"EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM LEVELS IN NEONATES RECEIVING PHOTOTHERAPY FOR NEONATAL JAUNDICE IN TERTIARY CARE HOSPITAL"

By

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“EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM LEVELS IN NEONATES RECEIVING PHOTOTHERAPY FOR NEONATAL JAUNDICE IN TERTIARY CARE HOSPITAL”

B.L.D.E (DEEMED TO BE UNIVERSITY)
VIJAYAPURA KARNATAKA

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LIST OF ABBREVATIONS USED

AAP	American Academy Of Paediatrics
AGA	Appropriate For Gestational Age
AN	Auditory Neuropathy
APGAR	Appearance Pulse Grimace (Reflex) Activity Respiration
BIND	Bilirubin-Induced Neurologic Dysfunction
CH	Conjugated Hyperbilirubinemia
CHD	Congenital heart disease
CI	Confidence interval
CNS	Central Nervous System
ECG	Electrocardiogram
ET	Exchange Transfusion
F	Female
FABP	Fatty Acid-Binding Protein
FTND	Full Term Normal Delivery.
G6PD	Glucose-6-Phosphate Dehydrogenase
gm	Grams
HB	Hyperbilirubinemia
Hrs	Hours

IUGR	Intrauterine Growth Retardation
LED	Light Emitting Diode
LGA	Large For Gestational Age
LMP	Last Menstrual Period

LSCS	Lower Segment Caesarean Section.
M	Male
MDA	Malondialdehyde
mg/dL	Milligram Per Deciliter
mg/mL	Milligram Per Milliliter
Min	Minutes
mmol/L	Millimoles Per Litre
MSAF	Meconium stained amniotic fluid
NA	Not Applicable
PIH	Pregnancy-Induced Hypertension
PT	Phototherapy.
PTH	Parathormone
SD	Standard Deviation
SGA	Small For Gestational-Age
SNHL	Sensorineural Hearing Loss
TAS	Total Antioxidant Status
TA	Thymine-Adenine

TcB	Transcutaneous bilirubinometer
TSB	Total Serum Bilirubin
UCH	Unconjugated Hyperbilirubinemia
UB	Unconjugated Bilirubin.
UDP	Uridine diphosphate
UDPGT	Uridine diphosphate glucanosyltransferase
UV	Ultraviolet
VATER	Vertebral Defects, Anal Atresia, Tracheoesophageal Fistula With Oesophageal Atresia, And Radial And Renal Abnormalities
(8-OH-dG)	8-hydroxydeoxyguanosin

ABSTRACT

BACKGROUND AND OBJECTIVES:

Hyperbilirubinemia is common and in most cases, benign problem in neonates. Phototherapy is the most common therapeutic intervention in these Neonates. However, it is not a harmless intervention. It can produce adverse effects such as dehydration, temperature instability, skin rashes, loose stools, retinal damage, hypocalcaemia, bronze baby syndrome, redistribution of blood flow and genotoxicity. The risk of hypocalcaemia due to phototherapy in preterm may be more than term neonates. This study is designed to observe the incidence of phototherapy induced hypocalcaemia in neonates, with unconjugated hyperbilirubinemia, after giving phototherapy.

METHODOLOGY:

A tertiary care teaching hospital based, prospective, Observational study done from December 2019 to May 2021 in the Neonatal intensive care unit of, SHRI B.M. Patil Medical college & Hospital ,VIJAYAPURA 100 neonates with unconjugated hyperbilirubinemia requiring phototherapy were selected for the study. Other causes of hypocalcaemia were ruled out. Pathologic hyperbilirubinemia requiring phototherapy was defined as per 2004 American Academy of Paediatrics (AAP) hyperbilirubinemia treatment guidelines. Serum calcium and total serum bilirubin levels, before and after phototherapy were estimated.

RESULTS

The mean of serum calcium which was 9.7 ± 0.7 mg/dL in neonates at the start of the phototherapy which had decreased to 8.2 ± 0.7 mg/dL after phototherapy. It was seen that after phototherapy, there was significant fall in calcium level in both term and preterm groups ($p<0.001$) compared to calcium levels before phototherapy. We observed that 34% of neonates developed hypocalcaemia after phototherapy. None of the neonates developed severe clinical manifestations of hypocalcemia like convulsions or apnea.

CONCLUSION

There is significant decrease in the serum calcium level after phototherapy in both term and late preterm neonates. 34% neonates developed hypocalcaemia after phototherapy. Serum calcium levels, are significantly lower in late preterm neonates as well as in term neonates. Thus this study emphasizes the need for monitoring calcium levels regularly in both term and preterm neonates undergoing phototherapy, for therapeutic interventions. Hypocalcemia due to phototherapy is not commonly associated with severe clinical manifestations like apnea or convulsions. There is no significant difference in occurrence of any other complications of phototherapy between term and preterm neonates.

KEY WORDS: Hypocalcemia; Phototherapy; Hyperbilirubinemia.

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INTRODUCTION

Neonatal hyperbilirubinemia is usually a benign problem in neonates and one of the leading causes of hospital readmission after birth. Neonatal jaundice is associated with increased unconjugated bilirubin concentration, caused by breakdown of Red blood cells. Around 66% of term Neonates and 80% of preterm Neonates develop jaundice in 1st week of life. The most common cause of hyperbilirubinemia in neonates is Physiological. Severe neonatal hyperbilirubinemia, can cause sensoneural hearing loss and Auditory neuropathy. If not controlled, Hyperbilirubinemia can lead to Hyperbilirubinemic encephalopathy or Neonatal death.

American Academy of Pediatrics recommends that, neonates discharged with in 48 hours should have follow up visits after 48-72 hrs for any significant jaundice.

Bilirubin is the final product of heme-protein metabolism, and its raised levels are potentially neurotoxic[1,2]. Newborns with low levels of bilirubin glucoronyl transferase and genetic deficiency of this enzyme are at greater risk of developing bilirubin toxicity.

The purpose of hyperbilirubinemia treatment is to prevent unconjugated Bilirubin from reaching neurotoxic levels.

There are mainly 2 modes of treatment for hyperbilirubinemia , Phototherapy & Exchange transfusion[3].

Phototherapy is safe , effective & most widely used treatment for hyperbilirubinemia. The mechanism of action of phototherapy is by three means, of which Photoisomerisation plays a major

role by converting Z isomer to E isomer.

Structural isomerization converts Bilirubin to lumirubin .

Photo oxidation has minor role.

Photoisomerisation occurs in skin layers which completes in nanoseconds, and reformation of non isomerized bilirubin collection takes 1-3 hrs[4].

Phototherapy can produce adverse effects such as Dehydartion, temperature instability, skin rashes, loose stools, retinal damage, hypocalcemia, bronze baby syndrome, redistribution of blood flow, and genotoxicity.

Hypocalcemia is one of the lesser known adverse effects of Phototherapy. Hypocalcemia may cause severe complications like irritability, convulsions & apnea. Hence, phototherapy induced hypocalcemia is a significant problem.

Romagnoli et al (1979) first time described the association of hypocalcemia with phototherapy in preterm newborns[11]. There are only few studies on the hypocalcemic effect of phototherapy[11-14].

There are very less published reports on the role of phototherapy inducing hypocalcemia in neonates. This study is planned to observe the occurance of phototherapy induced hypocalcemia in neonates with unconjugated hyperbilirubinemia after giving Phototherapy

OBJECTIVES

1. To study the occurrence of hypocalcemia, in neonates with unconjugated hyperbilirubinemia receiving phototherapy for neonatal jaundice admitted in NICU.

2. To assess the correlation of risk factors for hypocalcemia in Hyperbilirubinemic Neonates.

REVIEW OF LITERATURE

Neonatal jaundice is associated with increase in un conjugated bilirubin concentrations caused by breakdown of RBC's. Elevated serum bilirubin levels can cause Bilirubin induced neurologic dysfunction[1,2]. Bilirubin by itself is not completely detrimental, as it also has protective effects due to its antioxidant properties. Bilirubin is an antioxidant that can scavenge peroxyl radicals. Bilirubin is reported to protect against variety of pathological processes, including complement-mediated anaphylaxis, myocardial ischemia, pulmonary fibrosis, and cyclosporin nephrotoxicity[15,16].

The American Academy of Pediatrics has published guidelines for the management of neonatal jaundice in 1994[19]. Since then, many cases of kernicterus has been reported[20]. Other significant concern is that neonates are sometimes discharged from hospital early, before the onset of jaundice. This will again delay the diagnosis of severe hyperbilirubinemia and will increase the incidence of kernicterus[21]. Therefore, researchers have been found about identifying predictors of neonatal hyperbilirubinemia to help in early detection of neonates at risk of severe hyperbilirubinemia. The hour specific bilirubin nomogram is widely accepted , by most of them but has low sensitivity[22].

Neonatal jaundice is most common cause of morbidity in first week of life, occurring in approximately 60% of term and 80 % of preterm newborns. 60% of newborns become clinically jaundiced during the first week of life. Incidence of jaundice varies among different countries. It is 60-70% in western countries & even higher among Asian countries[23]. Indirect hyperbilirubinemia occurs as a result of excessive bilirubin formation and immaturity of the neonatal liver to clear Bilirubin from blood[24,25]**.** Many newborns with jaundice are healthy, but

they have to be monitored for toxicity of bilirubin levels to the central nervous system. Increased levels of Bilirubin lead to bilirubin encephalopathy and subsequently kernicterus, with permanent neurodevelopmental handicaps[26]. Currently, present interventions make severe sequelae rare. Neonatal jaundice is so common that most infants are monitored and treated to prevent substantial damage. Some data suggest that TSB can be 20mg/dl or higher in 1-2% of infants born at 35 weeks of gestation[27,28]. Hospital-based studies have shown that 5-40 per 1000 term infants & late preterm infants receive phototherapy before discharge from nursery and that almost equal number are readmitted for phototherapy after being discharged[28-30].

BILIRUBIN METABOLISM IN NEONATES –

Jaundice is said to be physiological when there is mild unconjugated hyperbilirubinemia that affects nearly all newborns and resolves within first few weeks after birth. The production of Bilirubin in term newborn babies is 2-3 times higher than in adults. This is mainly caused by increased production of Bilirubin, decreased bilirubin clearance and increased enterohepatic circulation.

The following are the factors that cause the development of physiological jaundice[19,20].

-Decreased hepatic excretion of unconjugated Bilirubin.

-Portal venous shunting through patent ductus venosus.

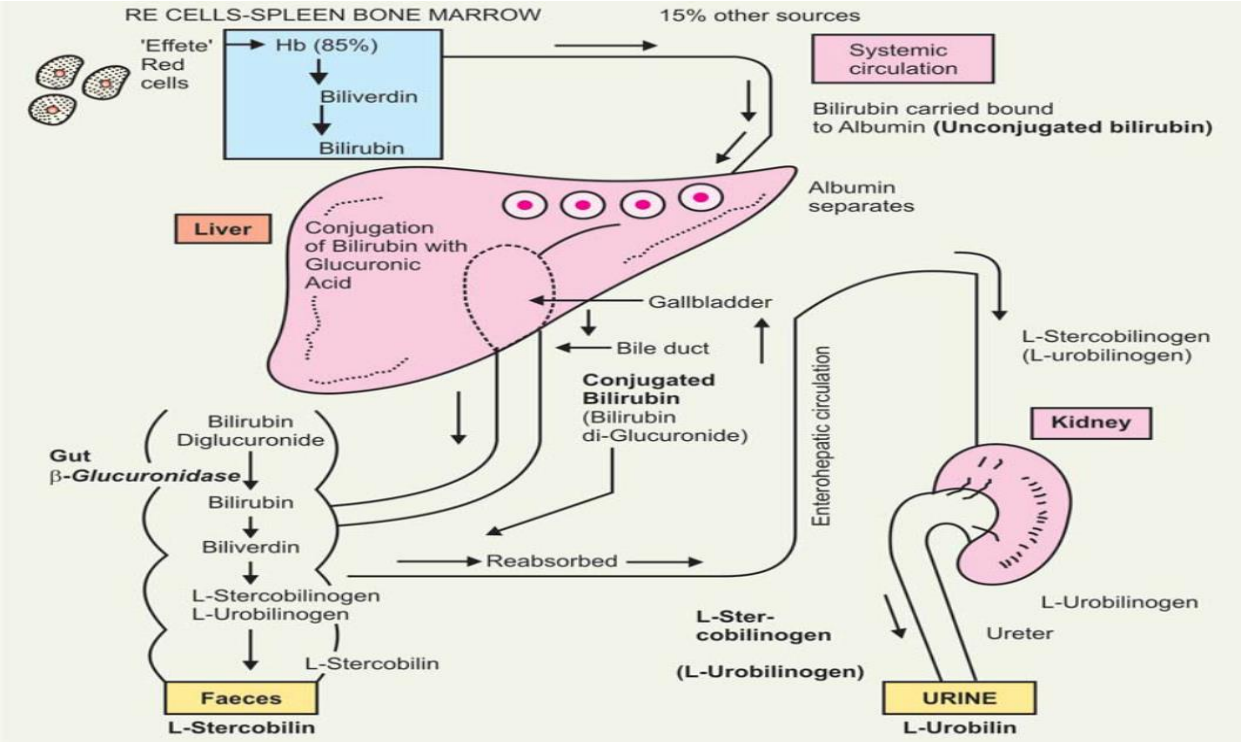
-Decreased RBC's life span.

-Immature hepatic bilirubin clearance.

At birth bilirubin-UGT activity is only 1 % of normal adult levels. Regardless of gestational age, enzyme activity increases by 14th week of life.

-Hydrolysis of conjugated Bilirubin- As beta glucuronidase increases in newborns, that leads to greater hydrolysis of conjugated Bilirubin to unconjugated form. The unconjugated Bilirubin reabsorbs from the intestine through the process of enterohepatic circulation.

-Decreased bacterial degradation of bilirubin-In neonates, the bilirubin degradation by bacteria is reduced because intestinal flora is not well developed, that leads to increased absorption of unconjugated Bilirubin.



Newborn infants, particularly premature ones, have an immature excretory system, resulting in neonatal jaundice with elevated levels of unconjugated bilirubin levels[10]. RBC mass at birth is high due to the relatively hypoxic environment, the short life span of RBC and increased

enterohepatic circulation due to sterile gut[14].

Normal infants after the age of 1 month, the process of hepatic uptake, conjugation, storage & biliary secretion of Bilirubin have matured to near-adult levels, so that concentration of UB in plasma is < 1.2 mg/dl. In utero, a very limited excretory function of liver is compensated by active transport of unconjugated Bilirubin across the placenta to maternal circulation. In addition to this, new born lacks anaerobic intestinal flora that converts UB to urobilinogen, leaving more unmetabolized UB free for absorption into portal blood, thus increasing enterohepatic circulation of Unconjugated hyperbilirubinemia. UB has potent antioxidant properties, the modest physiological jaundice of newborns is thought to be neuroprotective[15].

Physiological jaundice is usually not harmful, but bilirubin levels above 10mg/dl coupled with prematurity, decreased serum albumin, acidosis , substances that compete for binding sites of albumin increase the risk of kernicterus. Bilirubin increase in concentration, 3 to 5 days after birth and remains elevated for 14 days. Bilirubin is usually less than 5 mg/dl with 90% UB.[16].

Reference range for neonatal total bilirubin-

Birth-1 day : 1-6 mg/dl

1-2 days : 6-7.5 mg/dl.

2-5 days : 4-12 mg/dl.

5 days-1 month: 0-1.8mg/dl[17.]

CAUSES OF UNCONJUGATED HYPERBILIRUBINEMIA[31].

- INCREASED HEPATIC BILIRUBIN LOAD.

- DECREASED BILIRUBIN CLEARANCE BY LIVER.

A. INCREASED HEPATIC BILIRUBIN LOAD

1. Hemolytic disease-RBC membrane defects

a. Elliptocytosis.

b. Hereditary spherocytosis.

c. Stomatocytosis.

d. Pyknocytosis.

2. RBC enzyme abnormalities-

a. Glucose 6 phosphate dehydrogenase deficiency.

b. Pyruvate b kinase deficiency.

3. Haemoglobinopathies-

a. Alpha thalassemia.

4. Immune-mediated (positive direct coombs test)

a. RH isoimmunization.

b. ABO incompatibility.

c. Minor blood group incompatibility.

5. Increased enterohepatic circulation-

a. Intestinal obstruction.

b. Meconium ileus.

c. Breast milk feeding.

6. Polycythemia.

7. Extravascular blood accumulation-

a. Cephalohematoma.

B. DECREASED BILIRUBIN CLEARANCE BY LIVER

1. Late preterm gestation.

2. Endocrine Abnormalities.

a. Hypothyroidism.

b. Hypopituitarism.

3. Decreased hepatic biliary uptake –

a. Patent ductus venosus.

b.SLCO1B1 gene polymorphism.

4. Disorders of bilirubin conjugation-

a. Crigler-Najjar syndrome type I.

b. Crigler-Najjar syndrome type II.

c. Gilberts syndrome.

CLASSIFICATION BASED ON ONSET OF JAUNDICE[31].

WITHIN 24 HRS OF BIRTH-

- RH & ABO incompatibility.
- G6PD deficiency.
- Pyruvate kinase deficiency.
- TORCH infections.
- Crigler-Najjar syndrome.

24-72 HRS AFTER BIRTH-

- Physiological jaundice.
- ABO incompatibility.
- Extravascular bleed.
- Polycythemia.

- Neonatal sepsis.
- Breastfeeding jaundice.
- Increased enterohepatic circulation.

AFTER 72 HRS OF BIRTH-

- Sepsis.
- Increased enterohepatic circulation.
- Hypothyroidism.
- Hypopituitarism.
- Neonatal hepatitis.
- Galactosemia.
- Crigler-najjar syndrome.
- Gilbert's disease.

RISK FACTORS FOR DEVELOPMENT OF SEVERE HYPERBILIRUBINEMIA-

- Low birth weight.
- Prematurity.
- Blood group incompatibility.
- Problems in breastfeeding.
- Infants of diabetic mothers.
- Perinatal asphyxia.
- H/o jaundice in previous siblings.
- Cephalohematoma.

EFFECT OF HYPERBILIRUBINEMIA IN TERM & PRETERM NEONATES

Severe neonatal hyperbilirubinemia causes sensorineural hearing loss & auditory neuropathy[3,4].

If hyperbilirubinemia is not controlled, it can lead to hyperbilirubinemic encephalopathy or neonatal death. Severe hyperbilirubinemia(TSB>25mg/dl) is associated with an increased risk of BIND in term and late preterm neonates. Brain regions typically affected by bilirubin toxicity include basal ganglia, cerebellum, white matter & brain stem nuclei for oculomotor and auditory function.

Lipid peroxidation, DNA damage and antioxidant status were assessed in neonates with unconjugated hyperbilirubinemia.

BASU S et al compared neonates with hyperbilirubinemia with controls without hyperbilirubinemia, an overall increase in mean plasma malondialdehyde & 8 hydroxy deoxyguanosine levels and decrease in TAS levels were noted in unconjugated hyperbilirubinemia group[32]**.** An increase in MDA was documented if Bilirubin was >20mg/dl . An increase in 8 - OH-DG has seen if bilirubin levels were>16mg/dl1. Moderate to severe unconjugated hyperbilirubinemia was associated with higher oxidative stress & lower antioxidant defense. Alteration of oxidative stress parameters can be utilized as early predictors for poor outcomes. If there is serious DNA damage even at a low bilirubin level, it suggest the genotoxic effect of bilirubin[32].

Hyperbilirubinemia is one of the common clinical conditions requiring evaluation and treatment in late preterm newborns and is an important cause for readmission during the first postnatal week of life[33,34.]

The AAP practice guidelines for the treatment of unconjugated hyperbilirubinemia in newborn infants at 35 weeks' gestation and greater is based on three principles to reduce the occurrence of severe hyperbilirubinemia and also in reducing harm; universal systemic assessment before discharge, close follow up and prompt intervention when indicated.

In late preterm neonates of 36 weeks' gestation, even at a high intermediate risk zone (75% to 94%) TSB is associated with >10% chance of increasing TSB to >/20 mg/dl, a risk more significant than that of the full-term newborn with a TSB level _> 95%[37.]

The reason for this increased risk is the immature hepatic metabolic pathways for Bilirubin and

immaturity of gastrointestinal function and motility. This puts the late preterm infants at increased risk of elevated severe Bilirubin levels, and jaundice becomes more prolonged, prevalent and severe[29].

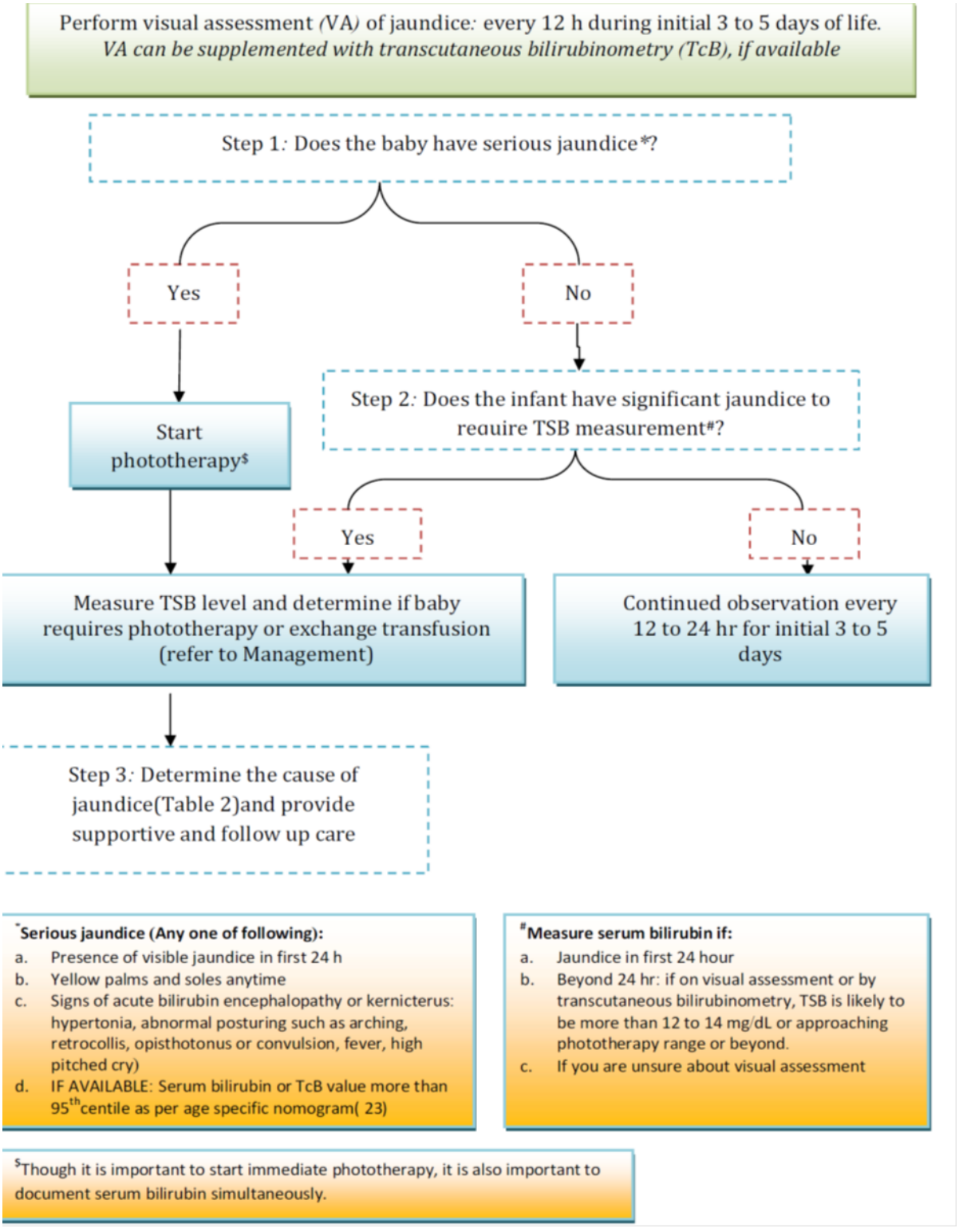
Late preterm neonates have same degree of RBC turnover and heme breakdown as term neonates, but UGT1A1 enzyme activity is lower in preterm Neonates, compared to term neonates. The maturation time of this enzyme appears to be slower in late preterm neonates during 1st week of life[39].

Clinical hyperbilirubinemia management guidelines for late preterm Neonates recommend treatment at lower TSB, Threshold than term neonates, a distinction that is an essential component of 2004 AAP practice guidelines on neonatal jaundice[40].

Along with other clinical factors observed in conjunction with late preterm gestation hyperbilirubinemia risk, Breast milk feeding has been identified most consistently, almost uniformly and appears to be equally important[33].

Late preterm neonates, due to their immature hepatic enzyme activities, less effective sucking & swallowing, and they may have difficulties in nutritive breastfeeding phenomena that may predispose these infants to varying degrees of lactation failure[41].

SCREENING PROTOCOL FOR DETECTION OF JAUNDICE IN NEWBORNS



DIAGNOSIS OF HYPERBILIRUBINEMIA[29].

- CLINICAL EXAMINATION OF NEONATE.
- MEASUREMENT OF TSB LEVELS.

CLINICAL EXAMINATION OF NEONATE WITH JAUNDICE

Dermal staining was recorded on a standard drawing of an infant divided into five dermal zones. For clinical examination, the newborn should be examined in good daylight. The skin should be blanched with digital pressure, and the colour of skin and subcutaneous tissue should be noted.

The following KRAMER'S criteria are used to estimate clinical jaundice

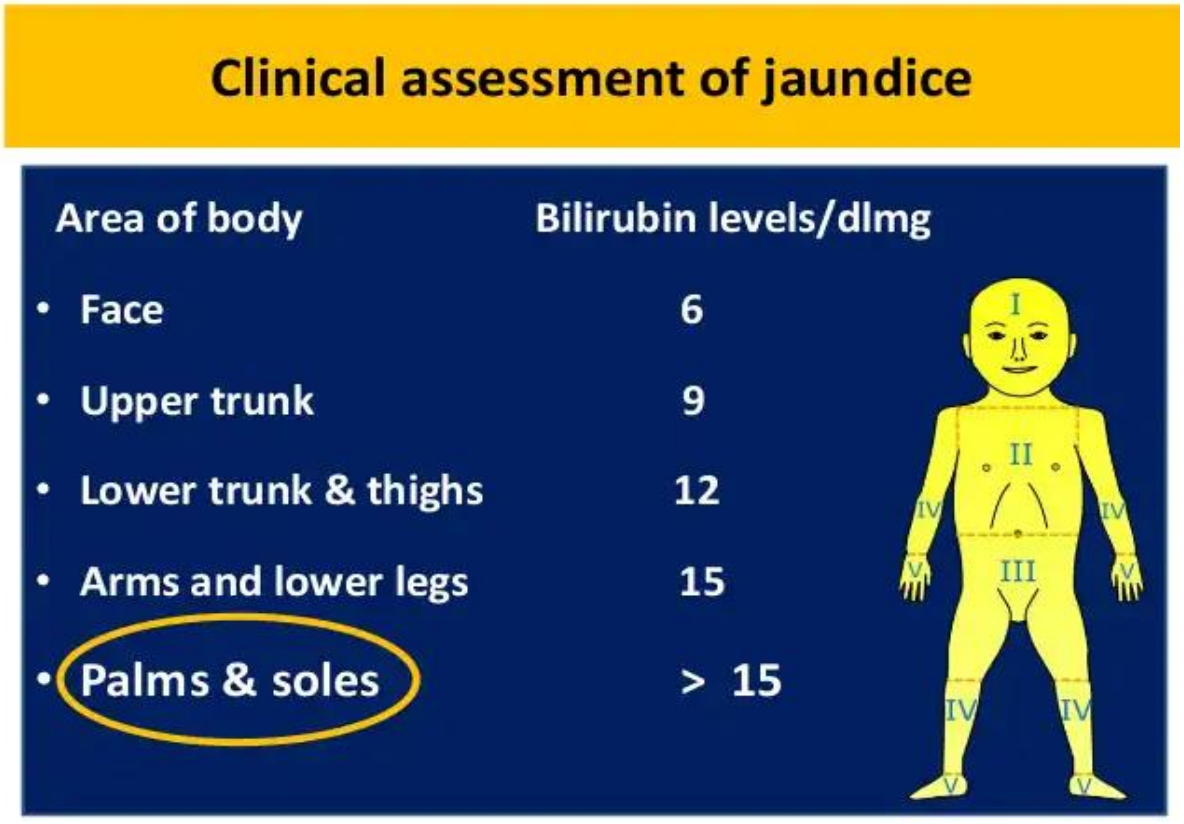


FIG-1 : CLINICAL ASSESMENT OF JAUNDICE.

CRITERIA TO ESTIMATE CLINICAL JAUNDICE :

CRITERIA TO ESTIMATE CLINICAL JAUNDICE	
AREA OF BODY	RANGE OF SERUM BILIRUBIN(mg/dl)
Face	4-6 mg/dl
Chest ,upper abdomen	8-10 mg/dl
Lower abdomen ,thighs	12-14 mg/dl
Arms, lower legs	15-18 mg/dl
Palms ,soles	15-20 mg/dl

Table – 1 : Estimation of clinical jaundice.

Newborns detected to have yellowish discolouration of skin, beyond the legs should have immediate laboratory confirmation, for levels of TSB. Clinical assessment is not reliable, if neonate has been receiving phototherapy and if the baby has dark skin.

MEASUREMENTS OF TSB LEVELS[42] :

BIOCHEMICAL:

High-performance liquid chromatography is the gold standard method for estimation of TSB, but this facility is unavailable in a few centres. So usually, laboratory estimation of TSB is done in labs based on Vanden Bergh reaction. It had marked inter-laboratory variability with the coefficient of variation up to 10-12% for TSB and over 20% for the conjugated fraction.

TRANSCUTANEOUS BILIRUBIN METER :

This is non-invasive and is reliable within 2-3mg/dl of total serum Bilirubin, it is equipped with a photoprobe with reflectometer, and a computerized spectrophotometer that provides a digital readout for total Bilirubin. It is based upon yellowish staining of the skin and subcutaneous tissue.

MICRO METHOD FOR ESTIMATION OF BILIRUBIN :

A number of automated sophisticated electric bilirubinometers are available, works based on spectrophotometry , which provide a reliable estimate of total serum Bilirubin on a capillary sample of blood.

MANAGEMENT OF UNCONJUGATED HYPERBILIRUBINEMIA :

- EXCHANGE TRANSFUION.
- PHARMACOTHERAPY.
- PHOTOTHERAPY.

The aim of therapy is to ensure that serum Bilirubin is kept at a safe level and brain damage is

prevented. Exchange transfusion remains the single most effective and reliable method to lower Bilirubin when it is at critical levels. It is important to remember that neonatal hyperbilirubinemia is a medical emergency, and delay in its management can lead to irreversible brain damage and death.

Phototherapy is the initial intervention used to treat and prevent severe hyperbilirubinemia in asymptomatic infants and should be provided in infants with the sign of acute Bilirubin encephalopathy while preparations are made for exchange transfusion.

EXCHANGE TRANSFUSION-

It is the most effective method for rapid removal of Bilirubin. In the case of isoimmunehaemolytic anaemia, exchange transfusion also removes antibodies & sensitized RBC, which are replaced by donor RBC lacking the sensitized antigen[42].

If there is an appearance of clinical signs of kernicterus, it indicates the need for exchange transfusion at any level of serum bilirubin. Double volume (160-180 ml/kg) exchange transfusion is performed if phototherapy fails to reduce serum bilirubin levels to a safe range.

Blood that is used for exchange transfusion is O RH negative irradiated packed RBC that are suspended in AB plasma and cross-matched against maternal plasma & cells. Individual aliquots should be appropriately 10% or less of infants blood volume, with a maximum volume of 20ml for term baby of 3 kg weight & smaller volumes in babies with physiologic instability.

CHOICE OF BLOOD FOR EXCHANGE TRANSFUSION-

In the case of RH isoimmunization- use of O RH Negative cells.

In the case of ABO incompatibility-blood group O type RH compatible with baby, Ideal is to use blood group O suspended in AB plasma.

The adverse events associated with exchange transfusion are asymptomatic electrolyte and blood abnormalities which are treatable. 74 % of exchange transfusion is associated with adverse effects ,most common is thrombocytopenia (44%) ,metabolic acidosis (24%) , & hypocalcemia (29%) of which 69% ,44% and 74% respectively require treatment.

PHARMACOTHERAPY

INTRAVENOUS IMMUNOGLOBULIN[42]

It has been used in infants with haemolytic disease caused by RH or ABO incompatibility. when total Bilirubin continuous to rise in infants receiving intensive phototherapy or within 2 or 3 mg/dl of threshold recommendation for Exchange Transfusion. Usually IVIG (0.5-1gm/kg) over 2 hrs. and repeat the dose in 12 hrs. if needed. The mechanism is unknown, but IVIG acts by occupying Fc receptors on macrophages, decreasing the removal of antibody-coated red cells from circulation.

DRUGS THAT INHIBIT BILIRUBIN FORMATION ARE

Orotic acid- It is metabolic precursor of uridine diphosphate glucuronic acid , and promotes conjugation of Bilirubin. Its utility is limited & the cost is prohibitive.

TIN-MESOPORPHYRIN-

These are structural analogues of heme molecule and in which central iron molecule has been replaced by metallic ions including mg, chromium. The mechanism of action is by competitive inhibition of heme oxygenase, a rate-limiting enzyme in heme metabolism. A single intramuscular dose of 6mg/kg is given on 1st day of life may reduce the need for phototherapy . Phototherapy if given after administration of tin mesoporphyrin, causes transient erythema.

BILIRUBIN TRANSPORT-ALBUMIN INFUSION

When administered (1gm/kg) as 5% salt-free albumin, half an hour to one hour before transfusion, it facilitates more effective removal of Bilirubin & improves bilirubin binding capacity . It should be avoided in babies with congestive cardiac failure because of the risk of overloading of circulation.

LIVER ENZYME INDUCERS :

Phenobarbitone induces maturation of microsomal enzymes, ligandin (Y receptor protein) and glucorynl transferase (UDPGA), thus improving uptake, conjugation & excretion of Bilirubin by the liver. The dosage is 5mg/kg/day twice daily. Due to a lag period of 48-72 hours before enzyme activity is induced by phenobarbitone, it is best administered prenatally during 1-2 weeks, prior to the expected date of delivery or given to neonate within 24 hrs. of birth.

PHOTOTHERAPY

Phototherapy is widely accepted as a relatively safe and effective method for the treatment of neonatal hyperbilirubinemia.

Regardless of the degree of skin pigmentation, gestational age, absence or presence of haemolysis,

phototherapy will reduce serum bilirubin in all neonates[9].

It is currently used as the treatment of choice to reduce the severity of neonatal hyperbilirubinemia, regardless of aetiology.

If intervention is done at the correct time in both term & preterm neonates, severe complications of hyperbilirubinemia can be prevented.

The three main factors that affect the efficacy of phototherapy are [46,47].

1. The best wavelength for phototherapy is at 420-480nm to induce photoisomerization. The lamps used for phototherapy are special blue lamps.

2. Irradiance: To increase the effectiveness of phototherapy, lamp energy output should be well above the levels that have been determined to be minimally effective in producing bilirubin degradation while not exceeding the level beyond which significant increases in response are evident. For providing standard therapy, irradiance is about 6-12 microwatt/cm2/nm and to provide intensive phototherapy, lamp energy output is increased to 25microwatt/cm2/nm or greater. The bili bed phototherapy can deliver up to 60microwatt/cm2/nm.

3. Distance of phototherapy lamps –

Usually, phototherapy lamps are positioned within 30cm of the patient. If we increase the distance of the lamp from the skin surface, it results in a diminution of light energy by a factor equal to the square of the increase in distance. The greater the surface area exposed, the more significant is the effectiveness of phototherapy[44].

The factors that increase the reflection of Phototherapy light on babies body surface can effectively increase the impact of phototherapy on serum bilirubin levels. Sometimes many phototherapy units are used to increase the therapeutic effect[43]. The more the surface area exposed, the greater is the effectiveness of phototherapy. So, for this purpose white covers are put around the phototherapy that reflects Phototherapy light to baby body surface. All these techniques can increase the effectiveness of phototherapy and favour the early discharge of neonates.

Phototherapy is the most widely used Therapeutic intervention in neonatal care. As phototherapy has developed through the years, it has almost completely replaced exchange transfusion because of the efficacy & safety of treatment[10]. The decrease in TSB during phototherapy is the result of photoisomers formation.

The efficacy of phototherapy in reducing TSB depends on several factors. The lamp energy output, exposed body surface area, spectrum of light emitted, duration of light exposure[48]. To give optimal treatment in an infant, regardless of design of the phototherapy unit , the committee on fetus & newborn of AAP has made a few recommendations for phototherapy treatment[49].

Optimal phototherapy is provided by blue light in spectrum of 460-490 nm at lamp energy output of >/30 microwatt/cm2/nm to maximum possible body surface area. These are based on previous studies of dose-response relationship between phototherapy with fluorescent tubes & decrease of TSB[50-51]. Some studies[50-52] have questioned this correlation. They all showed a dose-response relationship between Lamp energy output & decrease in TSB. According to tan(1982), there is no further decrease in TSB is seen with increasing irradiance[52] after reaching a saturation point of

30microwatt/cm2/nm.

Bilirubin is usually cleared from the body by hepatic conjugation with glucuronic acid, and it gets eliminated in bile in the form of bilirubin diglucuronides & monoglucuronides. Neonatal hyperbilirubinemia results from the transient decrease in conjugation of Bilirubin along with decreased lifespan of red cells . The condition that can cause jaundice are isoimmunization, hereditary hemolytic disorders, and cephaloheamotoma[31]. Genetic disorders, commonly gilberts syndrome, can also predispose to neonatal hyperbilirubinemia[53]. Late preterm infants and neonates who are exclusively breastfed (if breastfeeding is not taking well)[30,54,55]can lead to an increase in the enterohepatic circulation of bilirubin[56].

MECHANISM OF ACTION OF PHOTOTHERAPY-

BIOCHEMICAL BASIS OF PHOTOTHERAPY :

Phototherapy reduces Bilirubin by facilitating its excretion from the body via routes other than conjugation. When Bilirubin interacts with light, coming from phototherapy, three photochemical reactions can occur . There are photo-oxidation, photoisomerization & structural isomerization. Photooxidation is a slow process that converts Bilirubin to small polar products that are excreted in urine and is the least important mechanism of bilirubin elimination[57].

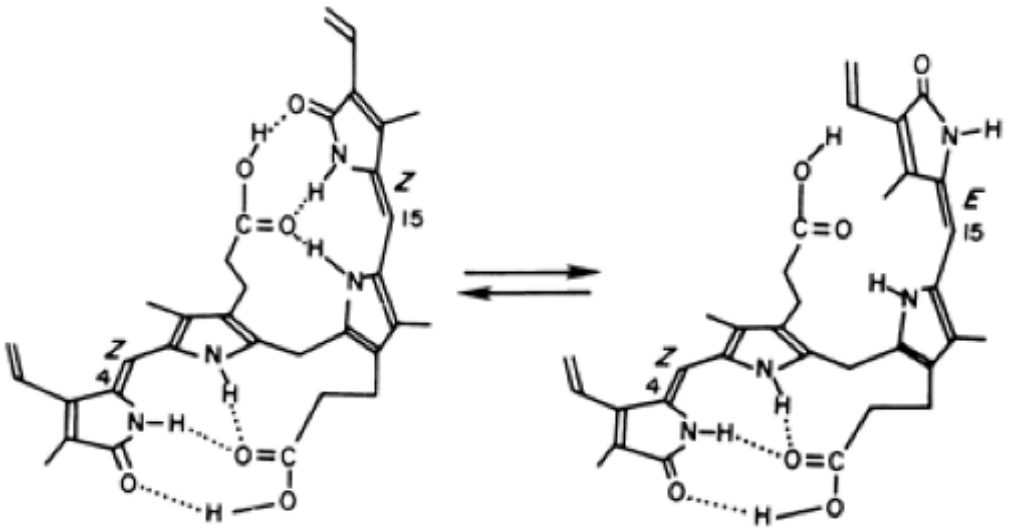


FIG-2 : Configurational photoisomerization of Bilirubin.

Photoisomerization rapidly converts about 15 % of 4Z,15Z bilirubin isomer to less toxic 4Z,15E form. This less-toxic isomer can be excreted into bile without conjugation, it is reversible, and clearance is slow. Standard laboratory tests do not distinguish between isomers, so TB may not change, even though it is less toxic.

In natural form, the arrangement of these double bonds, and hence arrange of pyrrole rings, is classified as 4Z ,15Z. When even phototherapy light strikes the bilirubin molecule, it can disturb this double bond and initiate 180-degree rotation of one or both end pyrrole rings to produce less toxic isomer forms[57].

If Bilirubin is bound to albumin, configurational isomers remain stable for many hours. In bile de configuration occurs and unconjugated Bilirubin, entering gut, undergoes enterohepatic circulation[57].

The main important role of phototherapy is to lower the concentration of circulating Bilirubin.

This is achieved by using light energy to change, shape & structure of Bilirubin, so that it can be easily excreted[57].

Absorption of light by dermal and subcutaneous Bilirubin causes the pigment to undergo several photochemical reactions that occur at very different rates . These reactions will produce yellow stereoisomers of Bilirubin & colorless derivatives of lower molecular weight. These products are less lipophilic than Bilirubin and can be excreted in bile or urine without the need for conjugation. Invitro and in vivo studies suggest that photoisomerization is important than photodegradation. Photoisomerization occurs rapidly during phototherapy, and isomers appear in blood before plasma bilirubin begins to decline[57].

Bilirubin absorbs light more strongly in the blue region of the spectrum near 460nm, in which rate of formation of bilirubin photoproducts highly depends on intensity & wavelength of phototherapy light used. An increase in wavelength cause increased penetration of tissue by light. So, the wavelength between 460-490 nm blue region of the spectrum is probably most effective for treating hyperbilirubinemia, UV light produce wavelength of < 400nm. So, using UV light to reduce serum bilirubin, instead of phototherapy lights is a misconception. Phototherapy lights do not emit significant erythemal UV radiation.

The effective alternative to phototherapy in infants with severe jaundice is exchange transfusion. The efficacy of phototherapy can be determined by a reduction in the number of exchange transfusions being performed[60,61]. Studies have shown that if phototherapy was withheld, 36% of infants with VLBW required an exchange transfusion[61]. When phototherapy was used, only 2

of 833 such VLBW received exchange transfusion.

The dose and effectiveness of phototherapy is affected by the type of light source commonly used. Lights in phototherapy units contain daylights, white or blue fluorescent tubes. However, when total serum bilirubin levels approach the range at which intensive phototherapy is recommended, it is important to use lights with a wavelength of 460-490 nm, especially blue lights. The AAP subcommittee currently recommends blue fluorescent lamps or LED lights that have been found to be effective for phototherapy[40]. The dose and effectiveness of phototherapy are also affected by infants distance from light, the nearer the light source, the more significant is irradiance and area of skin exposed. Many controlled trials have shown that the more surface area exposed, the greater the reduction in total serum bilirubin level.

When phototherapy light is placed 20cm above the infant, standard daylight phototherapy units should deliver spectral irradiance of 8 to 10 microwatt/cm2/nm in 430-490nm band. Blue fluorescent lamps will deliver 30-40 microwatt/cm2/nm. The AAP[40] defines intensive phototherapy as spectral irradiance of at least 30 microwatt/cm2/nm delivered as much of infants body surface area as possible.

This can be achieved by using a light source placed above & beneath the infant.

There is a direct relationship between irradiance used & the rate at which TSB declines.

NEWBORN CARE WHILE RECEIVING PHOTOTHERAPY[40].

- Breastfeeding on demand can be continued .10-20% extra iv fluids can be provided.
- Eyes & genitalia should be covered during phototherapy.
- Hydration should be maintained by checking urine colour, frequency.
- Change of posture is necessary.
- Temperature monitoring should be done to prevent hypothermia.
- Weight should be monitored daily.
- TSB should be measured every 12 hrs. or 6hrs in case of severe unconjugated Hyperbilirubinemia.

ADVERSE EFFECTS OF PHOTOTHERAPY SHOULD BE MONITORED :

- Dehydration
- Loose stools.
- Hypothermia/hyperthermia.
- Opening of patent ductus arteriosus in preterm babies.
- Hypocalcemia.
- Rashes.

- Retinal damage.
- Decrease in renal blood flow velocity
- Bronze baby syndrome.

USE OF PHOTOTHERAPY IN CLINICAL PRACTICE :

In term & late preterm infants phototherapy is used, according to AAP[40] guidelines. These guidelines take into consideration not only the level of TSB but also the gestational age of infant, age of the infant in hours since birth, presence or absence of other risk factors like isoimmune haemolytic anaemia.G6PD deficiency, lethargy, Asphyxia, Temperature instability, sepsis, Acidosis, Hypoalbuminemia.

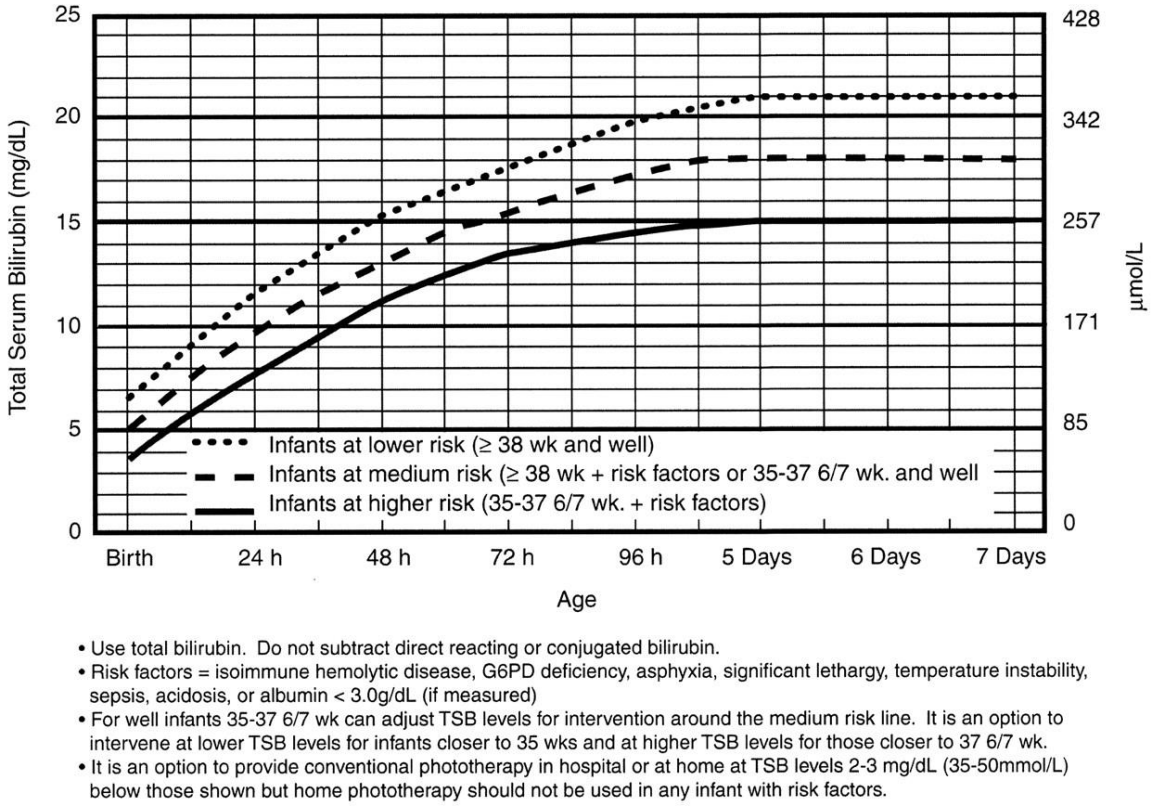


Figure -3 : Nomogram for assesment of TSB levels.

In preterm infants , phototherapy is used even at low levels of serum bilirubin levels, and in some places, phototherapy is used prophylactically in all babies with birth weight less than 1000gm[62].

COMPLICATIONS OF PHOTOTHERAPY

Significant complications with phototherapy are rare. The important clinical complication that is observed during phototherapy is the presence of direct hyperbilirubinemia or cholestatic jaundice. When these infants with cholestatic jaundice are exposed to phototherapy, they develop greyish-brown discolouration of skin, serum & urine (bronze baby syndrome)[63]. This is due to the accumulation of porphyrins or other pigments in plasma in the presence of cholestasis[63,64]**.** Sometimes bad complications with this syndrome have been described, two infants with this syndrome who died were shown to have kernicterus at Autopsy[65]**.** There are no other reports of significant complications in infants who develop the bronze baby syndrome, although impaired binding of Bilirubin to albumin has been seen in infants with this syndrome[66,67].

If there is a requirement of phototherapy, direct hyperbilirubinemia should not be taken as a contraindication to its use, particularly in sick newborns, and as a rule, direct hyperbilirubinemia should not be subtracted from total bilirubin concentrations. In the newborn with a bronze baby syndrome, exchange transfusion should be considered if phototherapy does not decrease TSB. Sometimes purpuric bullous lesions can be seen in infants with cholestatic jaundice requiring phototherapy[67].

The most common side effects include loose stools, hypothermia, dehydration, skin burn, retinal

damage, increased red cell osmotic fragility, vitamin B2 deficiency, DNA damage. A lesser-known side effect, but a complication of phototherapy is hypocalcemia[68].

An erythematous rash can be seen in infants treated with tin-mesoporphyrin and subsequently exposed to sunlight or daylight fluorescent bulbs[72].

The obsolete contraindication for phototherapy includes congenital porphyria, severe blistering, agitation that occurs during phototherapy could be seen in case of congenital porphyria[73].

Conventional phototherapy can cause thermal environmental, changes in infants leading to increased peripheral blood flow & insensible water loss[74,75]**.** This is not seen with LED lights, which has low heat output, and much less likely to cause insensible water loss.

Recent studies have shown that intensive phototherapy might increase the number of atypical melanocytic naevi that is seen at school age[76,77]**.** Intensive phototherapy will not cause haemolysis[78]. Swedish studies suggested that phototherapy is associated with type 1 DM and possibly asthma[79]. Bilirubin is a powerful antioxidant, lowering TSB levels, particularly in an infant with very low birth weight, will have undesirable consequences but not been clearly identified[80,81.]

FAILURE OF PHOTOTHERAPY[42]

It is defined as the inability to decrease Bilirubin of 1-2mg/dl after 4-6 hrs. and /or to keep Bilirubin below the exchange transfusion zone. Exchange transfusion is done if TSB increases despite intensive phototherapy.

HYPOCALCEMIA IN NEONATE

DEFINITION OF HYPOCALCEMIA

Neonatal hypocalcemia is defined as a total serum calcium concentration of <7mg/dl (1.75mmol/L) or an ionized calcium concentration of <4mg/dl (1 mmol/L) in preterm neonates & less than 8 mg/dl (2mmol/L) in term neonates[83]. In very low birth weight infants, ionized calcium values of 0.8-1mmol is common and not associated with clinical symptoms .

CALCIUM FUNCTION & METABOLISM-

After birth, newborns are capable of mounting a PTH response to hypocalcemia, but serum calcium levels depend on many other parameters like PTH secretion, dietary calcium intake, renal calcium reabsorption, skeletal calcium stores and vitamin D stores[82]. Usually, total serum calcium levels are done, but ionized calcium is active & physiologically important component. Total serum calcium levels include ionized calcium & bound calcium, it is usually affected by albumin, PH, serum levels of phosphate, magnesium, and bicarbonate and reduced by factors that bind calcium like the rapid infusion of citrate buffered blood and free fatty acids from parenteral nutrition. At normal pH of 7.4, 10% is bound to bicarbonate, phosphate or citrate, 40% is bound to albumin, and the remaining exists as free ionized calcium. The normal range of ionized calcium is 1-1.2mmol/L[82].

Hormonal regulation of calcium homeostasis -

Critical for blood coagulation.

Neuromuscular excitability.

Cell membrane integrity & function.

Activation of cellular enzyme cascades.

Secretory activity of various exocrine glands.

Hypocalcemia increases both cellular permeability to sodium ions and cell membrane excitability. Low calcium levels reduce the threshold for excitation of neurons & cause repetitive responses to a single stimulus. Because this effect will be seen in CNS & peripheral nervous system, both manifestations will be seen in children[82].

EPIDEMIOLOGY

The incidence of hypocalcemia varies in different studies. It occurs in 30% of infants with very low birth weight and 89 % of infants whose gestational age at birth was <32 weeks[82]. Neonates born to the infant of a diabetic mother and who had birth asphyxia have a high incidence of hypocalcemia. Late-onset hypocalcemia, more commonly seen in infants of developing countries, who are fed with cow's milk or formula containing a high amount of phosphate. Most pediatric patients are newborns. In older children, hypocalcemia is usually associated with an illness like acquired hypoparathyroidism, mutation of calcium-sensing receptor or defects in vitamin D supply or metabolism[68].

EARLY-ONSET NEONATAL HYPOCALCEMIA[42]

It occurs within 48-72 hrs. after birth, which can be due to the following factors.

- Birth asphyxia –Several neonatal birth depression is frequently associated with hypocalcemia, hypomagnesemia, hypophosphatemia & delayed introduction of feeds.
- Prematurity –Premature infants are capable of mounting PTH response to hypocalcemia, but target organ responsiveness to PTH may be diminished.
- Infants of diabetic mothers have 25-50% the incidence of hypocalcemia because in mothers, maternal depletion of calcium due to diabetes mellitus causes a hypomagnesemia state in the fetus, which induces functional hypoparathyroidism & hypocalcemia in the infant.
- IUGR infants may also have hypocalcemia if they are also preterm or had perinatal asphyxia.

LATE-ONSET NEONATAL HYPOCALCEMIA[42]

It is characterized by the onset of tetany at the age of 5-10 days in healthy term babies receiving animal milk or formula feeding. The ingestion of milk with high phosphate content or low calcium/phosphorus ratio. Whole cow's milk has seven times the phosphate load of breast milk (965 vs 140 mg/dl in breast milk)

Data have also suggested that an association exist between late-onset neonatal hypocalcemia and gentamycin use, with a newer dosing schedule of every 24 hrs[83,84].

From medical records of 78 term babies with hypocalcemia, moderate to severe late-onset neonatal hypocalcemia occurred more often in male infants & Hispanic infants[85].

CAUSES OF LATE ONSET HYPOCALCEMIA[68]

- Hypomagnesemia
- Increased phosphate load.
- Cow milk, renal insufficiency.
- Vitamin D deficiency.
- Low levels of Vitamin D
- Malabsorption.
- Hepatobiliary disorders.
- Renal insufficiency.
- PTH resistance
- Transient hypoparathyroidism.
- Hypoparathyroidism
- DiGeorge syndrome, CATCH 22 syndrome.
- Mutation of the calcium-sensing receptor.
- Secondary to maternal hyperparathyroidism.

- Activating mutations of calcium-sensing receptors

Secondary causes

Maternal hyperparathyroidism.

Metabolic syndromes

Kenny Caffey syndrome

LCHAD.

Kerns Sayre syndrome.

Iatrogenic-

Blood transfusion.

Intravenous lipid infusions.

Soda bicarbonate.

Furosemide infusion.

Steroids.

Phosphate therapy.

Gentamycin usage.

Alkalosis.

Phototherapy.

PRETERM NEONATES WITH HYPOCALCEMIA –

In preterm neonates during the postnatal period, there is a rapid decline in serum calcium; the magnitude of depression is inversely proportional to gestational age.

Untreated LBW infants and essentially all ELBW infants exhibit total calcium levels < 7mg/dl by day 1. However, a decrease in calcium is not proportional to a decrease in total serum calcium levels. The ratio of ionized to total calcium levels in preterm newborns is higher than in term[82].

The ionized calcium is not decreased due to low serum protein concentration and pH in prematurity. Due to this, hypocalcemic signs are frequently absent in preterm infants.

The parathyroid glands in neonates, despite prematurity, responds well to hypocalcemia.

A several days delay in phosphaturic and renal CAMP responses to PTH has been reported, suggesting that there might be a maturational delay in the renal response to PTH. High renal sodium loss also causes calciuric loss. If the exaggerated increase in calcitonin in preterm neonates can also promote hypocalcemia[82].

CLINICAL FEATURES OF HYPOCALCEMIA[42]-

In newborns they can present with any of the following:

Poor feeding

Lethargy.

Vomiting.

Abdominal distension.

Jitteriness.

Irritability.

Convulsions.

Hypertonia.

Apnea.

Tachypnea/tachycardia.

Laryngospasm.

Clonus, hyperreflexia.

Carpopedal spasm is less common

Screening is recommended only in at-risk neonates-

Preterm infants born before 32 weeks.

Neonates of diabetic mothers.

Neonates who are born after severe perinatal asphyxia, is defined as APGAR <4 at 1 min of age.

Time of screening :

At 24 to 48 hrs. of age in at-risk babies.

Difference between total & ionized serum calcium levels :

Ionized calcium levels are important to differentiate true hypocalcemia from a decrease in total serum calcium concentration. A decrease in total calcium can be due to low serum albumin and abnormal Ph[42].

INVESTIGATIONS :

First line :

- Serum magnesium levels.
- Serum phosphate.
- ALP.
- LFT.
- RFT.
- Arterial PH.

Second line :

- Serum parathormone levels.
- Urinary calcium creatinine ratio.
- Maternal calcium, phosphate & ALP.

Others –

CT brain for calcifications.

2D ECHO.

Vitamin D levels.

Hearing evaluation.

Cortisol levels.

Thyroid function tests.

TREATMENT OF HYPOCALCEMIA

Calcium therapy is the most effective treatment for hypocalcemia, iv calcium therapy is the most effective & rapid method of increasing serum calcium concentration. Once hypocalcemia is controlled, maintenance therapy with oral calcium can be given. In patients with asymptomatic hypocalcemia, only oral calcium is sufficient[42].

TREATMENT OF EARLY-ONSET HYPOCALCEMIA[42]

(1 ml of calcium gluconate (10%) gives 9mg of elemental calcium.)

1. In neonates who are at increased risk of hypocalcemia (prophylactic)

Preterm infants (</32 weeks), sick infants of diabetic mothers and those with severe perinatal asphyxia should receive 40mg/kg/day of elemental calcium (4ml/kg/day of 10 % calcium gluconate) for prevention of early-onset hypocalcemia. However, there is no evidence for this

practice. Infants who are on oral feeds will receive orally calcium every 6 hrs. Oral calcium preparation has high osmolality &should be avoided in babies with a high risk of NEC.

2. Neonates diagnosed to have symptomatic hypocalcemia(on screening)

For these infants ,they should receive 80mg/kg/day elemental calcium.(8ml/kg/day of 10% calcium gluconate) for 48 hrs.

This must be tapered by 50% dose for another 24 hrs. and then discontinued. Neonates tolerating oral feeds should be started on oral calcium.

3. Neonates diagnosed to have symptomatic hypocalcemia-

They should receive a bolus of 2ml/kg/dose diluted 1:1 with 5% dextrose over 10 minutes under cardiac monitoring. In case of severe hypocalcemia with poor cardiac function, calcium chloride 20mg/kg must be given through the central line over 10-30 minutes, followed by iv infusion of 80mg/kg/day elemental calcium for 48 hrs.

Calcium infusion is preferred to iv bolus dose (1ml/kg/dose q 6hrly). Infusion should be decreased to 50 % in next 24 hrs. and then discontinued. The infusion can be replaced by oral calcium on the last day.

Normal calcium values should be documented at 48 hrs. before weaning from the infusion.

The use of vitamin D formulations in neonates to prevent hypocalcemia is not effective. An important aspect of management is treating the primary cause (hypomagnesemia, hyperphosphatemia)

AAP published revisions to guidelines for adequate intake of vitamin D in infants, children &

adoloscents[86]. These guidelines now recommend a daily intake of 400U in the first few months following birth and continuing through adolescence.

Although not used routinely due to the risk of osteosarcoma, the administration of recombinant PTH in the infant with hypocalcemia refractory to calcitriol & calcium supplements was reported to be effective[86].

PHOTOTHERAPY INDUCED HYPOCALCEMIA

Romagnoli et al. (1979) first time showed the association of hypocalcemia with phototherapy in preterm newborns[11]. Similarly, Bergstrom & Hakanson saw this observation in newborn rats[12]. There are only a few studies on the hypocalcemic effect of phototherapy[12,13,14].

Hakanson & Bergstrom et al. (1981) reported prevention of phototherapy induced hypocalcemia in newborn rats by melatonin[12]. When rats are exposed to white light, the serum calcium levels decrease. This can be prevented by covering occiput, by inhibiting corticosterone synthesis, and exogenous melatonin. This exogenous melatonin prevents hypocalcemic response to cortisol. Light-induced hypocalcemia usually occurs when melatonin is inhibited by transcranial illumination.

Hunter (2004) hypothesized that phototherapy inhibits pineal gland secretion of melatonin, which usually block the effect of cortisol on calcium in bone. So, when cortisol increases, bone uptake of calcium increases and causes hypocalcemia[12,68].

In Kim(2001) study, hypocalcemia due to decreased secretion of parathormone[88].

In Hoomans (2005) study, hypocalcemia was due to increased urinary calcium excretion[89].

Yadav (2012) have observed that 60% of term & 80% preterm developed hypocalcemia after phototherapy[90].

A cross-sectional study was performed on 147 icteric term neonates by paymanch AH et al. (2013) that was done with title "prevalence of phototherapy induced hypocalcemia in term neonates" in Bahrami hospital in Tehran from 2008-2009[91]. Phototherapy is given with four blue-light fluorescent lamps, placed 20 cms from newborn. Serum calcium and Bilirubin was measured on arrival & at 48 hrs after phototherapy. There was a significant difference between serum calcium levels before & after phototherapy(p=0.03)

Jain et al. (1998)study, the prevalence of hypocalcemia was 30 % in full-term & 55% in preterm neonates. In this study, the prevalence of hypocalcemia was higher in patients with high levels of serum bilirubin.

In Yadav's study (2012), 80% of hypocalcemic term neonates became symptomatic after 48hrs of phototherapy. The most common sign was jitteriness[90].

In Eghbalian's study (2002), one of the hypocalcemic newborns had apnea[93]. It was found that blood calcium levels decreased considerably, and continued at times to threshold of hypocalcaemia. The duration of phototherapy correlated with hypocalcemic incidence.

In the karamifars study (2002), they found out a significant difference between the prevalence of hypocalcemia in premature (22.6%) and full tern neonates (8.7%). None of the hypocalcemic neonate was symptomatic clinically. Serum calcium returned to normal after 24 hrs after discontinution after phototherapy in almost all hypocalcemic infants[94].

Sethi H et al. (1993) study on phototherapy induced hypocalcemia,90% preterm neonates & 75% full-term neonates developed hypocalcemia after being subjected to phototherapy[14]. There was a significant fall in total calcium as well as ionized calcium in the study group in contrast to the control group. From this study, it is recommended that neonates should be given supplementary calcium to prevent hypocalcemia.

Zecca et al. (1983) reported that 25 hydroxyvitamin D3 did not reduce the incidence of phototherapy induced hypocalcemia in preterm neonates and concluded that vitamin D3 would not play an important role in the pathogenesis of phototherapy induced hypocalcemia[95].

Yadav et al. (2011) did a study with the title "evaluation of the effect of phototherapy on serum calcium level"[96]. In this study, they included 30 neonates (15 term & 15 preterms) with a control group of 20 neonates (10 term & 10 preterms) . Neonates in the study group is treated with phototherapy were as in the control group it is treated without phototherapy. Ionized calcium was measured before & 48 hrs after phototherapy . There was no statistically significant difference in mean serum calcium levels in term & preterm neonates of both the study and control group. After 48 hrs of phototherapy in the study group, a significant decrease in serum calcium level in 66.6% of term & 80% of preterm neonates was seen. But no difference was observed in the control group.

Marzich k et al. (2014) study, with the title "effect of head covering on phototherapy induced hypocalcemia in icterus newborns", A randomized control trial was done on 72 full-term neonates with indirect hyperbilirubinemia receiving phototherapy during march to September 2010[97]. Neonates were divided into two groups. The study group received phototherapy while wearing a hat, whereas the control group underwent phototherapy without wearing a hat. From this study, it was shown that 385 in the control group and 13.8% in the case group had hypocalcemia after 48 hrs after phototherapy, which was statistically significant.

NEED FOR THE STUDY

There are only limited reports which were published on the role of phototherapy in causing hypocalcemia in neonates. There is a difference in incidence reported of hypocalcemia after phototherapy in different studies[11,12,14,87-96].

As hypocalcemia is one of the lesser-known adverse effects of phototherapy, to study the effect of phototherapy on serum calcium levels is need for the study.

METHODOLOGY

Study Design:

This was a tertiary care teaching hospital based, prospective observational study done from December 2019 to May 2021 in the Neonatal intensive care unit of, SHRI B.M. Patil Medical college & Hospital ,VIJAYAPURA.

Sample Size:

100 neonates with unconjugated hyperbilirubinemia.

Tentative Statistical analysis

- Data will be represented using Mean ±SD, percentages and diagrams
- Significant difference of baseline and post-operative data will be compared using Paired t test/ Wilcoxon sign rank test.
- Significant difference between Qualitative data will be found using Chi square or Fisher's Exact test if necessary.

If $P \leq 0.05$, association or difference will be considered statistically significant.

Neonates with unconjugated hyperbilirubenemia were selected for the study and were given phototherapy.

Statistical methods used

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean±standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables. The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value. C= (number of rows-1)*(number of columns-1)

The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

s_1^2 = variance of sample 1 = $\frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$

s_2^2 = variance of sample 2 = $\frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$

The difference of the means of analysis variables between two time points in same group was tested by paired t test.

T-Statistic

The T-Statistic is the value used to produce the *p*-value (Prob Level) based on the *T* distribution. The formula for the T-Statistic is:

$$T - Statistic = \frac{\overline{x}_{diff} - Hypothesized\ Value}{SE_{\overline{x}_{diff}}}$$

DF

The degrees of freedom define the T *distribution* upon which the probability values are based. The formula for the degrees of freedom is the number of pairs minus one:

$$df = n - 1$$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23(IBM Statistics, Chicago, USA)and Microsoft office 2007.

Late Preterm birth defined as delivery between 34 0/7 weeks and 36 6/7 weeks of gestation .

Term birth defined as delivery after 37 0/7 weeks to 41 6/7 weeks

Inclusion criteria:

- Term neonates (37 0/7 weeks to 41 6/7 weeks) with unconjugated hyperbilirubinemia requiring phototherapy
- Late Preterm neonates (34 0/7 weeks to 36 6/7 weeks) with unconjugated hyperbilirubinemia requiring phototherapy .
- All the neonates included in the study group had unconjugated hyperbilirubinemia which required management with phototherapy as per AAP 2004 guidelines.
- Neonates weighing more than 2000 gms.

Exclusion Criteria:

- Hypocalcaemia before phototherapy.
- Apgar of less than 7 at 5 minutes after birth.
- Neonates of diabetic mothers
- Neonates on IV Calcium gluconate before Phototherapy.
- Syndromic babies
- Any high risk neonate requiring NICU admission

- Associated with co morbidities like Septicaemia, Renal Failure.

Study tool

- Predesigned proforma . (enclosed as Annexure 1)
- Gestational age is determined by New Ballard scoring .(enclosed as annexure 11)
- Complete history and thorough physical examination was carried out in the Neonates. Besides routine investigation, serum calcium and total serum bilirubin levels, before and after 48 hours of phototherapy were estimated.
- Serum bilirubin of the neonates was determined by Dual Wavelength Spectrophotometry (VITRUS by Johnson and Johnson). ·
- Neonates found with hyperbilirubinemia were further investigated as per standard protocol.
- Hyperbillirubinemia were managed as per standard protocol and phototherapy was given as per AAP [American Academy of Pediatrics] guidelines .

Procedure

- Clinical data, results of laboratory testing and administered medication, and outcome (death, resolving time or specific treatment) of the patients and maternal details were recorded from the patients‘ medical files.

- The neonate's birth weight, gestational age(**Annexure IV**), APGAR score(**Annexure V),** gestational history, intrapartum events (birth asphyxia, haemorrhages, etc.), feeding difficulties, adequacy of breast milk and other data were recorded.

- Pathologic hyperbilirubinemia requiring phototherapy was defined as any serum indirect (unconjugated) bilirubin level needing treatment with phototherapy during the first week of life, which was based on the 2004 American Academy of Pediatrics hyperbilirubinemia treatment guidelines .

- Phototherapy was performed according to AAP guidelines[40] .

- The infants were placed in a bassinet with the phototherapy device placed below and above them. All infants were exposed naked (apart from eye pads and diaper) to phototherapy .Phototherapy was interrupted only for feeding and nursing for 10-15 minutes every 2 hours. Our previous studies have shown that with this practice, the infants are treated 85% of the time on an average[102,103] .

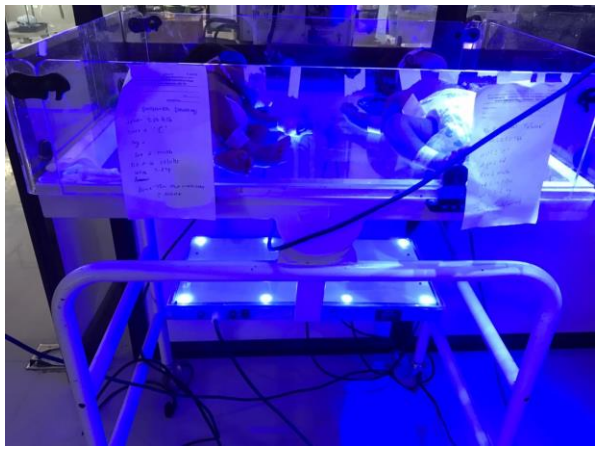


Fig 4 : Baby under phototherapy

Fig 5 : Phototherapy unit of PHOENIX MEDICALS

- Double surface phototherapy is given by placing blue light source [four 40- watt blue fluorescent tubes, PHOENIX MEDICALS] 20 cms above and 20 cms below the baby.
- Gestational age is determined by New Ballard scoring.
- All babies were on breast feeding.

- Detailed physical and systemic examination were done.
- The neonates were clinically assessed for features of hypocalcemia i.e. jitteriness, irritability/ excitability, letharginess and convulsions as well as other complications of phototherapy like rash, loose stool, fever and dehydration.
- Dehydration was assessed based on urine output, weight gain and sleep pattern.
- Those neonates fulfilling the inclusion criteria are subjected to blood test like serum calcium levels, at initiation and after phototherapy.
- 1 ml of venous blood was collected in pre-heparinized syringe.
- Serum calcium level less than 7 mg/dL in preterm infants and less than 8 mg/dL in term neonates was considered as hypocalcemia .

Written consent was taken from all participants in the study.

The patients declining to give consent were excluded from the study.

The consent form is enclosed as **Annexure II.**

The study design and proforma was approved by institutional ethical committee.

The approval letter from the ethical committee is enclosed in **Annexure I**

Sample Size of Estimation

Sample size : 100 cases includes

- Term neonates and

- Late Preterm neonates

with unconjugated hyperbilirubinemia were selected for the study and were given phototherapy.

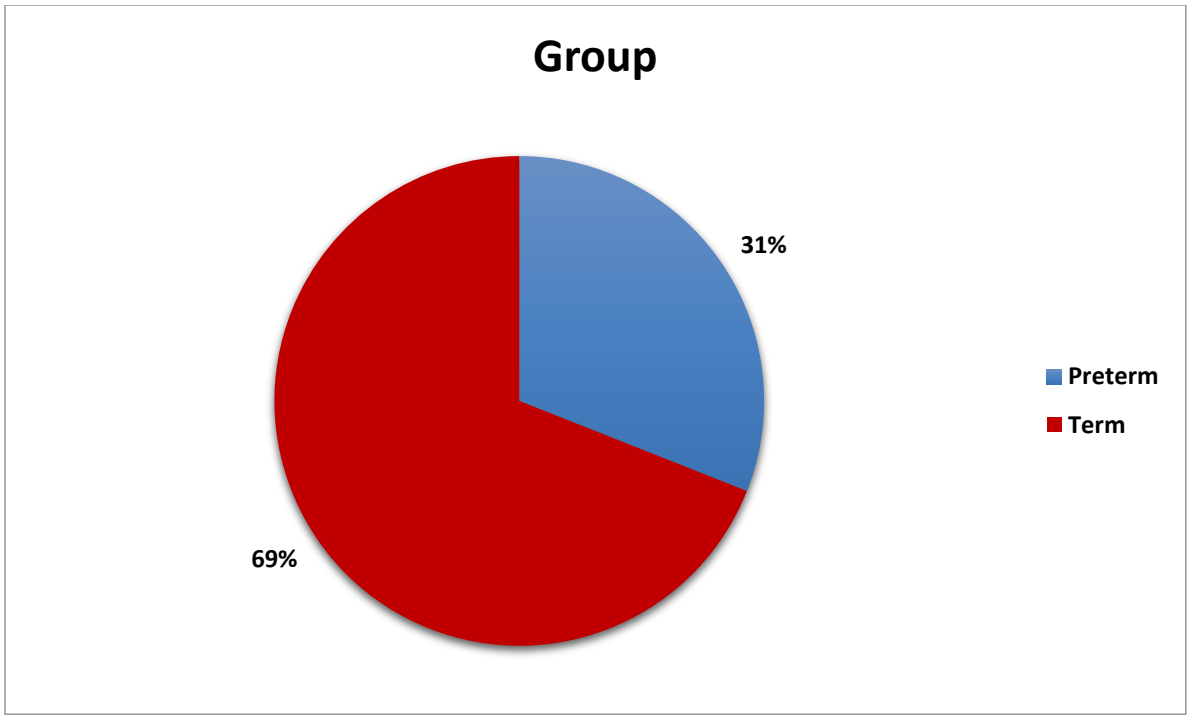
RESULTS

During the study period, a total of 100 hyperbilirubinemic neonates who met the criteria were enrolled into the study.

Table 1: Distribution of Cases according to Term/Late Preterm

Group	N	Percent
Preterm	31	31
Term	69	69
Total	100	100

Figure 1: Distribution of Cases according to Term/Late Preterm

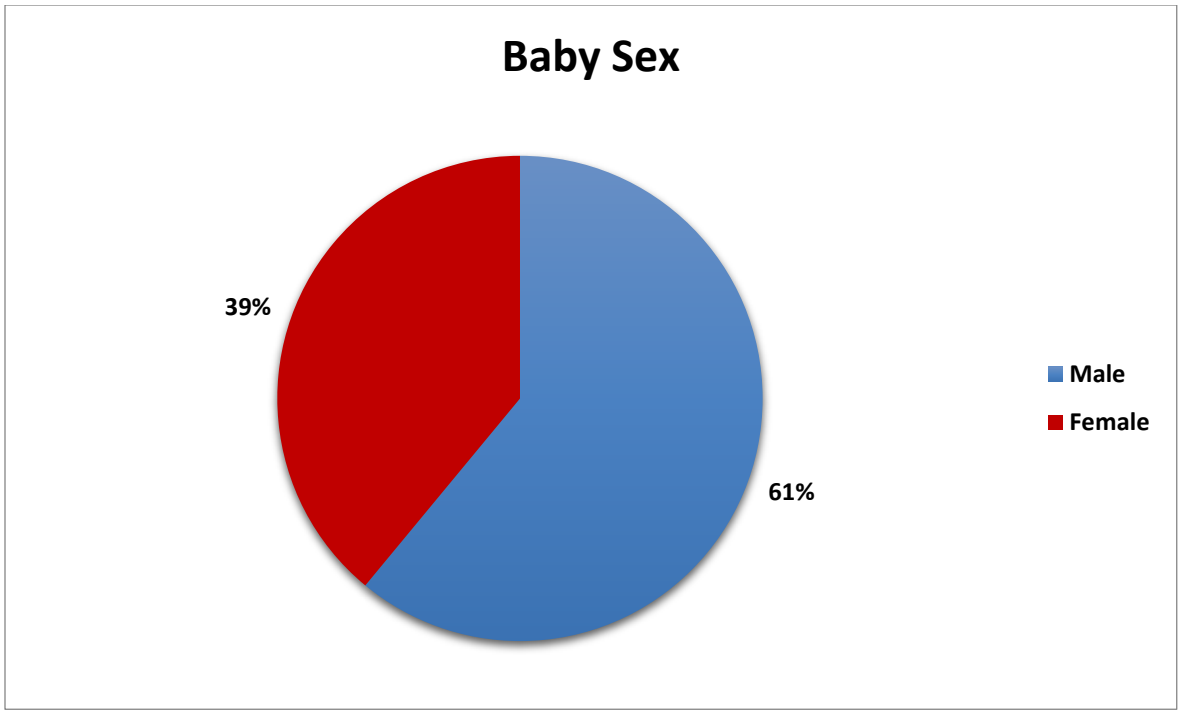


69% of babies were Term babies, and 31% were Late Preterm babies. (Table 1 & Figure 1)

Table 2 : Distribution of Cases according to Baby Sex

Baby Sex	N	Percent
Male	61	61
Female	39	39
Total	100	100

Figure 2 : Distribution of Cases according to Baby Sex

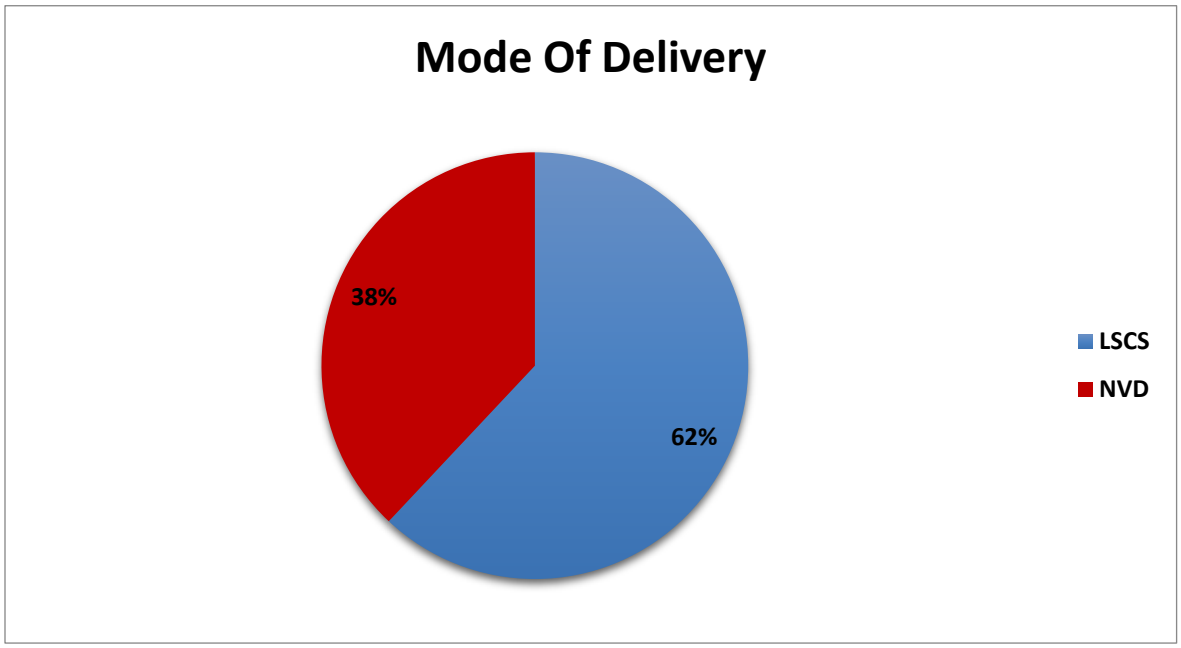


61% of Neonates were Males & 39% were Females. The Male : Female Ratio was found to be 1.56 : 1(Table 2 and Figure 2).

Table 3 : Distribution of Cases according to Mode Of Delivery

Mode Of Delivery	N	Percent
LSCS	62	62
NVD	38	38
Total	100	100

Figure 3 : Distribution of Cases according to Mode Of Delivery

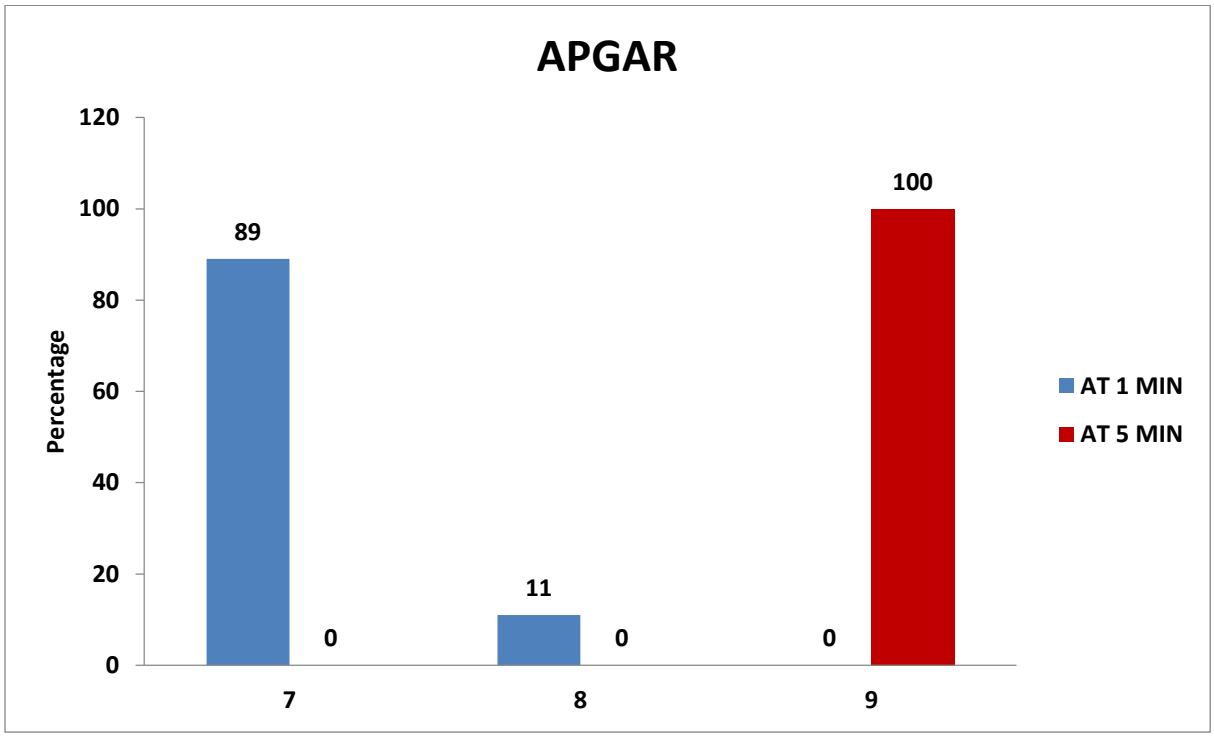


62% of Neonates were delivered by LSCS and 38% of neonates were delivered by Normal Vaginal Delivery.(Table 3 & Figure 3).

Table 4 : Distribution of Cases according to APGAR

APGAR	AT 1 MIN		AT 5 MIN	
	N	Percent	N	Percent
7	89	89	0	0
8	11	11	0	0
9	0	0	100	100
Total	100	100	100	100

Figure 4 : Distribution of Cases according to APGAR



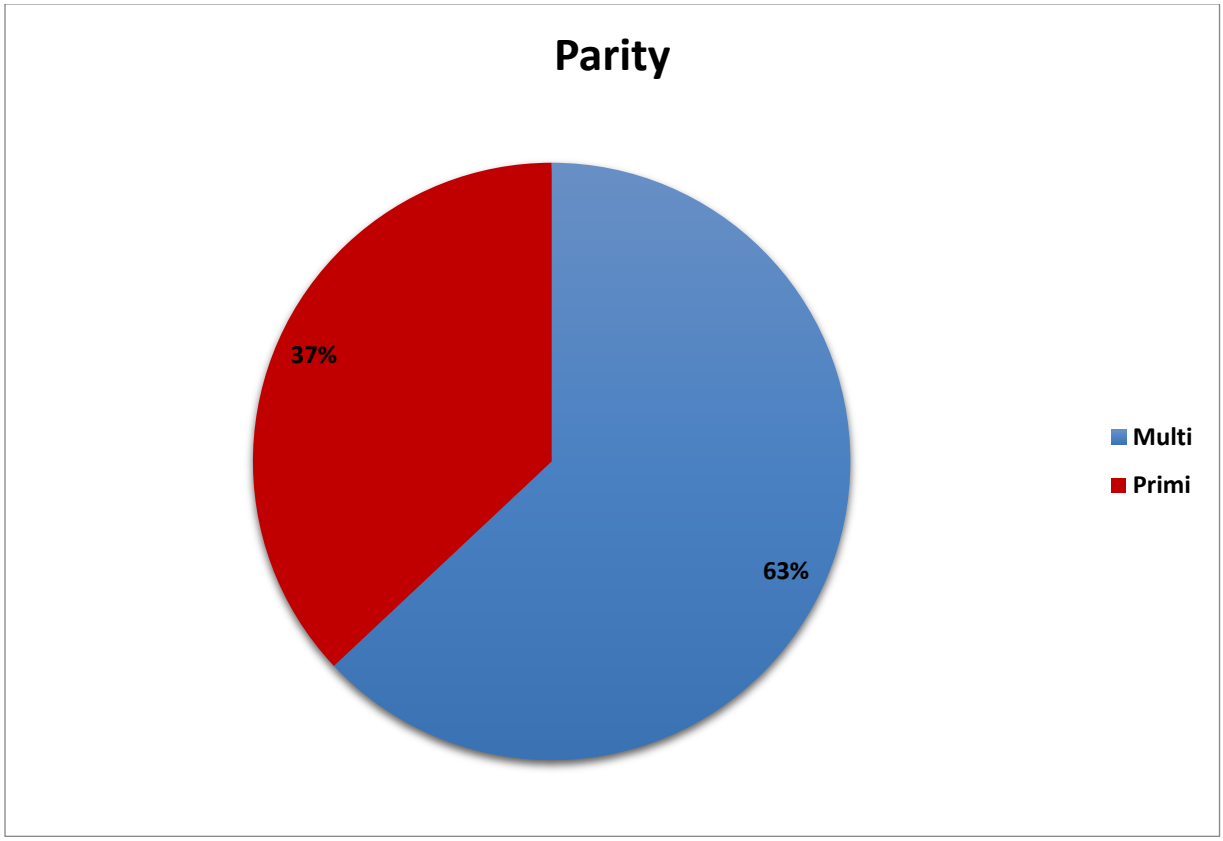
89% of Neonates had APGAR score of 7 at 1 Minute. 11% had APGAR score of 8 at 1 Minute.

100% of Neonates had APGAR score of 9 at 5 Minutes.(Table 4 & Figure 4).

Table 5 : Distribution of Cases according to Parity

Parity	N	Percent
Multi	63	63
Primi	37	37
Total	100	100

Figure 5 : Distribution of Cases according to Parity

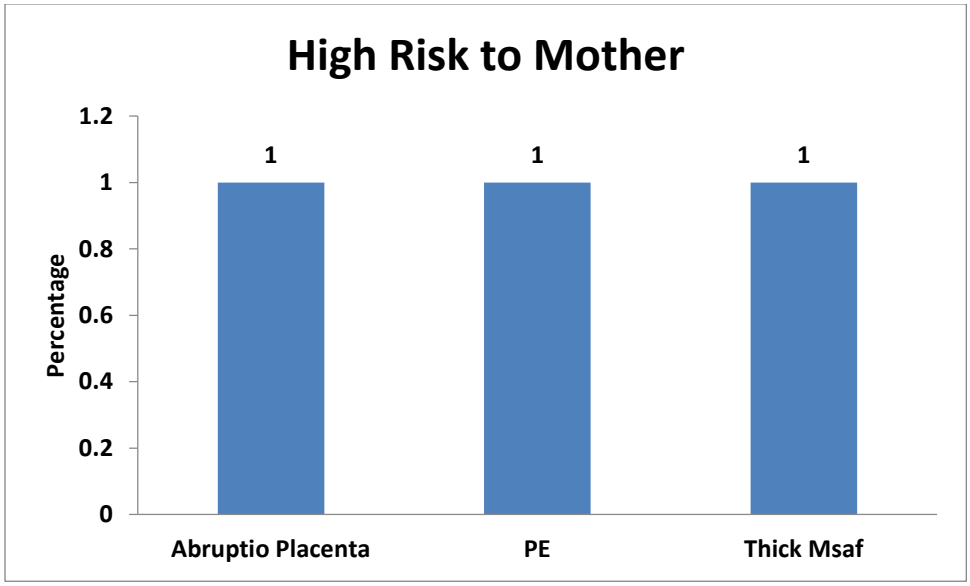


63% of Neonates were born to Multiparous Mothers & 37% of Neonates were born to Primiparous Mothers. (Table & Figure).

Table 6 : Distribution of Cases according to Risk factors in Mother

High Risk to Mother	N	Percent
Abruptio Placenta	1	1
PE	1	1
Thick MSAF	1	1

Figure 6 : Distribution of Cases according to Risk factors in Mother

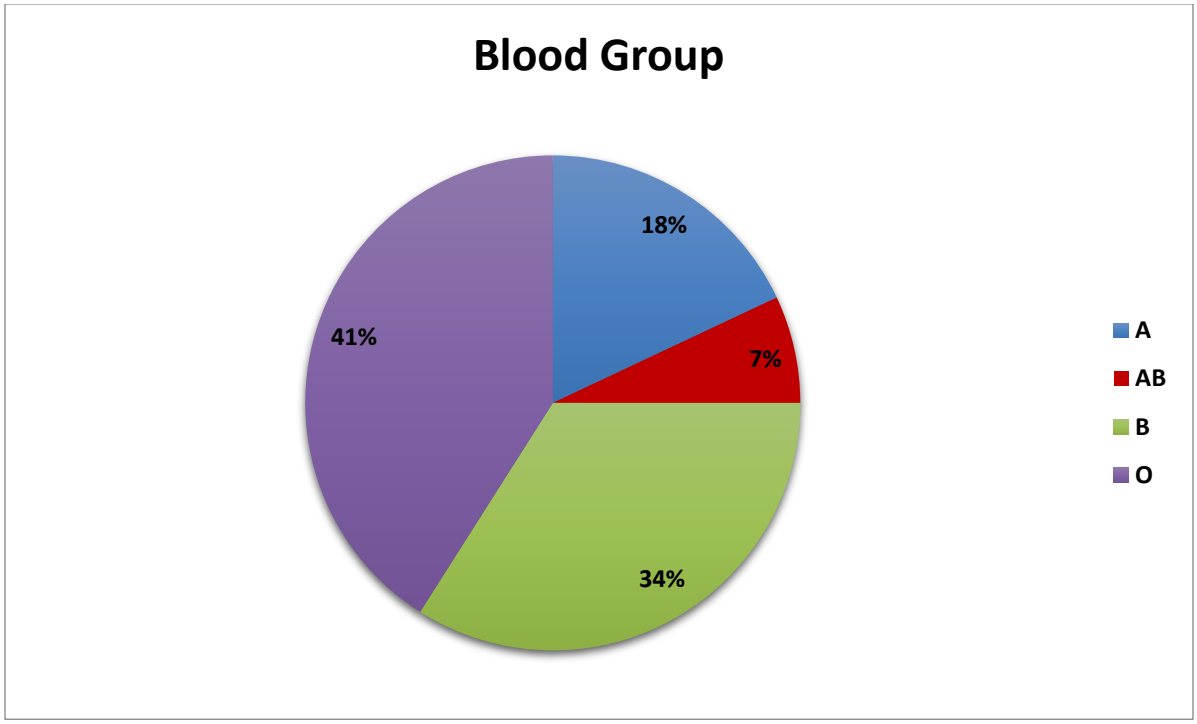


1% of Mothers had Abruptio Placenta. 1% of Mothers had Preeclampsia, 1% of Mothers had Thick MSAF. (Table 6 & Figure 6)

Table 7 : Distribution of Cases according to Blood Group

Blood Group	N	Percent
A	18	18
AB	7	7
B	34	34
O	41	41
Total	100	100

Figure 7 : Distribution of Cases according to Blood Group

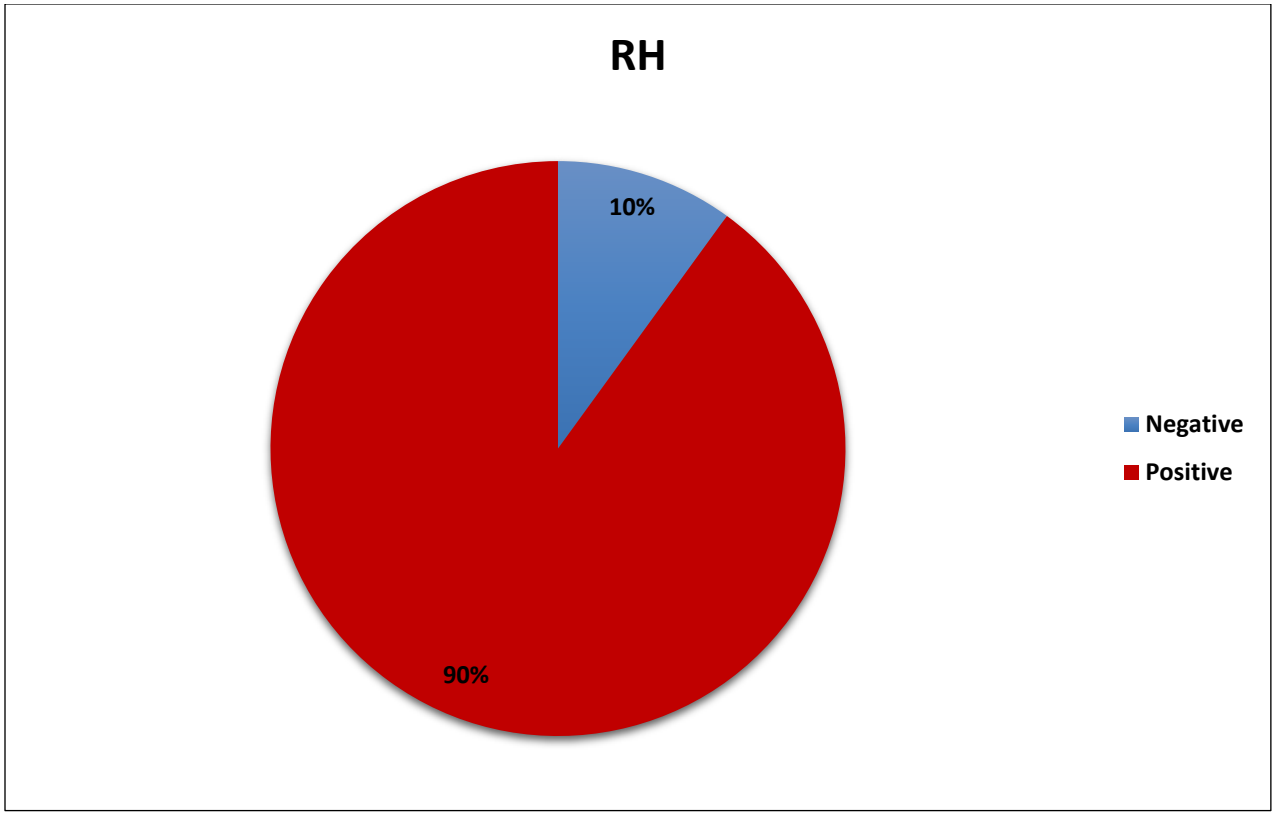


18% of Neonates had blood group A . 7% of Neonates had Blood group AB. 34% of Neonates had blood group B. 41% of Neonates had Blood Group O. (Table 7 & Figure 7).

Table 8 : Distribution of Cases according to RH

RH	N	Percent
Negative	10	10
Positive	90	90
Total	100	100

Figure 8 : Distribution of Cases according to RH

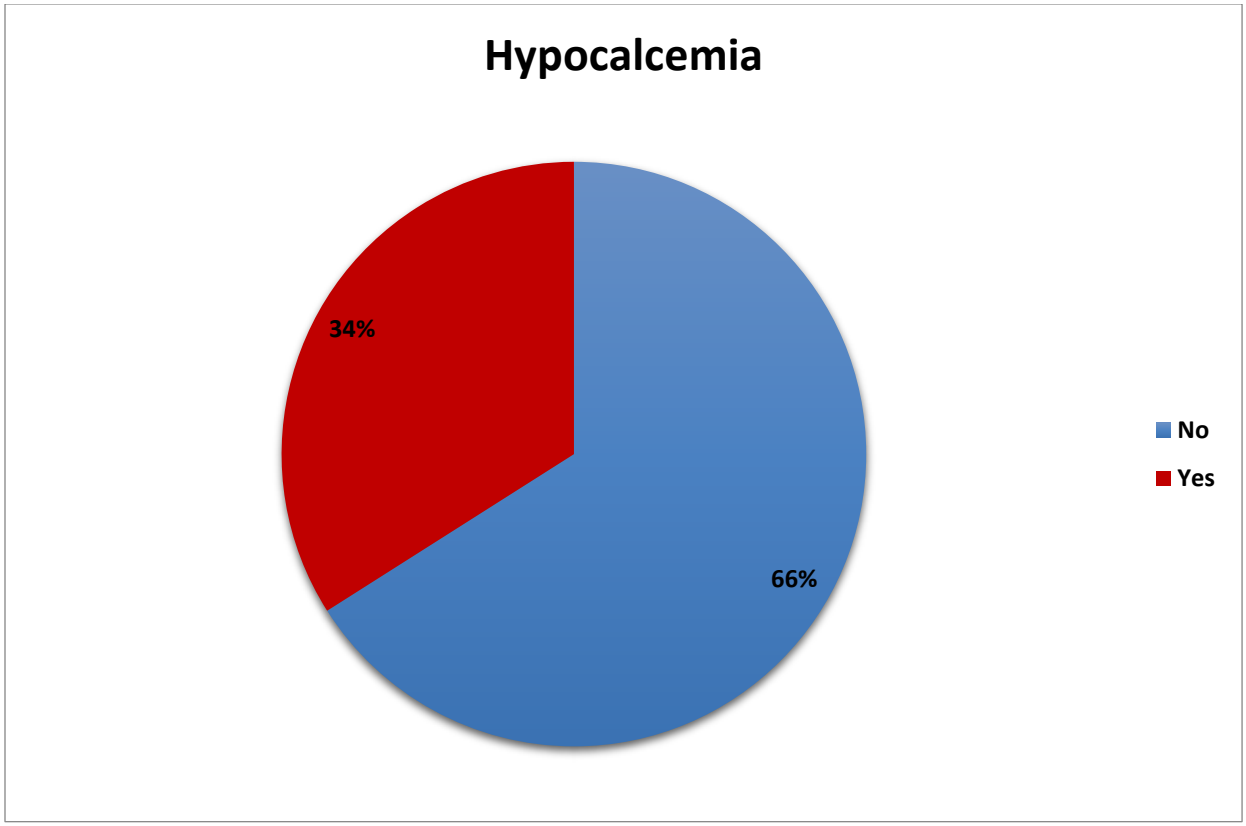


90% of Neonates were RH positive . 10% of Neonates were RH Negative.(Table 8 & Figure 8)

Table 9 : Distribution of Cases according to Hypocalcemia

Hypocalcemia	N	Percent
No	66	66
Yes	34	34
Total	100	100

Figure 9 : Distribution of Cases according to Hypocalcemia

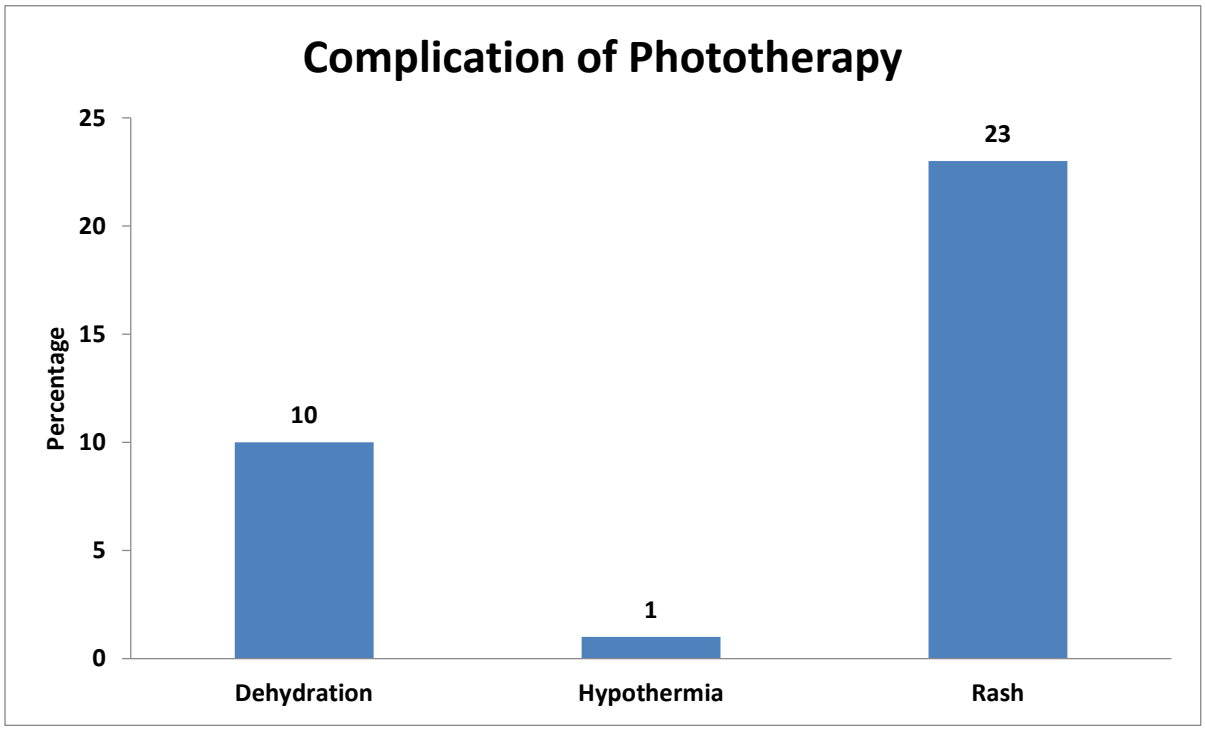


34% of Neonates had Hypocalcemia after Phototherapy. In 66% of neonates calcium levels were Normal after Phototherapy.(Table 9 & Figure 9).

Table 10 : Distribution of Cases according to Complication

Complication of Phototherapy	N	Percent
Dehydration	10	10
Hypothermia	1	1
Rash	23	23

Figure 10 : Distribution of Cases according to Complication

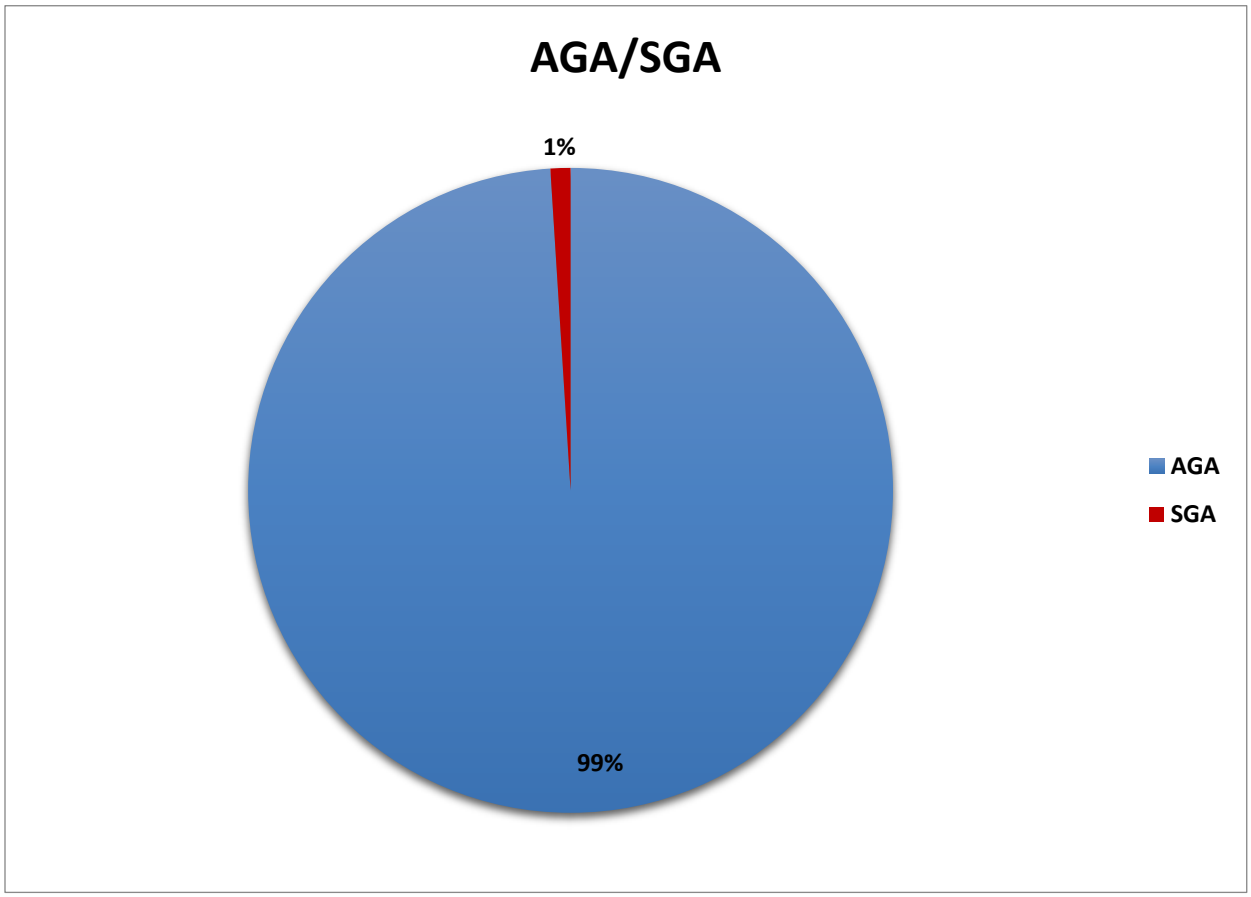


10% of Neonates had Dehydration after Phototherapy . 1% of Neonates had Hypothermia after Phototherapy. 23% of Neonates had Rash after Phototherapy.(Table 10 & Figure 10).

Table 11 : Distribution of Cases according to AGA/SGA

AGA/SGA	N	Percent
AGA	99	99
SGA	1	1
Total	100	100

Figure 11 : Distribution of Cases according to AGA/SGA

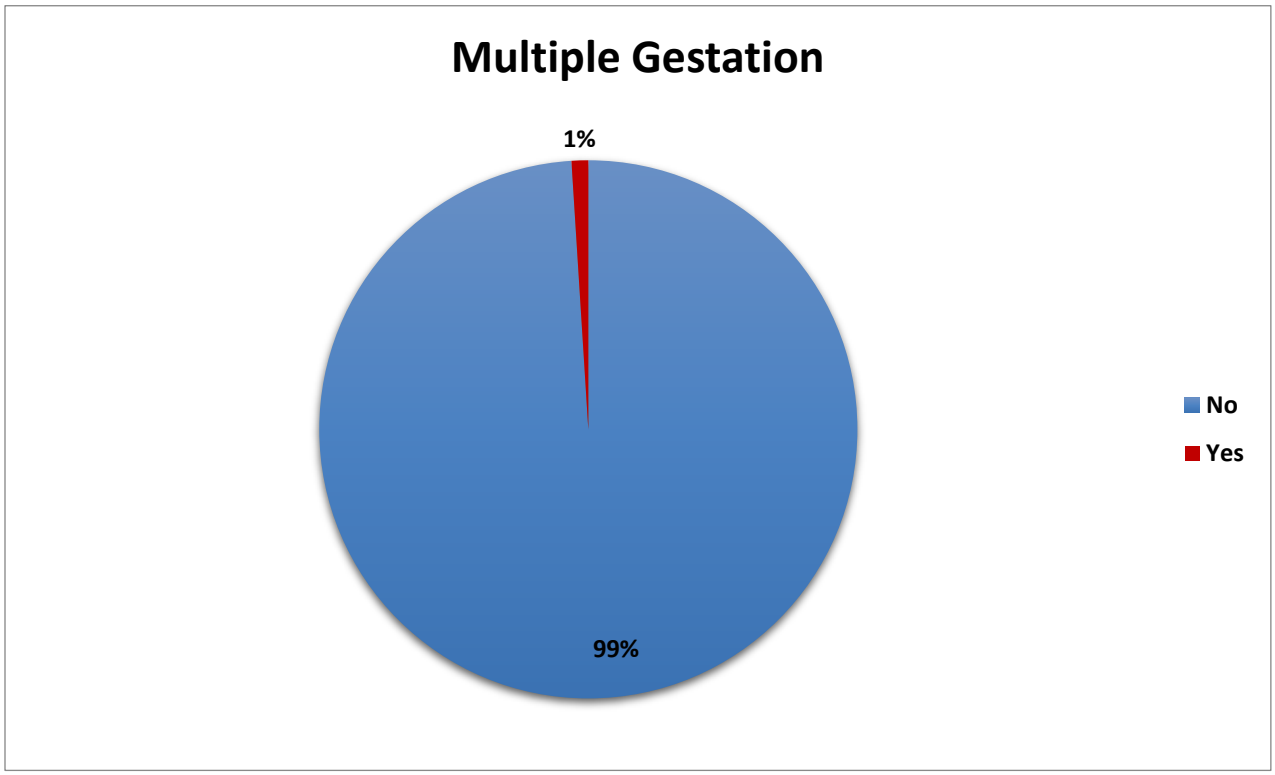


99% of Neonates were AGA. 1% of Neonates were SGA.(Table 11 & Figure 11).

Table 12 : Distribution of Cases according to Multiple Gestation

Multiple Gestation	N	Percent
No	99	99
Yes	1	1
Total	100	100

Figure 12 : Distribution of Cases according to Multiple Gestation



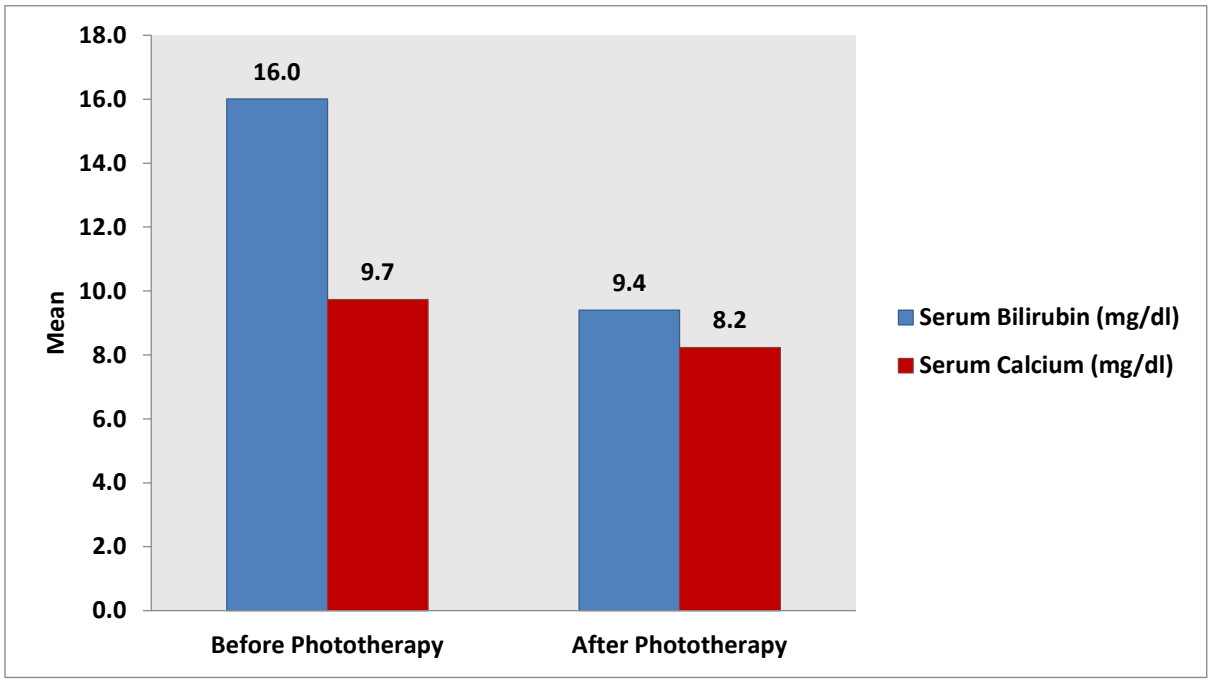
99% of Neonates were born to Single Gestation Pregnancy. 1% of Neonates were born to Multiple Gestation Pregnancy.(Table 12 & Figure 12)

Table 13 : Distribution of Serum Bilirubin and calcium according to Phototherapy

Parameter	Before Phototherapy		After Phototherapy		p value
	Mean	SD	Mean	SD	
Serum Bilirubin (mg/dl)	16.0	3.2	9.4	2.0	<0.001*
Serum Calcium (mg/dl)	9.7	0.7	8.2	0.8	<0.001*

Note: p value* significant at 5% level of significance (p<0.05)

Figure 13 : Distribution of Serum Bilirubin and calcium according to Phototherapy

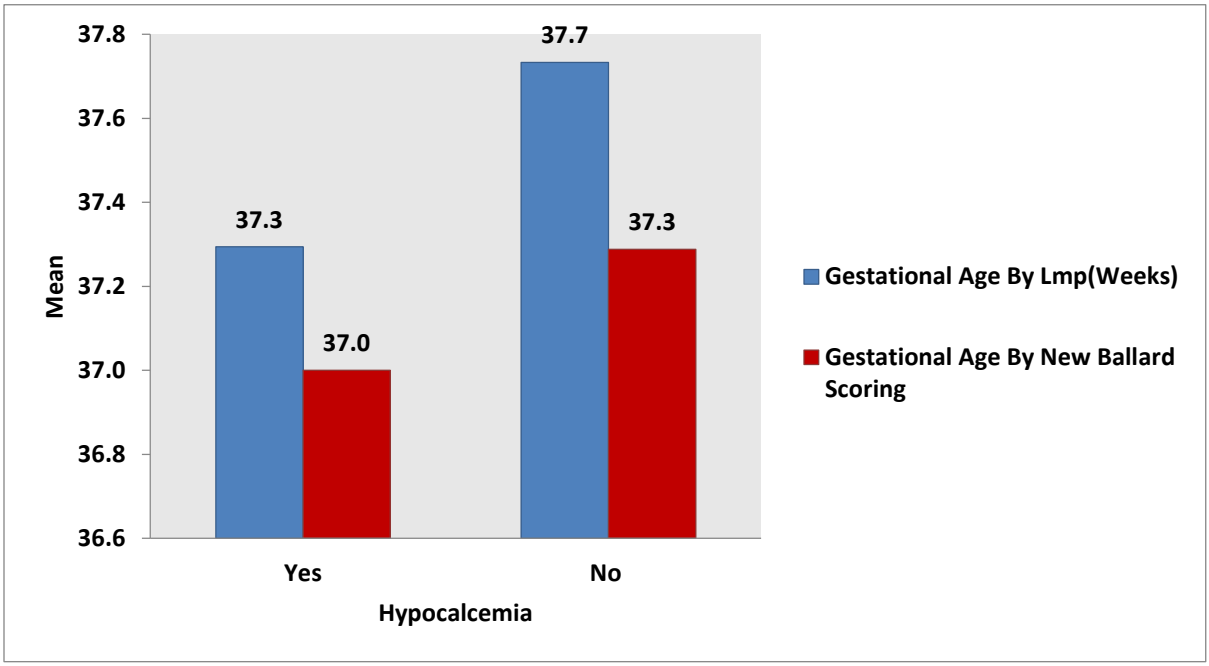


The Mean and SD of serum Bilirubin before Phototherapy was 16.0+_3.2.The Mean and SD of serum Bilirubin after Phototherapy was 9.4+_2.0.The Mean and SD of serum Calcium before Phototherapy was 9.7+-0.7.The Mean and SD of Serum Calcium after Phototherapy was 8.2+-0.8. **Which was Statistically Significant.** (Table 13 & figure 13)

Table 14 : Distribution of Gestational Age according to Hypocalcemia

Parameter	Hypocalcemia				p value
	Yes		No		
	Mean	SD	Mean	SD	
Gestational Age By LMP(Weeks)	37.3	1.3	37.7	1.6	0.169
Gestational Age By New Ballard Scoring	37.0	1.4	37.3	1.7	0.389

Figure 14 : Distribution of Gestational Age according to Hypocalcemia

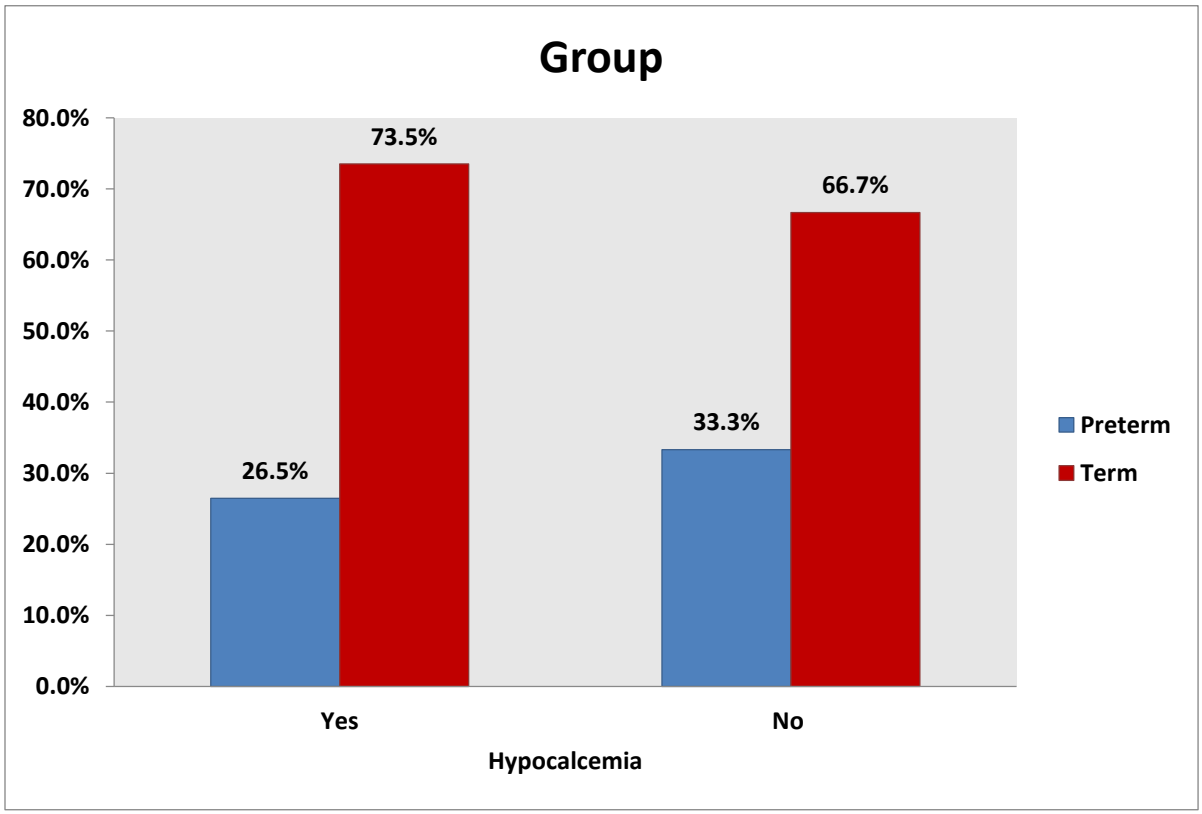


Among the Neonates with Hypocalcemia, the Mean Gestational age according to LMP was 37.3+_1.3 .The Mean Gestational age according to New Ballard Scoring was 37+_1.4. Which **was not statistically significant**.(Table 14 & Figure 14).

Table 15 : Distribution of Group according to Hypocalcemia

Group	Hypocalcemia				p value
	Yes		No		
	N	%	N	%	
Preterm	9	26.5%	22	33.3%	0.482
Term	25	73.5%	44	66.7%	
Total	34	100.0%	66	100.0%	

Figure 15 : Distribution of Group according to Hypocalcemia



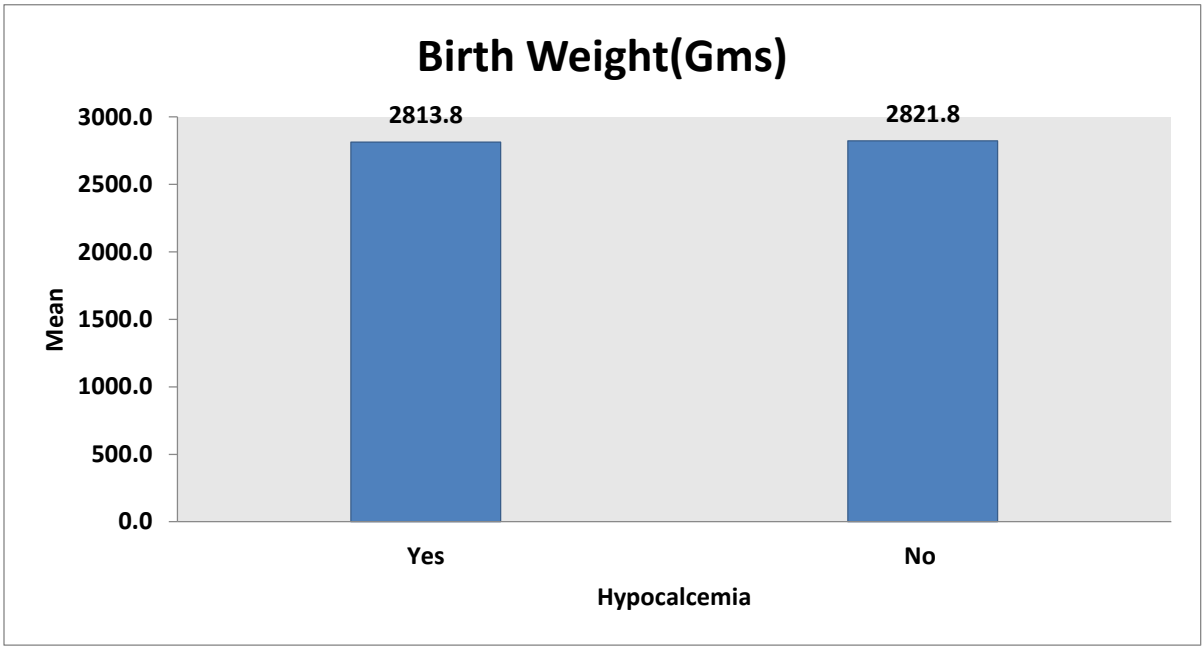
Among the Neonates with Hypocalcaemia, 26.5% were Preterm and 73.5% were Term neonates.

Which was **not statistically significant**.(Table 15 & Figure 15).

Table 16 : Distribution of Birth Weight according to Hypocalcemia

Parameter	Hypocalcemia				p value
	Yes		No		
	Mean	SD	Mean	SD	
Birth Weight(Gms)	2813.8	354.1	2821.8	361.9	0.917

Figure 16 : Distribution of Birth Weight according to Hypocalcemia



Among the Neonates with Hypocalcemia, the mean Birth weight was 2813 gms+-354 gms.

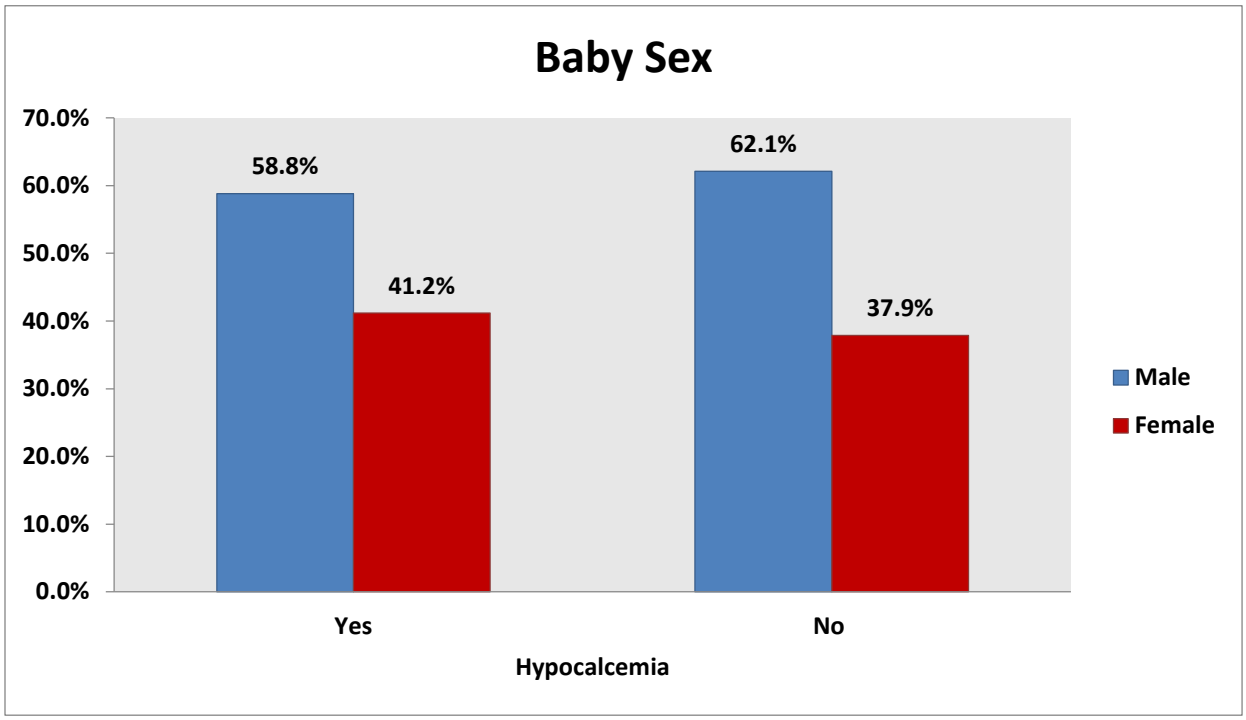
Among the Neonates without Hypocalcemia the mean Birth weight was 2821 gms+_361 gms.

The Comparison between the two groups **was not statistically significant**(Table 16 & Figure16)

Table 17 : Distribution of Baby Sex according to Hypocalcemia

Baby Sex	**Hypocalcemia**				**p value**
	Yes		**No**		
	N	**%**	**N**	**%**	
Male	20	58.8%	41	62.1%	0.749
Female	14	41.2%	25	37.9%	
Total	34	100.0%	66	100.0%	

Figure 17 : Distribution of Baby Sex according to Hypocalcemia

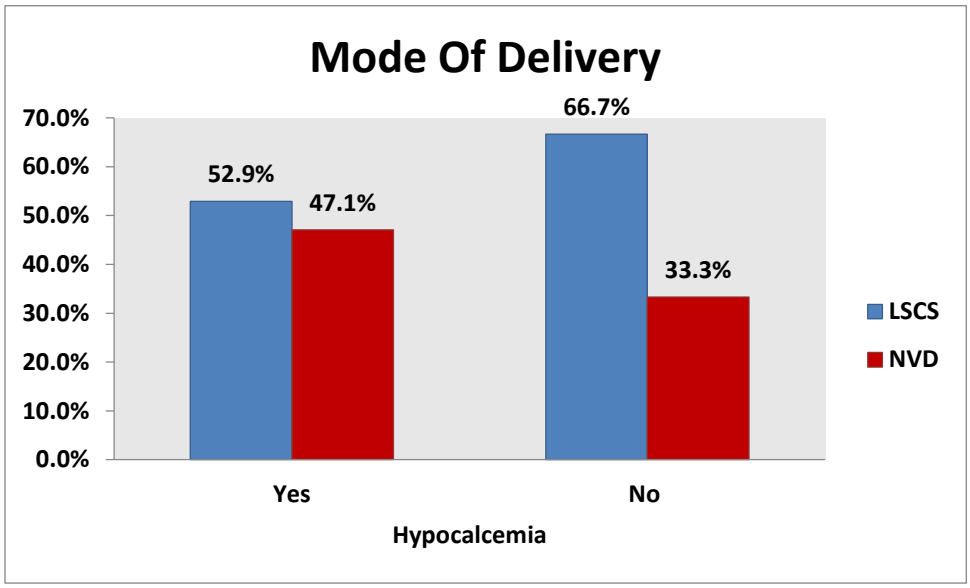


Among the Neonates with Hypocalcemia 58.8% were Males & 41.2% were females. And in neonates without Hypocalcemia 62.1% were males & 37.9% were Females. The comparison between the two groups **was not statistically significant**.(Table 17 & Figure 17).

Table 18 : Distribution of Mode Of Delivery according to Hypocalcemia

Mode Of Delivery	Hypocalcemia				p value
	Yes		No		
	N	%	N	%	
LSCS	18	52.9%	44	66.7%	0.180
NVD	16	47.1%	22	33.3%	
Total	34	100.0%	66	100.0%	

Figure 18 : Distribution of Mode Of Delivery according to Hypocalcemia

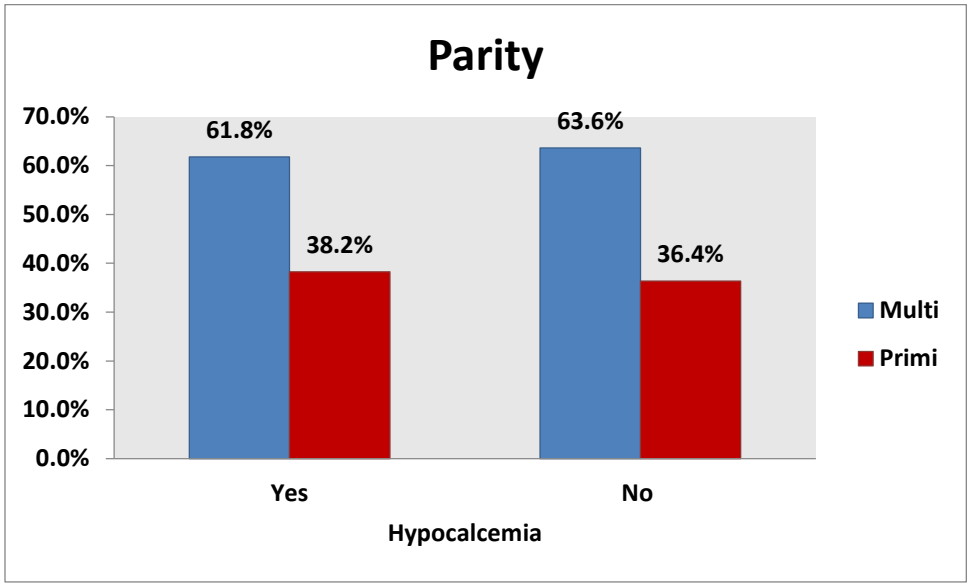


Among the Neonates with Hypocalcemia 52.9% of Neonates were delivered via LSCS, and 47.1% of Neonates were delivered via NVD. Among the Neonates without Hypocalcemia 66.7% were delivered via LSCS, and 33.3% of Neonates were delivered via NVD. The Comparison between the two groups **was not statistically significant**.(Table 18 & Figure 18)

Table 19 : Distribution of Parity according to Hypocalcemia

Parity	**Hypocalcemia**				**p value**
	Yes		**No**		
	N	**%**	**N**	**%**	
Multi	21	61.8%	42	63.6%	0.854
Primi	13	38.2%	24	36.4%	
Total	34	100.0%	66	100.0%	

Figure 19 : Distribution of Parity according to Hypocalcemia

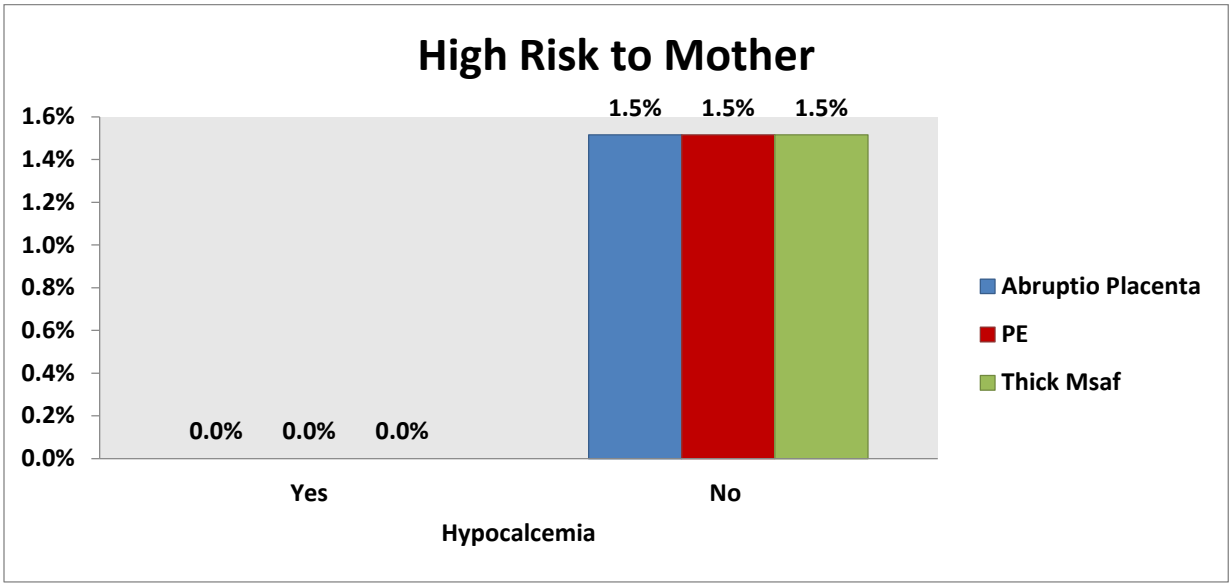


In Neonates with Hypocalcemia, 61.8% were born to Multiparous Mothers and 38.2% were born to primiparous mothers. In neonates without Hypocalcemia 63.6% of Neonates were born to Multiparous Mothers and 36.4% of Neonates were born to Primiparous mothers. The comparison between the two groups **was not statistically significant**.(Table 19 & figure 19)

Table 20 : Distribution of High Risk according to Hypocalcemia

High Risk to Mother	Hypocalcemia				p value
	Yes		No		
	N	%	N	%	
Abruptio Placenta	0	0.0%	1	1.5%	0.661
PE	0	0.0%	1	1.5%	
Thick MSAF	0	0.0%	1	1.5%	

Figure 20 : Distribution of High Risk according to Hypocalcemia

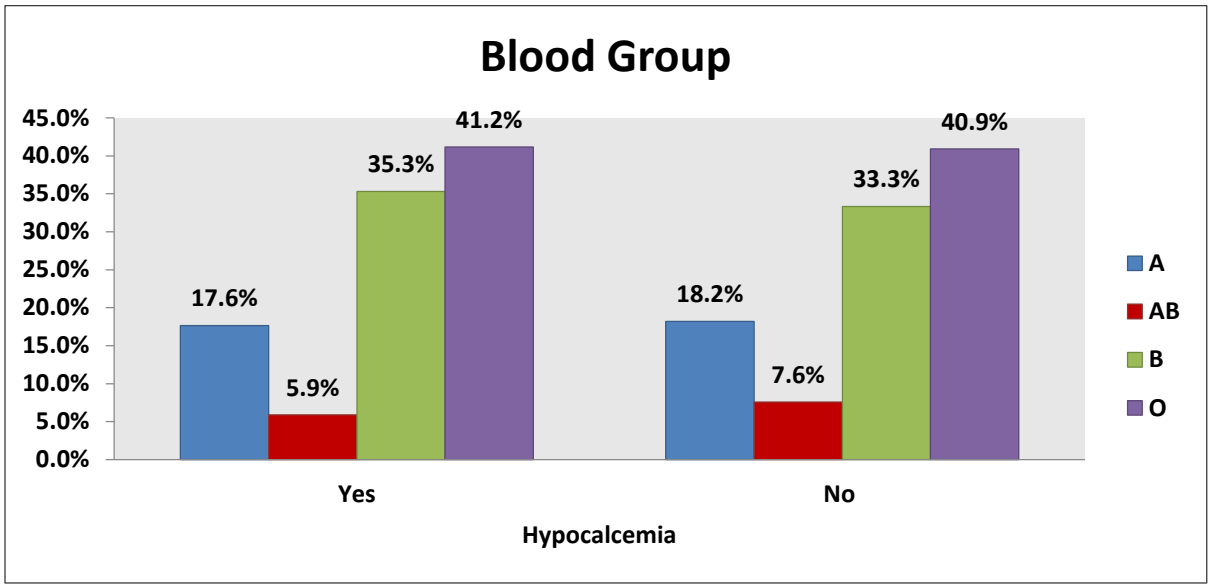


No Risk factors were identified in the mothers of the neonates who developed Hypocalcemia. Whereas in mothers of neonates who did not develop Hypocalcemia, Few risk factors were seen in the mothers. The comparison between two groups was not statistically significant.(table 20 & Figure 20).

Table 21 : Distribution of Blood Group according to Hypocalcemia

Blood Group	Hypocalcemia				p value
	Yes		No		
	N	%	N	%	
A	6	17.6%	12	18.2%	0.989
AB	2	5.9%	5	7.6%	
B	12	35.3%	22	33.3%	
O	14	41.2%	27	40.9%	
Total	34	100.0%	66	100.0%	

Figure 21 : Distribution of Blood Group according to Hypocalcemia

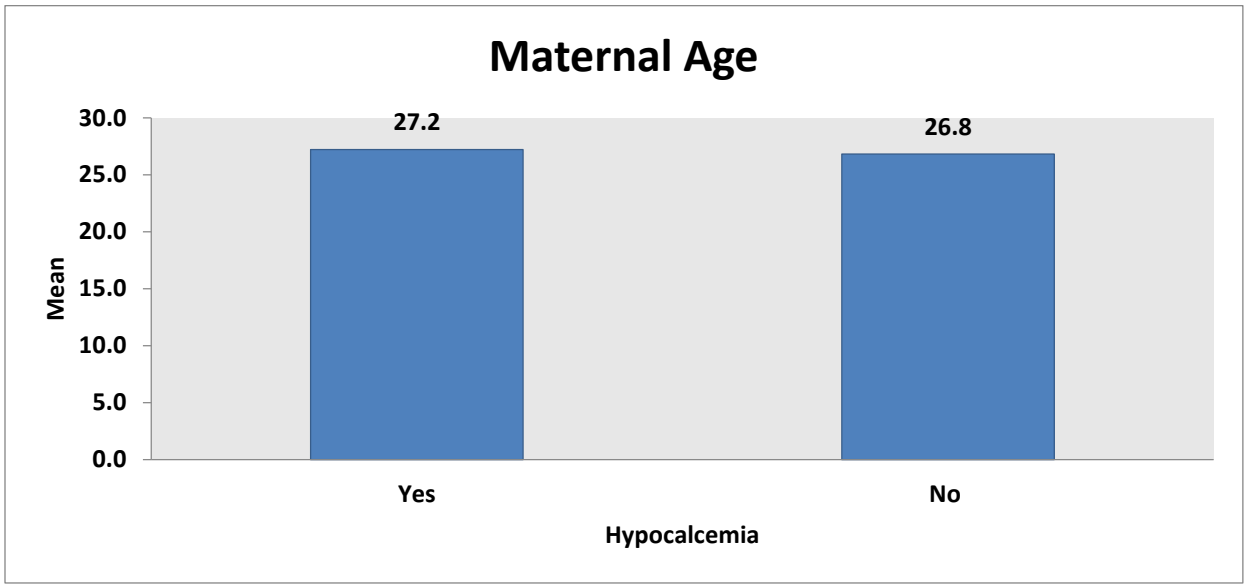


Among the Neonates with Hypocalcemia : 17.6% had blood group A ; 5.9% had blood group AB ; 35.3% had blood group B ; 41.2% had blood group O. There was **no statistically significant correlation** seen between blood groups and Hypocalcemia.(table 21 & figure 21)

Table 22 : Distribution of Maternal Age according to Hypocalcemia

Parameter	**Hypocalcemia**				**p value**
	Yes		**No**		
	Mean	**SD**	**Mean**	**SD**	
Maternal Age	27.2	1.1	26.8	1.1	0.109

Figure 22 : Distribution of Maternal Age according to Hypocalcemia

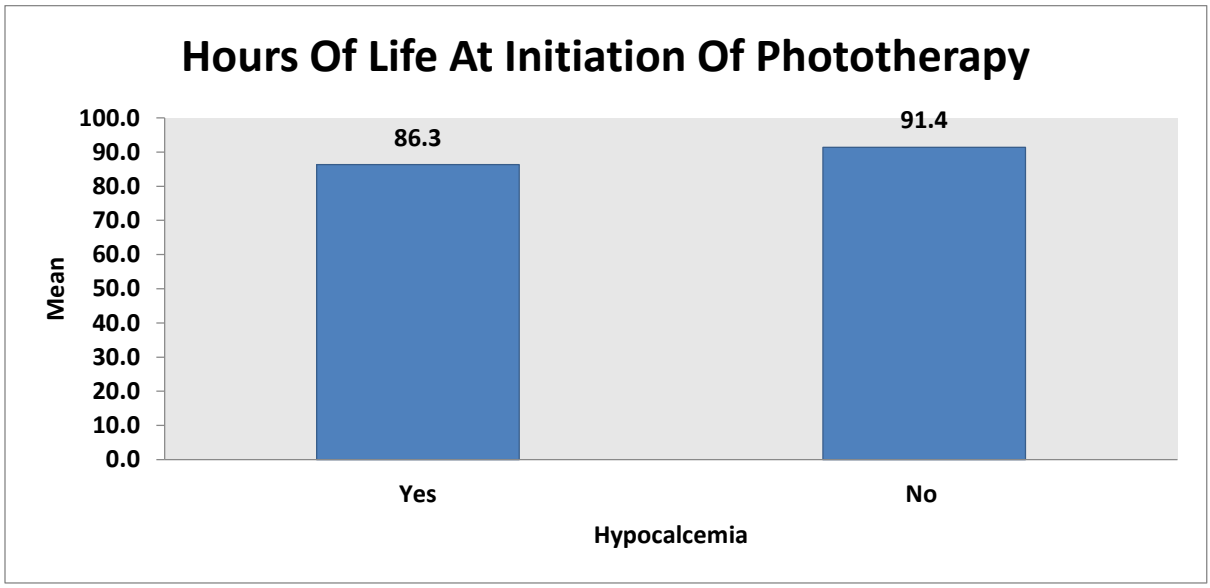


Among the Neonates with Hypocalcemia, the mean maternal age was 27.2+- 1.1 & among the Neonates without Hypocalcemia, the mean maternal age was 26.8+-1.1 .There was **no statistically significant** difference seen between the two groups (Table 22 & figure 22).

Table 23 : Hours of life at initiation of phototherapy according to Hypocalcemia

Parameter	Hypocalcemia				p value
	Yes		No		
	Mean	SD	Mean	SD	
Hours of life at initiation of phototherapy	86.3	30.7	91.4	51.4	0.599

Figure 23 : Hours of life at initiation of phototherapy according to Hypocalcemia



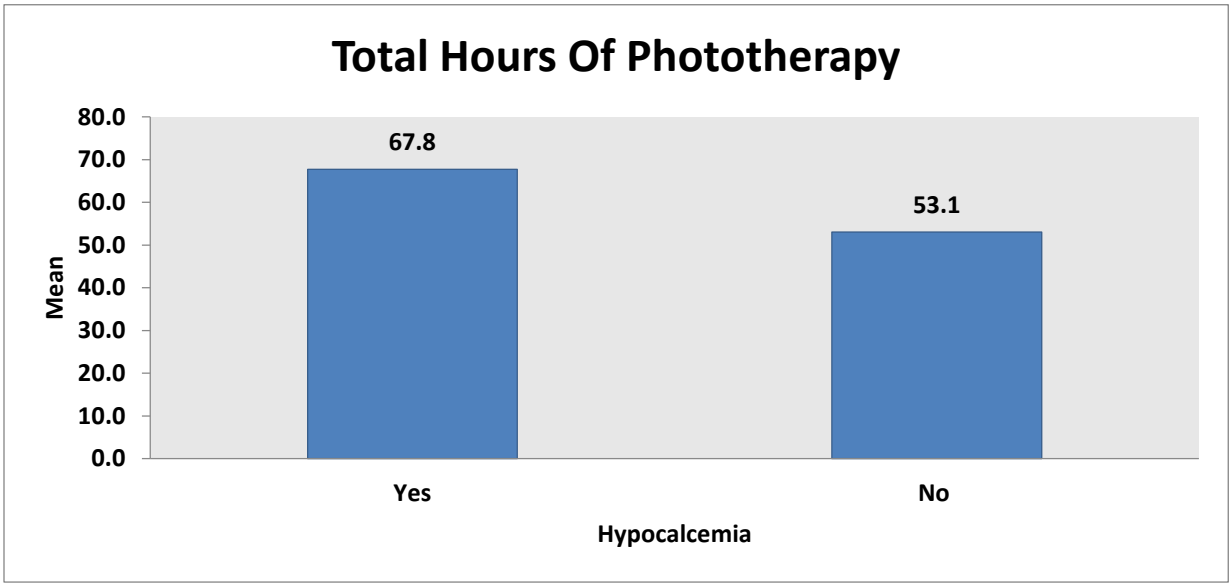
Among the Neonates with Hypocalcemia, the mean hours of life at Initiation of Phototherapy was 86.3+- 30.7 and in neonates without Hypocalcemia, the mean hours of life at initiation of Phototherapy was 91.4+_51.4. The Comparison between the two groups was **not statistically significant.(Table 23 & figure 23).**

Table 24 : Total Hours of Phototherapy according to Hypocalcemia

Parameter	**Hypocalcemia**				**p value**
	Yes		**No**		
	Mean	**SD**	**Mean**	**SD**	
Total Hours of Phototherapy	67.8	16.1	53.1	11.5	<0.001*

Note: p value* significant at 5% level of significance (p<0.05)

Figure 24 : Total Hours of Phototherapy according to Hypocalcemia

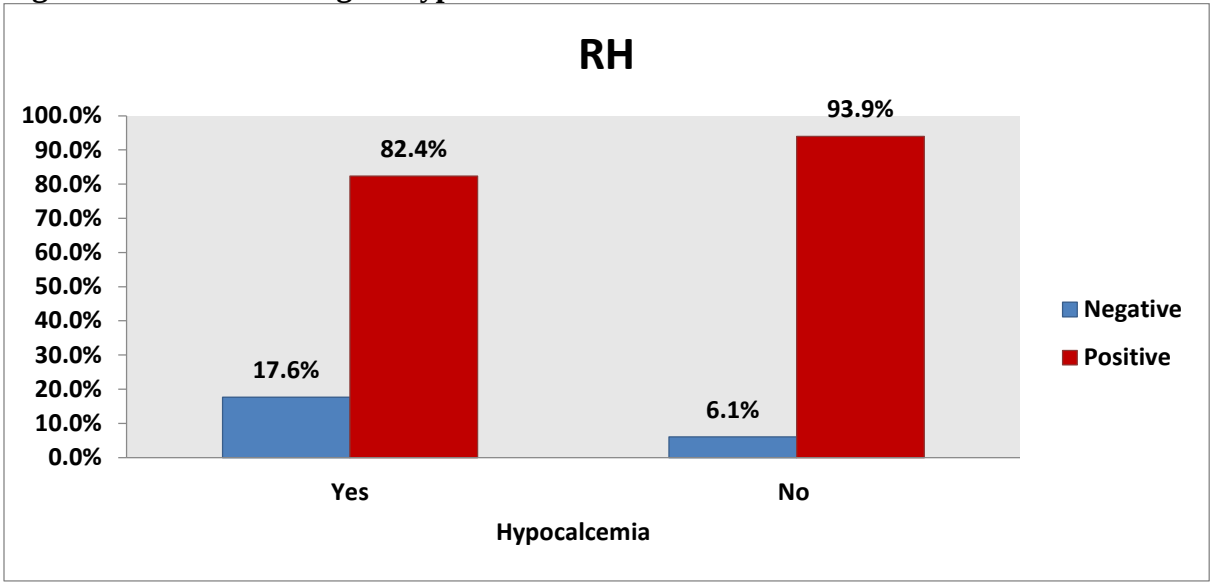


Among the Neonates with Hypocalcemia, the mean duration of hours of phototherapy was 67.8+-16.1.In neonates without Hypocalcemia, the mean duration of hours of Phototherapy was 53.1+_11.5. Among the neonates in whom phototherapy was given for longer duration, the calcium levels are significantly decreased, compared to neonates in whom phototherapy was given for shorter duration. The comparison between two groups **was statistically significant**.

Table 25 : RH according to Hypocalcemia

RH	Hypocalcemia				p value
	Yes		No		
	N	%	N	%	
Negative	6	17.6%	4	6.1%	0.067
Positive	28	82.4%	62	93.9%	
Total	34	100.0%	66	100.0%	

Figure 25 : RH according to Hypocalcemia



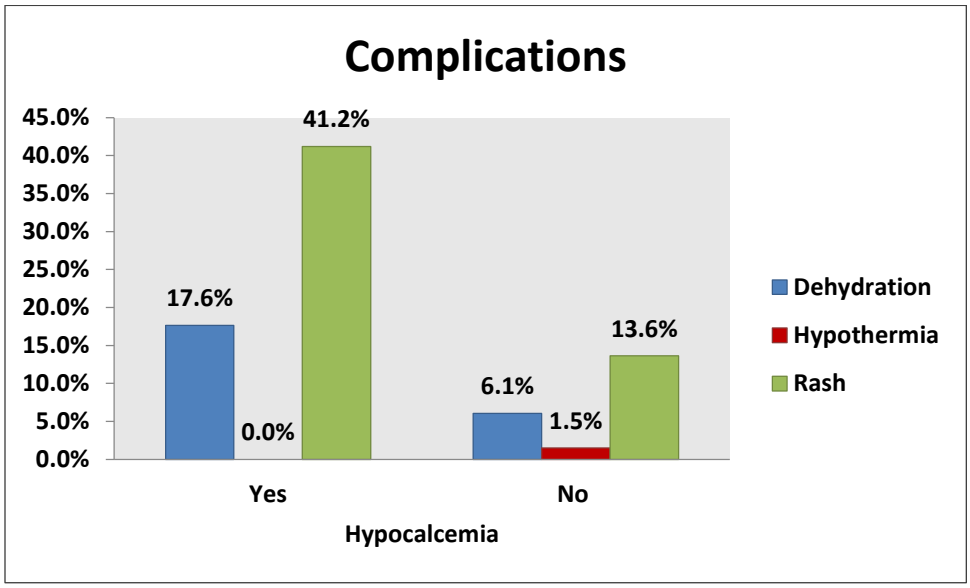
Among the Neonates who developed Hypocalcemia 17.6% were born to RH negative Mothers, were as 82.4% were born to RH positive mothers. Among the neonates in whom calcium levels remained normal after phototherapy, 6.1% were born to RH negative mothers & were as 93.9% were born to RH positive mothers. The comparison between two groups **was not statistically significant.(**Table 25 & Figure 25)

Table 26 : Complications according to Hypocalcemia

Complication of Phototherapy	**Hypocalcemia**				**p value**
	Yes		**No**		
	N	**%**	**N**	**%**	
Dehydration	6	17.6%	4	6.1%	0.003*
Hypothermia	0	0.0%	1	1.5%	
Rash	14	41.2%	9	13.6%	

Note: p value* significant at 5% level of significance (p<0.05)

Figure 26 : Complications according to Hypocalcemia



In Neonates who developed Hypocalcemia after Phototherapy 41.2% of Neonates developed Rash, were as only 17.6% of them had Dehydration. In neonates with normal calcium levels with Phototherapy around 13.6% developed Rash and 6.1% had dehydration, also 1.5% of these Neonates were Hypothermic. Complications such as Dehydration & Rash were seen more in Neonates who were given Phototherapy for longer duration compared to Neonates in whom Phototherapy was given for shorter duration. The Comparison between two groups **was statistically significant.(table 26 & figure 26)**

DISCUSSION

Jaundice is most common problem faced during first week of life .It is of important concern for physician & source of anxiety for parents .High bilirubin level is toxic to developing brain & cause neurological impairment even in term newborns. Nearly 60 % of newborns are visibly jaundiced during first week of life. In most of the times ,it is physiological & no intervention is required. But around 5-10% of newborns have clinically significant hyperbilirubinemia & use of phototherapy becomes mandatory.[105]

The mainstay of treatment is phototherapy with wavelength of 450 nm. It acts by photoisomerization of bilirubin, forming lumirubin, which is water soluble and gets excreted in urine. Phototherapy can be usually delivered by fluorescent lights , spot lights or fiberoptics, among which fiberoptics generate less heat. Unless the bilirubin is in exchange transfusion zone ,phototherapy can be discontinued for an hour for neonatal care.

The common side effects of phototherapy are hypothermia, loose stools ,dehydration, fluid loss, skin burn, photoretinitis, thrombocytopenia, increased red cell osmotic fragility, bronze baby syndrome, DNA damage. A lesser known side effect ,but potentially important is hypocalcemia, defined as serum calcium levels of <7 mg/dl or ionized calcium of <4mg/dl (<1mmol/L)[68]. Ionized calcium is important for many biochemical process, neuromuscular excitability, cell membrane integrity & cellular enzymatic & secretory activity .

Romagnoli et al (1979) first time have shown association of hypocalcemia with phototherapy in preterm newborns[11].Hakonson & Berstrom (1981) documented same observation in newborn

rats[12].There are only few studies on effect of phototherapy on calcium levels[12,13,14].Phototherapy is one of the most common modalities used for neonatal jaundice. So, several investigations have been done to find out safety of phototherapy for treatment of neonatal jaundice .The detrimental effects of phototherapy was seen on eyes & genitals. No change in other metabolic parameters have been reported other than calcium levels, drop is serum calcium have been seen in neonates undergoing phototherapy. This decrease in serum calcium levels is statistically significant in most of the cases, but there is of no clinical significance in most cases[94-97].

The mechanism for phototherapy induced hypocalcemia is not well understood , but it is known to involve changes in serum melatonin levels, which is regulated by pineal gland. In normal humans, pineal gland is shown to be influenced by diurnal variation in light & dark cycle. Colour of skin of neonate and colour of the light used for phototherapy are known to influence results of phototherapy as shown by Karamifar et al (2002)[94]. Hakanson Do et al(1987) reported that when young rats are exposed to white lights, serum concentration of calcium has decreased[87]. In his study it is shown that decrease in calcium was accompanied by decrease in serum melatonin levels as well. This effect on melatonin can be prevented by covering the occiput, by inhibiting corticosterone synthesis & by administrating exogenous melatonin[10]. It has been shown that propranolol also reduce serum calcium by inhibiting melatonin synthesis. Light induced hypocalcemia can also be because of increased calcium uptake by the bone, once blocking effect

of melatonin decreases after pineal inhibition by the transcranial illumination[87].

Hunter (2004) have given hypothesis that phototherapy inhibits pineal secretion of melatonin, which blocks the effect of cortisol on bone calcium. As the cortisol level increases ,it shows direct hypocalcemic effect & increases bone uptake of calcium as well[68].

Phototherapy was evaluated in many number of randomized control trials those were conducted from 1960s through the early 1990s[58-60].Though these trials helped to know the effect of phototherapy as it was used during this period, but no study have used the relatively high doses used today . According to current ethical standards, it would prevent any trial comparing phototherapy with placebo.

This prospective, observational study was done in department of paediatrics (NICU) of SHRI B.M.Patil Medical college & hospital, VIJAYAPURA, to evaluate occurrence of phototherapy induced hypocalcemia .

In this study total of 100 cases ,term neonates(n=69) and late preterm neonates (n=31) with unconjugated hyperbilirubinemia, who were given phototherapy were selected.

Neonates with other risk factors of hypocalcemia like infants of diabetic mothers, birth asphyxia, sepsis etc were excluded from the study. Neonates with hypocalcemia before phototherapy and neonates who received blood transfusion or calcium supplementation were also excluded from the study.

NEONATAL PARAMETERS

In this study, in the term group (n=69) 28 were females & 41 were males. In the Hypocalcemic group (n=34),20 were males & 14 were females. The comparison between two groups in relation with hypocalcemia was not statistically significant. In the study done by Karamifar (2002) on 62 preterm neonates ,39 were males & 23 were females and 91 full term neonates 49 were males & 42 were females[94].

In this study, birth weight (mean value 2813+_354gms.)among hypocalcemia group and birth weight among neonates in whom calcium levels were normal after phototherapy(mean value 2821+_361 gms).The comparison between two groups in relation to hypocalcemia was not statistically significant.

Gestational age by LMP (mean value 37.3+_1.3 in hypocalcemia group vs mean value 37.7+_1.6 in neonates in whom calcium levels were normal after phototherapy). Gestational age by New Ballard Scoring (mean value 37+_1.4 in hypocalcemia group vs 37.3+_1.7 in neonates in whom calcium levels were normal after phototherapy.) The comparison between two groups were found to be statistically insignificant.

According to the study done by karamifer et al (2002) which also showed significant difference in mean birth weight of the two study groups(term and preterm)[94].The gestational age by New Ballard scoring and LMP have shown similar observations in the study done by Eghbalian et al[93].

28(40%) mothers of term neonates and 13(41%) of preterm neonates had O blood group. Comparison of mothers blood group between preterm & Term neonates was not statistically significant.

There was no major difference in the coexisting neonatal morbidities & abnormal physical findings between the two groups.

Among the term neonates (n=69)98%(68/69) neonates were AGA ,1.4%(1/69) were SGA and in preterm neonates (n=31)100%(31/31) were AGA. The difference was not statistically significant in this study. Lowest birth weight was 1540 in preterm group.

MATERNAL PARAMETERS :

In the present study, 61.8% of neonates in Hypocalcemic group were born to Multiparous mothers compared to 63.6% of neonates in whom calcium levels were normal after phototherapy. 38.2% of neonates in hypocalcemic group was born to primiparous mothers compared to 36.4% of neonates in whom calcium levels were normal after phototherapy. The comparison was found to be statistically insignificant. A study done by Rajesh et al (2012) showed same type of result. The comparison was similar in both groups in the study done by them also[96].

44% (31/69) of term neonates and 22%(7/31) neonates of preterm group were born via NVD .The difference between the two groups were statistically not significant.(p=>0.05).

Maternal parameters like maternal age and number of high risk pregnancies did not show any

difference between the two groups.

1.4%(1/69) neonates in term group had multiple gestational problem, and none in the preterm group which was statistically not significant.

Most of the mothers of both term neonates & preterm neonates had O blood group.

PHOTOTHERAPY INDUCED HYPOCALCEMIA :

On the basis of findings of present study, we observe that mean value of serum bilirubin was 16.08+-3.2 before giving phototherapy .Mean value of serum bilirubin has decreased to 9.4+-2.0 after giving phototherapy. There was statistically significant difference between the two groups (p=<0.05). In the study done by Rajesh et al (2012) there was no significant difference between the term and preterm groups in their bilirubin levels[96].Another study done by Karamifar et al(2002), showed mean serum bilirubin concentration before phototherapy was 18.0+_ 2.4 mg/dL in full term neonates and 16.2 +-3.0 mg/dL in preterm infants[94].

Hours of life at initiation of phototherapy and total hours of phototherapy .Hours of life at initiation of phototherapy in Hypocalcemia group (mean value 86.3+-30.7) compared to hours of life at initiation of phototherapy in whom calcium levels are normal after phototherapy(mean value 91.4+_51.5) and total hours of phototherapy in hypocalcemia group was (mean value 67.8+_16.1) Compared to total hours of phototherapy in whom calcium levels are normal after Phototherapy (mean value 53.1+_11.5).

From our study, it was found that hypocalcemia was seen more in the neonates in whom phototherapy was given for longer duration.

Karamifar et al (2002) in their study, found that day of life at initiation of phototherapy was 112 hours in term neonates and 88 hours in preterm neonates[94].

The mean value of serum bilirubin was 16.08+-3.2 before giving phototherapy .Mean value of serum bilirubin has decreased to 9.4+-2.0 after giving phototherapy.

It was observed There was statistically significant difference between the two groups (p=<0.05). There was significant fall in serum calcium levels, compared to serum calcium levels before phototherapy.

In the study done by Paymanch(2013) on term neonates ,the mean serum calcium level before and after phototherapy were 9.8+-0.8 and 9.5+-0.9 mg/dl respectively[91].There were significant difference in calcium levels before & after phototherapy.

In study done by Eghbalian and Mosef (2012) on full term neonates, it showed that mean serum calcium level have decreased significantly (p=<0.001) from minimum value of 9.85+-1.23 mg/dl (before giving phototherapy) to 9.09 +-0.93mg/dl, after putting on phototherapy.

In the study done by Rajesh Kumar Yadav et al (2011) among 30 neonates , before giving phototherapy ,there was no statistically significant difference in mean serum calcium levels among both term and preterm neonates in both study & control groups. After 48 hrs of phototherapy in study group, significant decrease in serum calcium level, in 66.6% of term & 80% of preterm neonates were seen[96].

In our study, it was also seen that mean value of serum calcium before giving phototherapy was 9.7(0.7) and after giving phototherapy mean value of serum calcium was 8.2(0.7). This was statistically significant.

Observations of present study are also in agreement with studies undertaken by Sethi et al (1993) & Medhat et al (2006) at university of Cario[14,106].

Sethi et al have studied the effects of phototherapy in 20 term & 20 preterm neonates with neonatal jaundice[14]. In their study it was seen that 20 term & 20 preterm hyperbilirubinemic neonates[14]. From their study, they observed that 75% of term & 90% of preterm neonates developed hypocalcemia after phototherapy . Similarly, Medhat (2006) from university of Cario observed 75% of term & 90% preterm developed hypocalcemia after phototherapy[106].

Jain et al (1998) have observed hypocalcemic effect of phototherapy, in 30% term & 55% late preterm neonates[92].

Karamifer et al (2002) found that 14.4% of neonates developed hypocalcemia after 48 hrs of phototherapy[94].There was significant difference on effect of phototherapy on hypocalcemia in preterm(22.6%) & full term neonates (8.7%)(p=0.018) .

A cross sectional study was done by Paymanch AH et al titled “Prevalence of phototherapy

induced hypocalcemia in Term neonates '' in Tehran on 147 icteric term neonates[91]. The mean serum calcium level during admission and after 48 hrs after phototherapy was 9.8+-0.8 & 9.5+-0.9 mg/dl respectively.56%(n=83) babies had decrease in serum calcium levels. Only 7 % (n=10)newborns developed hypocalcemia after phototherapy. They have observed significant difference in serum calcium levels before & after phototherapy. However, occurrence of hypocalcemia was less compared to our study.

In our study clinical features of hypocalcemia like convulsions were also studied. Among total neonates, term 21(30.3%) & preterm 13(41.8%) developed other complications of phototherapy. The two groups were statistically not significant. None of the infants developed severe clinical manifestations of hypocalcemia like convulsions or apnoea. In Yadava's study, 80% of hypocalcaemia term neonates became symptomatic, the most common sign was jitteriness[90].

In the study done by Rajesh Kumar Yadav et al ,67% (10/15) of term neonates had hypocalecmia, of which 80%(8/10) is symptomatic.i..e 30%(3/10) developed jitteriness,20%(2/10) developed irritability/excitibility,30%(3/10) neonates were lethargic & none of the neonate developed convulsion[96].All the preterm neonates who developed hypocalcemia after phototherapy were symptomatic,i..e 50% (6/12) developed jitteriness,25% was having irritability,25% had lethargy & no one had convulsions.

BK Jain et al, in their study with the title "Phototherapy induced hypocalcemia'' done at department of pediatrics , Ludhiana observed that ,among preterm neonates with hypocalcemia 67% had jitteriness & 27.3% of the neonates had irritability. Among full term neonates with

hypoclcemia,50% had jitteriness & 16.7% had irritability[92].

In the study done by Eghbalian et al found that in majority of cases, decrease in calcium under the effect of phototherapy was not associated with symptoms & signs of hypocalcemia such as jitteriness, convulsions , cyanosis. Only one case of symptomatic hypocalcemia in the form of apnea as observed[93].

In this study, Among total neonates, with Hypocalcemia, 17% of neonates developed Dehydration after Phototherapy.41.2% of neonates in hypocalcemia group developed Rash after phototherapy . Which was significantly higher among neonates of hypocalcemic group compared to neonates in whom calcium levels were normal after phototherapy. Dehydration was assessed by urine output ,weight gain and sleep pattern. Hence, complications of Phototherapy has to be monitored regularly in whom Phototherapy was given for longer duration.

Thus, this study clearly explains the need for monitoring serum calcium levels regularly both in term & preterm neonates and watch for complications of hypocalcemia after undergoing phototherapy ,for neonatal jaundice.

Multicentric & Analytical studies will give better definitive results .

CONCLUSIONS

There is significant decrease in serum calcium below normal levels after giving phototherapy in both term & preterm neonates . Mean Serum calcium with standard deviation before giving phototherapy was 9.7(0.7) and after giving phototherapy mean value of serum calcium was 8.2(0.7). This was statistically significant. Thus, this study emphasizes the need for monitoring calcium levels frequently in both term and preterm infants undergoing phototherapy for therapeutic interventions.

Hypocalcemia due to phototherapy is not commonly associated with severe clinical signs & symptoms of hypocalcemia like apnea, convulsions. Hypocalcemia is also commonly associated with complications of phototherapy like Rash, Dehydration, which was significantly higher among neonates in hypocalcemic group compared to neonates in whom calcium levels were normal after phototherapy.

LIMITATIONS OF STUDY

1. Single Centre study.

2. Small sample size.

3. Other parameters like magnesium, phosphorous, parathyroid hormone levels were not known.

4. Serum albumin that affects the serum calcium levels were not studied.

5. Maternal factors that affect the serum calcium levels of neonate, like maternal hypocalcemia and levels of vitamin D were not studied.

SUMMARY

Neonatal Jaundice is common and in most of the neonates it is benign problem, and in whom phototherapy is the therapeutic intervention of choice in these neonates.

This study is planned to observe effect of phototherapy on serum calcium levels among neonates with unconjugated hyperbilirubinemia, after giving phototherapy.

A total of 100 patients were enrolled in the study. 69 term neonates & 31 preterm neonates with unconjugated hyperbilirubinemia requiring phototherapy were selected for phototherapy. Neonates with other risk factors like birth asphyxia, sepsis & convulsions were excluded from the study. Neonates in whom calcium level is low before initiation of phototherapy, who has received blood transfusion before phototherapy, or calcium supplementation before phototherapy was excluded from the study.

Pathologic hyperbilirubinemia requiring phototherapy was taken based on criteria as per 2004 American Academy of Pediatric guidelines. Serum calcium & serum bilirubin levels were measured before & after phototherapy.

In our study we made the following observations:

- 69% of babies were Term babies, and 31% were Late Preterm babies.
- 61% of Neonates were Males & 39% were Females. The Male : Female Ratio was found to be 1.56
- 62% of Neonates were delivered by LSCS and 38% of neonates were delivered by Normal Vaginal Delivery
- 89% of Neonates had APGAR score of 7 at 1 Minute. 11% had APGAR score of 8 at 1 Minute. 100% of Neonates had APGAR score of 9 at 5 Minutes
- 63% of Neonates were born to Multiparous Mothers & 37% of Neonates were born to Primiparous Mothers
- 1% of Mothers had Abruptio Placenta. 1% of Mothers had Preeclampsia, 1% of Mothers had Thick MSAF
- 18% of Neonates had blood group A . 7% of Neonates had Blood group AB. 34% of Neonates had blood group B. 41% of Neonates had Blood Group
- 90% of Neonates were RH positive . 10% of Neonates were RH Negative
- 34% of Neonates had Hypocalcemia after Phototherapy. In 66% of neonates calcium levels were Normal after Phototherapy
- 10% of Neonates had Dehydration after Phototherapy . 1% of Neonates had Hypothermia after Phototherapy. 23% of Neonates had Rash after Phototherapy
- 99% of Neonates were AGA. 1% of Neonates were SGA
- 99% of Neonates were born to Single Gestation Pregnancy. 1% of Neonates were born to Multiple Gestation Pregnancy
- The Mean and SD of serum Bilirubin before Phototherapy was 16.0+_3.2.The Mean and SD of serum Bilirubin after Phototherapy was 9.4+_2.0.The Mean and SD of serum Calcium before Phototherapy was 9.7+-0.7.The Mean and SD of Serum Calcium after Phototherapy was 8.2+-0.8. **Which was Statistically Significant.**
- Among the Neonates with Hypocalcemia, the Mean Gestational age according to LMP was 37.3+_1.3 .The Mean Gestational age according to New Ballard Scoring was 37+_1.4. Which **was not statistically significant**
- Among the Neonates with Hypocalcaemia, 26.5% were Preterm and 73.5% were Term neonates. Which was **not statistically significant**
- Among the Neonates with Hypocalcemia, the mean Birth weight was 2813 gms+-354 gms. Among the Neonates without Hypocalcemia the mean Birth weight was 2821 gms+_361 gms. The Comparison between the two groups **was not statistically significant**

- Among the Neonates with Hypocalcemia 58.8% were Males & 41.2% were females. And in neonates without Hypocalcemia 62.1% were males & 37.9% were Females. The comparison between the two groups **was not statistically significant**
- Among the Neonates with Hypocalcemia 52.9% of Neonates were delivered via LSCS, and 47.1% of Neonates were delivered via NVD. Among the Neonates without Hypocalcemia 66.7% were delivered via LSCS, and 33.3% of Neonates were delivered via NVD. The Comparison between the two groups **was not statistically significant**
- In Neonates with Hypocalcemia, 61.8% were born to Multiparous Mothers and 38.2% were born to primiparous mothers. In neonates without Hypocalcemia 63.6% of Neonates were born to Multiparous Mothers and 36.4% of Neonates were born to Primiparous mothers. The comparison between the two groups **was not statistically significant**
- No Risk factors were identified in the mothers of the neonates who developed Hypocalcemia. Whereas in mothers of neonates who did not develop Hypocalcemia, Few risk factors were seen in the mothers. The comparison between two groups was not statistically significant.
- Among the Neonates with Hypocalcemia : 17.6% had blood group A ; 5.9% had blood group AB ; 35.3% had blood group B ; 41.2% had blood group O. There was **no statistically significant correlation** seen between blood groups and Hypocalcemia.
- Among the Neonates with Hypocalcemia, the mean maternal age was 27.2+- 1.1 & among the Neonates without Hypocalcemia, the mean maternal age was 26.8+-1.1 .There was **no statistically significant** difference seen between the two groups
- Among the Neonates with Hypocalcemia, the mean hours of life at Initiation of Phototherapy was 86.3+- 30.7 and in neonates without Hypocalcemia, the mean hours of life at initiation of Phototherapy was 91.4+_51.4. The Comparison between the two groups was **not statistically significant**
- Among the Neonates with Hypocalcemia, the mean duration of hours of phototherapy was 67.8+-16.1.In neonates without Hypocalcemia, the mean duration of hours of Phototherapy was 53.1+_11.5. Among the neonates in whom phototherapy was given for longer duration, the calcium levels are significantly decreased, compared to neonates in whom phototherapy was given for shorter duration. The comparison between two groups **was statistically significant**
- Among the Neonates who developed Hypocalcemia 17.6% were born to RH negative Mothers, were as 82.4% were born to RH positive mothers. Among the neonates in whom calcium levels remained normal after phototherapy, 6.1% were born to RH negative mothers & were as 93.9% were born to RH positive mothers. The comparison between two groups **was not statistically significant**

- In Neonates who developed Hypocalcemia after Phototherapy 41.2% of Neonates developed Rash, were as only 17.6% of them had Dehydration. In neonates with normal calcium levels with Phototherapy around 13.6% developed Rash and 6.1% had dehydration, also 1.5% of these Neonates were Hypothermic. Complications such as Dehydration & Rash were seen more in Neonates who were given Phototherapy for longer duration compared to Neonates in whom Phototherapy was given for shorter duration. The Comparison between two groups **was statistically significant.**

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ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE

IEC/NO - 121/2019
22-11-19

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Effect of phototherapy on serum calcium levels in neonates receiving phototherapy for neonatal jaundice in tertiary care hospital

Name of PG student: Dr Siri Chandana P, Department of Paediatrics

Name of Guide/Co-investigator: Dr A S Akki, Professor Department of Paediatrics

DR RAGHVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDE(U)'s Shri B.M. Patil
Medical College, BIJAPUR-586103

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

ANNEXURE-II

CONSENT FORM

Shri B.M. PATIL Medical College, Hospital & Research Centre, Vijayapura 586103

TITLE OF THE PROJECT: EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM LEVELS IN NEONATES RECEIVING PHOTOTHERAPY FOR NEONATAL JAUNDICE IN TERTIARY CARE HOSPITAL

GUIDE : **Dr. A.S.AKKI, MD**

PROFESSOR

DEPARTMENT OF PEDIATRICS

PG STUDENT: **Dr. SIRI CHANDANA**

PG DEPARTMENT OF PEDIATRICS

(MD PEDIATRICS)

PURPOSE OF RESEARCH

I have been informed that this study will help in screening for bilirubin induced neurological dysfunction among hyperbilirubinemic neonates.

PROCEDURE

I am aware that in addition to routine care received, I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations which will help the investigator in this study

BENEFITS

I understand that participation in the study will help the investigator to help in the early detection of neonatal hyperbilirubinemia and bilirubin induced neurological dysfunction.

CONFIDENTIALITY

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file. If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION

I understand that I may ask more questions about the study at any time; Dr Siri Chandana at the department of paediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might

influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr Siri Chandana may terminate my participation in the study after she has explained the reasons for doing so.

INJURY STATEMENT

I understand that in the unlikely event of injury to the baby resulting directly from participation in this study, if such injury were reported promptly, the appropriate treatment would be available to the baby. But, no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights. I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

Dr Siri Chandana Date

(Investigator)

ANNEXURE III

PROFORMA

Name | Birth weight

Age | Sex

Address | IP/OP no

DOB | DOA

Gestational age ..... Term / Preterm

ANTENATAL FACTORS

Age | Parity

High risk mothers: PIH , Preeclampsia , Eclampsia | Others specify ……..

PROM : YES / NO | If yes , specify duration –

H/o intake of drugs : Yes / No | If yes , specify

INTRANATAL FACTORS

Type of delivery –

FTND : Yes / No

Instrumentation : Vacuum : Yes / No | Forceps: Yes / No

LSCS : Elective / Emergency

Multiple Gestations If Any :

BIRTH DETAILS

APGAR : 1 min - 5 min -

Resuscitation required : Yes / NO

Gestational Age –

By Dates : ..…….. weeks

Term / Preterm SGA / AGA / LGA

POST NATAL FACTORS

Any illness in the Neonate : Yes / No

CLINICAL FEATURES –

- Jitteriness : Yes / No
- Lethargy : Yes / No
- Apnea : Yes / No
- Seizures : Yes / No
- Rash : Yes / No
- Loose stool : Yes / No
- Fever : Yes / No
- Dehydration : Yes / No

Exchange transfusion, if any : Yes / No

Drugs given : Yes / No

CLINICAL EXAMINATION-

i)HR

ii) RR

iii) CFT

SYSTEMIC EXAMINATION :

· CVS

· Respiratory System

· CNS

· Abdomen

Any other significant finding:

Mother Blood group :

Baby Blood group :

Hours of life at initiation of phototherapy :

Total hours of phototherapy given :

Serum Calcium [mg/dL] at initiation of phototherapy:

Serum Bilirubin [mg/dL] at initiation of phototherapy:

Serum Calcium [mg/dL] after phototherapy:

Serum Bilirubin[mg/dl] after phototherapy.

KEY TO MASTER CHART

AGA	Appropriate for gestational age
LGA	Large for gestational age
LSCS	Lower segment cesarean section
MSAF	Meconium stained amniotic fluid
NR	Non reactive
PE	Pre-eclampsia
SGA	Small for gestational age
VD	Vaginal delivery
PT	Phototherapy

MASTER CHART

S No	IP Number	GROUP	Sex	Gestational Age by LMP (weeks)	B WT (gms)	APGAR AT 1 MIN	APGAR AT 5 MIN	Gestational age by new Scoring	Mode Of Delivery	Neonatal Morbidity	Clinical Features of Hyopcalcemia	Birth Asphyxia	Abnormal Physical Finding	Maternal Age	Parity	History	High Risk to Mothe	Drugs Given t Mother	Blood Group	RH	SGA/ AGA/ LGA	Multiple Gestation	Hours Of Life At Initiation of PT	Total Hours of PT	S. Bilirubin At Initiation of PT (mg/dl)	S. Bilirubin after PT (mg/dl)	DCT	S.Calcium Before PT (mg/dl)	S.Calcium After PT(mg/dl)	Hypocalcemia	Complication of PT
1	9078	TERM	F	41	2940	7	9	39	NVD	No	No	No	no	26	PRIMI	NO	no	no	A	+	AGA	NO	48	48	10.6	8	-	9.8	9.3	No	
2	10354	PRETERM	M	35	2600	7	9	34	LSCS	no	No	No	no	26	MULTI	NO	No	No	B	+	AGA	NO	48	48	11.8	7.2	-	9.2	9.1	No	RASH
3	10564	TERM	M	38	2800	7	9	37	NVD	No	No	No	No	25	MULTI	NO	No	No	B	+	AGA	NO	144	48	19	13	-	9.9	9.6	No	No
4	12003	TERM	M	37	2800	7	9	36	NVD	no	No	No	no	24	PRIMI	NO	No	No	O	+	AGA	NO	72	72	16.8	5.6	-	10.4	9.3	No	
5	12186	TERM	F	37	2600	7	9	37	NVD	No	No	No	No	25	MULTI	NO	No	No	B	+	AGA	NO	72	48	13.4	8.7	-	9.1	9	No	
6	10897	TERM	F	38	3000	7	9	38	NVD	no	No	No	No	26	MULTI	NO	NO	NO	B	+	AGA	NO	144	72	21.8	11.7	-	10.2	7	YES	RASH
7	11205	TERM	F	38	3000	7	9	37	NVD	NO	No	No	NO	25	MULTI	NO	NO	NO	A	+	AGA	NO	120	48	13.4	10.2	-	8.9	8.2	No	DEHYDRATION
8	13124	TERM	M	37	3500	7	9	37	NVD	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	+	AGA	NO	48	72	17	8.5	-	10	7.5	YES	DEHYDRATION
9	13486	PRETERM	M	36	3000	7	9	35	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	B	+	AGA	NO	92	48	13.2	9.3	-	8.8	8.1	No	RASH
10	13471	PRETERM	F	36	2500	7	9	35	LSCS	NO	No	No	NO	25	MULTI	NO	NO	NO	O	+	AGA	NO	44	48	16.8	9.3	-	9	8	No	RASH
11	14335	TERM	F	37.5	3000	7	9	37	NVD	NO	No	No	NO	26	PRIMI	NO	NO	NO	O	+	AGA	NO	312	48	10.4	8.8	-	10.5	8.5	No	
12	13938	TERM	F	38	2800	7	9	37	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	A	+	AGA	NO	168	48	14.7	12.1	-	10.2	8.2	No	RASH
13	13817	TERM	F	37	3200	7	9	36	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	120	72	18	10	-	9.6	7.2	YES	
14	14166	PRETERM	M	36.5	2800	7	9	36	NVD	NO	No	No	NO	25	PRIMI	NO	NO	NO	A	+	AGA	NO	96	72	14.8	10	-	9.2	7.9	YES	
15	14167	TERM	M	37	3100	7	9	37	NVD	NO	No	No	NO	26	PRIMI	NO	NO	NO	B	+	AGA	NO	48	48	12.3	11	-	9.6	8	No	
16	14171	PRETERM	M	36	2240	7	9	35	NVD	NO	No	No	NO	25	MULTI	NO	NO	NO	B	+	AGA	NO	96	72	15	10.8	-	9.5	8.2	No	
17	17631	TERM	F	38.5	2500	7	9	38	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	AB	+	AGA	NO	120	48	15.7	10.5	-	9.7	7.5	YES	
18	17696	PRETERM	F	36.2	3000	7	9	36	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	+	AGA	NO	96	48	12.6	9.8	-	9	8.4	No	RASH
19	18321	TERM	F	38	2800	7	9	37	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	A	+	SGA	NO	168	96	22.5	8.2	-	10.6	7	YES	
20	18054	TERM	M	38	3160	7	9	37	LSCS	NO	No	No	NO	26	PRIMI	NO	NO	NO	O	+	AGA	NO	120	48	14.6	10.4	-	9.8	8	No	
21	18565	PRETERM	M	35	3200	7	9	35	LSCS	NO	No	No	NO	25	MULTI	NO	NO	NO	AB	-	AGA	NO	96	48	16	8	-	9	8	No	
22	18581	TERM	F	38.5	3200	7	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	120	48	15.3	10.8	-	9.8	9	No	
23	18762	TERM	M	40	2700	7	9	39	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	120	48	10.1	8.1	-	9.7	9	No	DEHYDRATION
24	344	PRETERM	M	34	2500	7	9	34	NVD	NO	No	No	NO	26	MULTI	NO	NO	NO	A	-	AGA	NO	78	96	24	12.6	-	10.2	7	YES	RASH
25	3230	PRETERM	M	36.4	3200	7	9	34	LSCS	NO	No	No	NO	25	MULTI	NO	NO	NO	A	+	AGA	NO	96	48	15.8	12.9	-	10.5	10	No	
26	5371	PRETERM	F	34	2000	7	9	34	LSCS	NO	No	No	NO	26	PRIMI	NO	NO	NO	B	+	AGA	NO	72	48	15.9	8	-	8.5	7.9	YES	DEHYDRATION
27	3600	PRETERM	F	37	3300	7	9	37	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	72	15	8	-	9.1	8.9	No	
28	4608	PRETERM	M	37.5	3500	7	9	37	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	A	+	AGA	NO	96	48	11	9	-	10.6	9	No	
29	5377	PRETERM	M	36	2000	7	9	35	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	72	48	13.7	10	-	10.5	8.5	No	
30	5349	TERM	M	39.5	2700	7	9	39	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	A	+	AGA	NO	96	48	16	10	-	10.3	9	No	
31	5846	TERM	M	38	2700	7	9	37	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	120	72	18.2	8.3	-	10.9	7.5	YES	DEHYDRATION
32	6212	TERM	M	41	2900	7	9	39	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	120	48	18	11	-	10.6	9	No	
33	6769	PRETERM	M	36	2600	7	9	35	NVD	NO	No	No	NO	26	MULTI	NO	NO	NO	B	+	AGA	NO	48	96	16	10	-	9.6	7.6	YES	RASH
34	7285	TERM	M	40	2700	7	9	39	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	96	72	16.8	8.9	-	9.5	8.1	No	
35	1385	PRETERM	M	36	2700	7	9	36	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	A	+	AGA	NO	96	48	15.6	12.5	-	10.1	9	No	
36	8899	TERM	M	39	3000	7	9	39	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	A	+	AGA	NO	120	48	17.7	12	-	9.7	8.1	No	
37	11469	TERM	F	38	2300	8	9	37	NVD	NO	No	No	no	27	PRIMI	NO	NO	NO	B	+	AGA	NO	72	72	19	9.5	-	9.9	7	YES	RASH
38	11773	TERM	M	37	2600	7	9	37	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	A	-	AGA	NO	96	72	21	9	-	9.6	7.1	YES	RASH
39	13928	TERM	M	38	3300	7	9	37	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	B	-	AGA	NO	72	48	14.9	8	-	10.2	8.5	No	RASH
40	18541	PRETERM	M	36	3000	7	9	35	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	96	72	19	10	-	12.2	7.9	YES	RASH
41	3511	TERM	F	38	3000	7	9	37	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	A	+	AGA	NO	204	48	14	8	-	9.5	8	No	DEHYDRATION
42	3664	PRETERM	M	36.4	2600	8	9	36	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	120	72	12	10	-	10	8.9	No	RASH

S No	IP Number	GROUP	Sex	Gestational Age by LMP (weeks)	B WT (gms)	APGAR AT 1 MIN	APGAR AT 5 MIN	Gestational age by new Scoring	Mode Of Delivery	Neonatal Morbidity	Clinical Features of Hyopcalcemia	Birth Asphyxia	Abnormal Physical Finding	Maternal Age	Parity	History	High Risk to Mothe	Drugs Given t Mother	Blood Group	RH	SGA/ AGA/ LGA	Multiple Gestation	Hours Of Life At Initiation of PT	Total Hours of PT	S. Bilirubin At Initiation of PT (mg/dl)	S. Bilirubin after PT (mg/dl)	DCT	S.Calcium Before PT (mg/dl)	S.Calcium After PT(mg/dl)	Hypocalcemia	Complication of PT
43	17701	TERM	M	37	2500	7	9	37	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	72	19.9	12.6	-	9.5	8.1	No	
44	19397	TERM	M	37.4	3000	7	9	37	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	14	10	-	9.6	9	No	
45	4545	TERM	M	41	2500	7	9	41	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	O	+	AGA	NO	144	48	14	10	-	10	9	No	
46	4430	TERM	F	39	3300	7	9	39	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	72	72	23	12	-	10	7	YES	DEHYDRATION
47	4647	TERM	M	38	2600	7	9	37	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	B	-	AGA	NO	96	72	19.5	9.3	-	9.8	7.6	YES	
48	24596	TERM	F	38	2800	7	9	38	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	264	48	15.4	10	-	10	9.5	No	
49	4738	PRETERM	F	36.5	2400	8	9	36	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	+	AGA	NO	100	48	10.6	9	-	12	9	No	
50	23998	TERM	M	38	3600	7	9	38	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	B	+	AGA	NO	72	48	13	10	-	9.9	9	No	RASH
51	22612	PRETERM	F	36	2300	7	9	36	LSCS	NO	No	No	NO	28	PRIMI	NO	PE	YES	O	+	AGA	NO	96	48	12.6	8.1	-	9.6	7.8	No	DEHYDRATION
52	43954	PRETERM	F	36	2400	7	9	36	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	72	72	15	8	-	9	6.9	YES	
53	22612	PRETERM	F	36	2300	7	9	36	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	72	48	15	8	-	9.6	9	No	
54	4815	TERM	M	40	3300	7	9	40	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	+	AGA	NO	96	48	13	8.7	-	10	9	No	
55	24574	TERM	M	40	3100	7	9	39	NVD	NO	No	No	NO	28	MULTI	NO	NO	NO	AB	+	AGA	NO	96	48	15.7	13.6	-	10.2	9	No	
56	23658	TERM	M	39	2700	8	9	39	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	12.6	8.5	-	8.5	7.9	YES	
57	23389	TERM	F	38	2800	7	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	13.7	10	-	10.7	7.8	YES	
58	5219	TERM	M	37	2800	7	9	37	NVD	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	120	48	20	16	-	10	7.4	YES	
59	72401	PRETERM	M	36	2500	7	9	35	LSCS	NO	No	No	NO	26	MULTI	NO	THIOK	NO	B	+	AGA	NO	70	24	14	8	-	10.6	9	No	RASH
60	79447	PRETERM	M	36	3500	7	9	35	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	96	48	17	12	-	9.9	7.8	YES	DEHYDRATION
61	85777	TERM	M	38	2100	8	9	38	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	AB	+	AGA	NO	216	48	16	7.9	-	10	9	No	
62	82719	TERM	M	37	3400	7	9	37	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	144	48	15	10	-	10.2	7.9	YES	RASH
63	84241	TERM	M	38	2500	7	9	38	NVD	NO	No	No	NO	25	MULTI	NO	NO	NO	A	+	AGA	NO	72	72	17.5	12	-	9.6	7.5	YES	
64	4958	TERM	M	40	3300	7	9	39	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	B	+	AGA	NO	120	72	14.1	7.2	-	10	9.5	No	
65	5250	TERM	F	39	3200	7	9	39	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	-	AGA	NO	72	72	17	10	-	9.5	7	YES	
66	5540	TERM	M	40	2500	7	9	39	LSCS	NO	No	No	NO	25	PRIMI	NO	NO	NO	A	-	AGA	NO	72	72	15.2	6.8	-	9.7	7.6	YES	DEHYDRATION
67	5641	TERM	F	40	3360	8	9	40	LSCS	NO	No	No	NO	25	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	18	12	-	9.9	8	No	
68	6166	TERM	M	37	2500	7	9	37	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	AB	+	AGA	NO	96	48	19.3	12	-	8.2	7.4	YES	
69	6102	PRETERM	M	36	2400	7	9	35	NVD	NO	No	No	NO	27	PRIMI	NO	ABRUI	NO	O	+	AGA	NO	96	48	17	12.1	-	9.5	8	No	
70	6123	TERM	M	37	3200	7	9	37	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	18.1	12	-	8.1	6.8	YES	RASH
71	6045	TERM	M	40	3400	7	9	39	NVD	NO	No	No	NO	27	PRIMI	NO	NO	NO	B	+	AGA	NO	72	48	18.7	10	-	9.3	8.5	No	
72	6148	PRETERM	M	35.5	2400	7	9	35	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	96	48	14.4	7.8	-	8.9	8	NO	
73	1E+05	TERM	M	38	2500	7	9	38	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	B	+	AGA	NO	48	72	17.8	7	-	9.1	8.5	No	
74	8428	TERM	F	38	2500	8	9	38	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	B	+	AGA	NO	72	48	15.4	9	-	9.7	9.5	No	
75	8425	PRETERM	F	36	3000	7	9	36	LSCS	NO	No	No	NO	30	PRIMI	NO	NO	NO	B	+	AGA	NO	72	48	14	9	-	8	6.9	YES	
76	2E+05	PRETERM	M	36	3200	7	9	36	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	72	72	23	9	-	10	6.7	YES	RASH
77	9170	TERM	M	38	2700	7	9	38	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	72	48	14.2	6	-	9.3	9.1	No	
78	9304	TERM	F	38	2600	7	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	A	+	AGA	NO	72	48	14.4	5	-	9.3	8	No	
79	2E+05	PRETERM	F	36	2600	7	9	36	LSCS	NO	No	No	NO	27	PRIMI	NO	NO	NO	B	+	AGA	NO	72	48	18.4	10	-	10.3	9	No	
80	9501	TERM	M	38	2800	8	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	72	48	14.4	9.7	-	9	7.8	YES	RASH
81	2E+05	TERM	M	39	3300	7	9	39	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	72	72	14.8	7	-	9.8	8	No	

S No	IP Number	GROUP	Sex	Gestational Age by LMP (weeks)	B WT (gms)	APGAR AT 1 MIN	APGAR AT 5 MIN	Gestational age by new Scoring	Mode Of Delivery	Neonatal Morbidity	Clinical Features of Hyopcalcemia	Birth Asphyxia	Abnormal Physical Finding	Maternal Age	Parity	History	High Risk to Mothe	Drugs Given t Mother	Blood Group	RH	SGA/ AGA/ LGA	Multiple Gestation	Hours Of Life At Initiation of PT	Total Hours of PT	S. Bilirubin At Initiation of PT (mg/dl)	S. Bilirubin after PT (mg/dl)	DCT	S.Calcium Before PT (mg/dl)	S.Calcium After PT(mg/dl)	Hypocalcemia	Complication of PT
83	2E+05	TERM	F	39	2700	7	9	39	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	B	+	AGA	NO	48	72	14.3	7	-	10.3	7.8	YES	RASH
84	11669	PRETERM	M	36	2900	7	9	35	LSCS	NO	No	No	NO	28	PRIMI	NO	NO	NO	A	+	AGA	NO	96	72	15.8	7.4	-	9.9	7.9	NO	
85	11863	TERM	F	39	3000	8	9	39	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	B	+	AGA	NO	96	72	16.3	9.4	-	9.4	8.5	NO	
86	16623	TERM	M	38	2500	7	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	O	+	AGA	NO	120	96	28	14.9	-	10.2	7	YES	RASH
87	22577	TERM	M	39	2900	7	9	39	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	AB	-	AGA	NO	72	72	15.2	8.1	-	9	8.7	NO	
88	31227	TERM	F	38	2800	7	9	38	NVD	NO	No	No	NO	26	PRIMI	NO	NO	NO	O	+	AGA	NO	48	48	12.3	8.9	-	10.6	9	No	
89	32521	TERM	M	38	2700	7	9	38	LSCS	NO	No	No	NO	28	MULTI	NO	NO	NO	B	+	AGA	NO	48	24	12	8	-	10.6	10	No	
90	77183	TERM	M	38	2600	7	9	39	NVD	NO	No	No	NO	27	MULTI	NO	NO	NO	B	+	AGA	NO	24	48	19	10	-	9	8.5	No	
91	80036	TERM	M	37	2500	7	9	37	NVD	NO	No	No	NO	28	PRIMI	NO	NO	NO	O	+	AGA	NO	48	72	18	6	-	10	7.8	YES	RASH
92	73819	PRETERM	F	36	2400	7	9	35	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	48	48	16	8.8	-	9	8	No	
93	81697	TERM	F	37	2800	8	9	37	NVD	NO	No	No	NO	27	PRIMI	NO	NO	NO	O	+	AGA	NO	24	48	12	8	-	10	8.9	No	
94	95427	TERM	M	37	3100	7	9	37	NVD	NO	No	No	NO	27	PRIMI	NO	NO	NO	B	+	AGA	NO	24	48	16	9	-	9.2	8.1	No	HYPOTHERMI
95	98248	PRETERM	M	35	2500	7	9	35	LSCS	NO	No	No	NO	25	MULTI	NO	NO	NO	AB	-	AGA	NO	24	72	12	5	-	8.7	8	No	
96	99806	TERM	F	37	3000	7	9	38	LSCS	NO	No	No	NO	26	MULTI	NO	NO	NO	O	+	AGA	NO	48	72	16	9	-	9	7.8	YES	
97	1E+05	TERM	F	39	2750	7	9	39	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	A	+	AGA	NO	48	48	17	10	-	10	8.6	No	
98	1E+05	TERM	F	38	2586	8	9	39	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	48	72	19	8	-	10.9	8.7	No	
99	1E+05	TERM	F	38	2870	7	9	37	NVD	NO	No	No	NO	28	MULTI	NO	NO	NO	B	-	AGA	YES	48	96	25	6	-	9	7.6	YES	RASH
100	1E+05	TERM	M	40	3600	7	9	40	LSCS	NO	No	No	NO	27	MULTI	NO	NO	NO	O	+	AGA	NO	48	72	17	8	-	11	8.7	No	

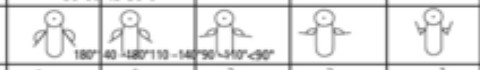
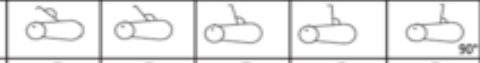
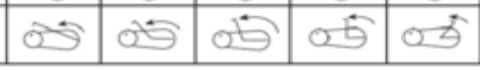
ANNEXURE –IV

NEW BALLARD SCORE

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score)

NAME_____ SEX _____
HOSPITAL NO._____ BIRTH WEIGHT_____
RACE _____ LENGTH _____
DATE/TIME OF BIRTH_____ HEAD CIRC._____
DATE/TIME OF EXAM_____ EXAMINER _____
AGE WHEN EXAMINED _____
APGAR SCORE: 1 MINUTE_____ 5 MINUTES _____ 10 MINUTES_____

NEUROMUSCULAR MATURITY

NEUROMUSCULAR MATURITY SIGN	SCORE							RECORD SCORE HERE
	-10 1	2 3 4 5						
POSTURE								
SQUARE WINDOW (Wrist)	 >90°	 90°60°45°30°0°						
ARM RECOIL		 180° 140°110 - 140°90 - 110°<90°						
POPLITEAL ANGLE							90° 100°120° 140° 160° 180°	
SCARF SIGN								
HEEL TO EAR								
							TOTAL NEUROMUSCULAR MATURITY SCORE	

SCORE
Neuromuscular _____
Physical _____
Total _____

MATURITY RATING

SCORE	WEEKS
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

GESTATIONAL AGE (weeks)
By dates_____
By ultrasound_____
By exam_____

PHYSICAL MATURITY

PHYSICAL MATURITY SIGN	SCORE							RECORD SCORE HERE
	-10 1	2 3 4 5						
SKIN	sticky friable transparent	gelatinous red translucent	smooth pink visible veins	superficial peeling & / or rash, few veins	cracking pale areas rare veins	parchment deep cracking no vessels	leathery cracked wrinkled	
LANUGO	none	sparse	abundant	thinning	bald area	mostly bald		
PLANTAR SURFACE	heel-toe 40–50 mm: -1 < 40 mm: -2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
BREAST	imperceptible	barely perceptible	flat areola no bud	stippled areola 1–2 mm bud	raised areola 3–4 mm bud	full areola 5–10 mm bud		
EYE / EAR	lids fused loosely: -1 tightly: -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff		
GENITALS (Male)	scrotum flat, smooth	scrotum empty faint rugae	testes in upper canal rare rugae	testes descending few rugae	testes down good rugae	testes pendulous deep rugae		
GENITALS (Female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora		
							TOTAL PHYSICAL MATURITY SCORE	

Reference
Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991; 119:417–423. Reprinted by permission of Dr Ballard and Mosby—Year Book, Inc.

ANNEXURE-V

APGAR SCORING FOR NEONATES

A score is given for each sign at one minute and five minutes after birth. If there are problems with the baby an additional score is given at 10 minutes. A score of 7-10 is considered Normal, while 4-7 might require some resuscitative measures, and a baby with APGAR's of 3 and less require immediate resuscitation.

	Sign	0 point	1 point	2 points
A	Activity(muscle tone)	Absent	Arms & Legs Flexed	Active Movement
P	Pulse	Absent	Below 100bpm	Above 100 bpm
G	Grimace	No response	Grimace	Sneeze, cough ,pulls away.
A	Appearance(skin colour)	Blue-gray, pale, all over	Normal, except for extremities	Normal over entire body.
R	Respiration	Absent	Slow ,irregular	Good ,crying.