2.81pg/ml	-	-	-	NO
37	312321	LAKSHMAMMA	SRINIVASA	CHIKKADATHURU,OODDAKADTHURU,MALUR	32W5D	CEPHALIC	LSCS	28.11.23	06.49PM	MALE	AGA	1.76KG	30.5CM	1-7/10 5-8/10	1.60KG	9.09%LOSS	DAY 2	NO	TILL DAY 2	ON DAY 7	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.24ng/ml	2.0pg/ml	-	-	-	NO

SL NO	UHID	MOTHERS NAME	FATHERS NAME	ADDRESS	GESTATIONAL AGE	PRESENTATION	MODE OF DELIVERY	DOB	TOB	SEX	WEIGHT FOR GESTATIONAL AGE	WEIGHT AT BIRTH	HC	APGAR	WT ON DAY 10	WT GAIN OR LOSS %	FEEDS STARTED ON	DHA GIVEN	RESP DISTRESS	ABDOMINAL DISTENSION	VOMITINGS	BLOOD IN STOOLS	HYPOGLYCEMIA	HYPERBILIRUBINEMIA	ACTIVITY	CRP	PROCALCITONIN	IL-6	BPD	NEC	SEPSIS	ROP CHANGES
38	314705	MOUNIKA	NAGARAJ	SWIMMING BATHLINE;OORGAUM,KGF-KOLAR	33W5D	CEPHALIC	LSCS	03.12.23	01.13PM	FEMALE	SGA	1.64KG	32CM	1-8/10 5-9/10	1.56KG	4.80%LOSS	DAY 1	YES	-	-	-	-	-	-	NORMAL	NEGATIVE	0.16ng/ml	2.2pg/ml	-	-	-	NO
39	314706	MOUNIKA	NAGARAJ	SWIMMING BATHLINE;OORGAUM,KGF-KOLAR	33W5D	BREECH	LSCS	03.12.23	01.14PM	MALE	SGA	1.52KG	31.5CM	1-8/10 5-9/10	1.40KG	7.89%LOSS	DAY 1	YES	-	-	-	-	-	-	NORMAL	NEGATIVE	0.20ng/ml	2.41pg/ml	-	-	-	NO
40	314742	RAMADEVI	MK DEVARAJ	MANCHINEELAKOTE,KOLAR ,KARNATAKA	33W3D	CEPHALIC	LSCS	03.12.23	10.54PM	FEMALE	SGA	1.60KG	31CM	1-5/10 5-8/10	1.47KG	8.10%LOSS	DAY 1	NO	TILL DAY 3	ON DAY 2	ON DAY 2	-	-	ON DAY 2	NORMAL	NEGATIVE	0.28ng/ml	2.32pg/ml	-	-	-	NO
41	316587	ZIGUNA	MAHABOOB PASHA	BELATHUR COLONY,BENGALURU	33W3D	CEPHALIC	LSCS	06.12.23	07.07PM	FEMALE	AGA	1.58KG	29.5CM	1-6/10 5-8/10	1.42KG	10.12%LOSS	DAY 5	NO	TILL DAY 10	-	-	-	-	-	NORMAL	1:2 POSITIVE	1.22ng/ml	5.81pg/ml	-	-	-	NO
42	326991	NAVYA	NARAYANASWAMY	SHIVARAPURA(V&P); KARNATAKA	32W2D	CEPHALIC	LSCS	23.12.23	10.28AM	FEMALE	SGA	1.00KG	29CM	1-5/10 5-7/10	0.93KG	7% LOSS	DAY 2	YES	TILL DAY 8	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.82ng/ml	2.8pg/ml	-	-	-	MILD ROP CHANGES
43	327276	DIVYA	HEMANTH YADAV	ATTURU;TELAGAVARA,KARNATAKA	32W6D	BREECH	LSCS	24.12.23	07.18AM	FEMALE	SGA	1.32KG	29CM	1-6/10 5-8/10	1.24KG	6% LOSS	DAY 2	YES	TILL DAY 5	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.14ng/ml	2.0pg/ml	-	-	-	NO
44	327277	DIVYA	HEMANTH YADAV	ATTURU;TELAGAVARA,KARNATAKA	32W6D	CEPHALIC	LSCS	24.12.23	07.23AM	FEMALE	AGA	1.52KG	31CM	1-6/10 5-8/10	1.34KG	11.8% LOSS	DAY 2	YES	TILL DAY 5	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.20ng/ml	2.0pg/ml	-	-	-	NO
45	327373	JYOTHI.N	SRINIVAS	KANNIGANAHELLI,KARNATAKA	32W	CEPHALIC	LSCS	25.12.23	01.01AM	MALE	AGA	1.44KG	30CM	1-7/10 5-9/10	1.28KG	11.1%LOSS	DAY 2	NO	TILL DAY5	-	-	-	-	-	NORMAL	1:4 POSITIVE	3.6ng/ml	8.2pg/ml	-	-	-	NO
46	328857	AMREEN TAJ	IMRANKHAN	REHAMATH NAGAR,KOLAR	33W5D	CEPHALIC	LSCS	27.12.23	12.35PM	FEMALE	AGA	1.68KG	30.5CM	1-6/10 5-8/10	1.46KG	13.09%LOSS	DAY 3	NO	TILL DAY 5	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.28ng/ml	2.6pg/ml	-	-	-	NO
47	329050	VEENA	V.PRASAD	VALBAI ROAD,SRINIVASAPURA	33W6D	CEPHALIC	LSCS	27.12.23	11.05PM	FEMALE	AGA	1.92KG	31.5CM	1-8/10 5-9/10	1.70KG	11.4%LOSS	DAY 3	NO	TILL DAY 6	-	-	-	-	ON DAY 6	NORMAL	NEGATIVE	0.24ng/ml	2.2pg/ml	-	-	-	NO
48	331213	S.SHILPA	G.V CHALAPATHI	GOWDAHALLI,SRINIVASAPURA,KOLAR	32W3D	CEPHALIC	LSCS	30.12.23	08.59PM	MALE	AGA	1.52KG	31CM	1-7/10 5-8/10	1.42KG	6.5% LOSS	DAY 2	YES	TILL DAY 3	-	-	-	-	ON DAY 3	NORMAL	NEGATIVE	0.16ng/ml	2.2pg/ml	-	-	-	NO
49	332597	VEENA	SRINIVAS	NALLURU(V),HANUMANAHALLI(P),MULAGAL,KARNATAKA	32W5D	CEPHALIC	VAGINAL	02.01.24	12.13PM	FEMALE	AGA	1.52KG	31CM	1-8/10 5-9/10	1.40KG	7.8%LOSS	DAY 1	NO	TILL DAY 5	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.30ng/ml	2.41pg/ml	-	-	-	NO
50	332599	VEENA	SRINIVAS	NALLURU(V),HANUMANAHALLI(P),MULAGAL,KARNATAKA	32W5D	BREECH	VAGINAL	02.01.24	12.23PM	FEMALE	AGA	1.72KG	31CM	1-8/10 5-9/10	1.60KG	6.9% LOSS	DAY 2	YES	TILL DAY 3	-	-	-	-	ON DAY 2	NORMAL	NEGATIVE	0.18ng/ml	2.20pg/ml	-	-	-	NO