STUDY OF ELECTROLYTE CHANGES IN TERM NEONATES RECEIVING PHOTOTHERAPY FOR JAUNDICE

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BONAFIDE CERTIFICATE

This is to certify that the dissertation titled **"STUDY OF ELECTROLYTE CHANGES IN TERM NEONATES RECEIVING PHOTOTHERAPY FOR JAUNDICE"** is a bonafide work done by **Dr.M.Usharani**, under my direct supervision and guidance, submitted to The Tamilnadu Dr. M. G. R. Medical University in partial fulfilment of University regulation for **M.D., Branch – V (Physiology).**

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DECLARATION

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INTRODUCTION

Neonatal hyperbilirubinemia has been the most common uncharacteristic physical finding during the earliest week of life. Over two third of neonates build up clinical jaundice. The physical finding like yellowish discolouration of the mucous membrane in newborn is due to accumulation of indirect bilirubin. Unconjugated hyperbilirubinemia is a normal physiological occurrence in most of the infants. Neonatal hyperbilirubinemia nearly influences 80% preterm and also 60% term neonates during initial week of life **.**

Among term newborn 6.1% contain a serum bilirubin over 12.9 mg%. Serum bilirubin over 15 mg% is present in 3% of term newborns. Nevertheless untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic **.**

Hyperbilirubinemia in neonate's being a manifestation of undeveloped conduit of excretion of bilirubin by the liver. It is largely the frequent cause for newborns getting admitted again in primary days of living in current era of postnatal discharge from hospital. Neonatal hyperbilirubinemia is a cause of concern for the parents . Premature infants have neonatal jaundice at very elevated frequency of which necessitate curative interference when compared to term neonates.

High values of unconjugated bilirubin could proceed towards bilirubin encephalopathy and later kernicterus through overwhelming permanant neurological development problems. Conjugated hyperbilirubinemia reflects impending systemic illnesses or severe hepatic disorders of the liver . Hence aptly managing neonatal hyperbilirubinemia is of supreme significance.

Hyperbilirubinemia can be treated either by phototherapy or exchange transfusion or pharmacologic agents.

Phototherapy plays a major function in prevention and management of hyperbilirubinemia. Phototherapy transforms bilirubin into isomers that are dissolvable in water which are capable of being excreted devoid of conjugation that occur in the liver **(Stokowski, 2006)**.

Ultimate value of phototherapy relies on the kind of light source used (i.e. dosage, spectral release curve, deepness of infiltration), the space amidst the light and the infant, the surface area to be treated, the etiology of the jaundice and also value of total serum bilirubin at phototherapy's onset**.**

The aims of phototherapy are to avoid the previously high total serum bilirubin level from increasing, to thwart the happening of encephalopathy or kernicterus and to stop the total serum bilirubin from getting higher to a level that needs exchange transfusion**.**

The foremost exhibited phototherapy's value has been diminishing the need for exchange transfusion. As any treatment has its side effects, phototherapy also has its adverse effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, hypocalcemia, redistribution of blood flow and genotoxicity **.**

Numerous investigations have been carried out to establish the security of phototherapy in the management of neonatal hyperbilirubinemia. Unlike other side effects, a few studies are currently available that depicts the adverse effects of

phototherapy on serum electrolytes. Hypocalcemia is one of the known adverse effects.

90% of preterm and 75% of fullterm neonates develop hypocalcemia after being subjected to phototherapy. Hypocalcemia can cause serious complication like irritability, jitteriness, convulsion and apnea. Phototherapy induced hypocalcemia is a significant problem. Hence emphasis is given in special reference to hypocalcemia.

Therefore this study is aimed in determining the changes in serum electrolytes sodium, potassium, chloride and bicarbonate in addition to calcium in term babies receiving phototherapy for jaundice.

AIMS AND OBJECTIVES

1. To estimate the serum electrolytes in term neonates before and after phototherapy.
2. To compare the occurrence of phototherapy induced electrolyte changes in term neonates before phototherapy and after phototherapy.

REVIEW OF LITERATURE

HISTORICAL ASPECTS

The record of bilirubin actually reverses several centuries, when neonates were found with jaundice. Towards the **eighteenth century's** ending latest reports of jaundice in newborns appears to have started. One of the works was done through **Jean Baptiste Thimotee Baumes** (1806).

He elaborates lethargy, poor intake, symptoms of cerebral association and a setback in passage of meconium would have been linked in the company of or itself reason of neonatal jaundice.

Association of newborn jaundice with absence of free discharge of meconium was stated by **Condie** (1853).

The first depiction of bilirubin related discoloration of the brain in a kernicteric neonate had been attributed by **Johannes Orth** (1875). He suggested the occurrence of yellowish and reddish tincture and substances in the appendages of neonates.

Assessment of the brain with help of microscope by him, exposed to facilitate neurons within the basal ganglia were stained with yellowish colour while that of adjacent parts have not been stained.

The term "Kernicterus " was initially invented by **Christian Schmorl in Dresden** (1904).

The yellowish tint of brain vanished later if not that tissue be safeguarded within formalin which was first noted by Schmorl .

In 1908 a case of icterus gravis neonatorum in families was published by **Hermann J. Pfannenstiel**.

Cases in which single families had jaundice and kernicterus were published by **Arkwright, J.A.** (1910), **Rolleston, H.D**. (1910).

The relationship among hyperbilirubinemia and brain injury in a newborn infant with **erythroblastosis fetalis** was made by **Guthrie L** (1914) and was attributed as the first to issue an explanation of kernicterus.

Diamond, et. al., in 1932, issued a key paper that explained the clinical setting of erythroblastosis fetalis (**Blackfan, K., Baty, J., and Diamond, L**1932) .

A more rigorous type of neonatal jaundice accepted was **Icterus gravis,** often related with intense anaemia, atypical neurological conclusion and demise.

Several years later the grounds of icterus gravis equivalent to **alloimmune hemolytic disorder** would not have been acknowledged till the blood groups of human were studied.

In 1940 danger of recurrence in families was established by the **invention of the Rh group** which were present as red cell antigens .

When development took place in the methods for exchange transfusion in neonates the etiology of hemolytic disease which occurred in newborn was eventually illustrated. A book disorders of blood in case of children was in print in 1944 **Blackfan, et. al.,(Blackfan, K., Leister, C., and Diamond, L)**.

The difficult method of exchange transfusion when needed was included and done by **John Barrett, MD, Edwin Forman, MD, Frank Giunta, MD**, in 1940s - 1960s .

By1950, **Vaughan, et. al.,** related erythroblastosis and kernicterus (**Allen F., Diamond, L ., and Vaughan V).**

Unconjugated bilirubin crosses the placenta without difficulty and in the perceptive of how fetal hyperbilirubinemia was absent and its levels tending to augment soon after birth was shown by **Schenker** (1963) (**Dawber, N., Schmid, R., and Schenker, S.,** 1964).

Simultaneous drop of birth rates in 1970s was associated with discovery of **Rh – immune antiglobulin** in 1968.

Appearance of red- blue pigment was found during 1883 when **Ehrlich** added diazo reagent with bilirubin in urine.

In 1918 **Van den Bergh** introduced diazo reaction.

Bilirubin glucuronide produced the direct moiety was stated by **Schmid, et. al.,** in 1956 . (**Billing, B., Lathe, G., Schmid, R., Talafant, E., and Cole, P.**)

In 1959, **Odell** studied binding of bilirubin with the protein (1959).

In **1956** the foremost discovery of utilization of phototherapy happened by chance, at England in **Rochford Hospital** which was located in Essex. Clean air and sunshine in the lawn benefitted the infants was the belief of the sister in the ward (Incharge Nurse) of the preterm baby unit.

Subsequent to publications **of Dr. Cremer's** in the Lancet during **1958** paediatricians in the United Kingdom started to employ phototherapy .

Lucey, et. al., published an additional very significant document in 1968 (**Hewitt, J., Ferreiro, M., and Lucey, J.,** 1968). The most honest adherent of the uses of

phototherapy was Dr. Lucey, with excellent humor called himself the “Prince of Light ” .

Avoidance of hyperbilirubinemia and kernicterus in neonates by means of photo therapy were critically studied by Dr Lucey .

Swift excretion of products of phototherapy which were photo-degradable were in bile and urine .This idea was put forth by **Ostrow, J** (Ostrow, J. 1967).

BILIRUBIN METABOLISM

1) SYNTHESIS OF BILIRUBIN:

The final product of metabolism of heme is bilirubin . Hemoglobin and various oxidative enzymes including cytochromes present in the mitochondria and cytochromes of the microsomes (P-450) in the liver possess heme . So bilirubin present in the plasma is approximately 85 % erythropoietic and15% non-erythropoietic. The two sources from which erythropoietic fraction originates are: normal aging erythrocytes in the circulation and the juvenile faulty red cells present in the bone marrow **(Stevenson et al., 2001).**

As per the significance monocytic macrophages, reticulo-endothelium in each organ more particularly in the spleen, liver and bone marrow produce bilirubin from erythropoietic heme. The hepatocytes produce bilirubin from non-erythropoietic heme. An oxygenase breaks the tetrapyrrolic ring present in heme . A tetrapyrrolic sequence devoid of iron is formed from the tetrapyrrolic molecule **(Dennery et al., 2001)**.

During the end of 1960s heme oxygenase was identified as the enzyme very indispensable for bilirubin production. Heme of hemoglobin or proteins which contain heme are degraded forming biliverdin, the green coloured pigment. Biliverdin reductase reduces biliverdin to unconjugated bilirubin, which is the orange-yellow coloured pigment.

The alpha- bridge carbon that is oxidized is extruded as carbon monoxide and exhaled through the lungs . There is release of Iron in this course of action and preserved for reuse **(Verman et al., 2004).**

2) BILIRUBIN TRANSPORT IN BLOOD

The reticulo endothelial cells set free bilirubin in the general circulation which quickly gets attached to albumin. One gram of albumin can bind with 8.3 mg of bilirubin at the primary binding site. However in the neonate, decreased albumin levels and presence of substances competing with bilirubin for the same binding sites can reduce the binding capacity e.g. long chain fatty acids from breast milk, sulphonamides and salicylate **(Gourley, 2001).**

Only bilirubin which is not bound to albumin enters the brain by crossing an intact blood-brain barrier **(Maisels, 2008)**.

3) HEPATIC UPTAKE OF BILIRUBIN

Hepatocytes take up bilirubin on their sinusoidal surface. There is breakage in the bond of albumin bilirubin . Albumin remains in the plasma. There is entry of free molecule of bilirubin into the hepatocyte. There is very quick uptake. The impairment in taking up of bilirubin by hepatocytes will result in unconjugated hyperbilirubinemia **(Moersehel et al., 2008).**

4) HEPATIC INTRACELLULAR BILIRUBIN TRANSPORT:

Within the hepatocyte cytoplasmic proteins: ligandins and Z protein are found attached with bilirubin . 2% of cytosolic proteins are constituted by collection of enzymes called Ligandins . Fatty acids are seen bound with Z protein . The avoidance of reflux of free bilirubin from hepatocytes into the circulation is the primary function of the Z proteins **(Hansen, 2009).**

5) CONJUGATION WITH GLUCURONIC ACID:

Glucose is normally present in hepatocytes. UDP-glucose dehydrogenase act on glucose to form Glucuronic acid **(Huang et al., 2002)**. Unconjugated (indirect) bilirubin is converted to water soluble conjugated (direct) bilirubin in the smooth endoplasmic reticulum by uridine diphosphate glucuronyl transferase (UDPGT) enzyme. This enzyme catalyzes the formation of bilirubin monoglucuronide which may be further conjugated to bilirubin diglucuronide. Both mono and diglucuronide forms can be excreted into the bile canaliculi against the concentration gradient.

Inherited deficiencies of the conjugating enzyme uridine diphosphate glucuronyl transferase (UDPGT) can cause severe hyperbilirubinemia in neonates (Criggler Najjar syndrome) **(Huang et al., 2002).**

By augmenting the action of bilirubin transferase bilirubin conjugation and excretion is favoured on administration of substances that induce microsomal enzyme such as phenobarbital, glutethimide and antipyrine **(Wong et al., 2007)**.

In summary: Glucose on combining with UDP-Glucose-dehydrogenase; UDP glucuronic acid is formed.

UDPGA combines with bilirubin and Glucuronyl transferaseto form bilirubin mono & di- glucuronides.

6) SECRETION OF BILE BY HEPATOCYTES:

The liver has an endocrine part and an exocrine part. Products such as blood proteins and coagulation factors produced by the liver are secreted internally into the blood through the sinusoidal surface **(Thaler M 1996).** The bile

and several other substances such as the final products of detoxification are secreted externally into the biliary tract **(Wong et al., 2007)**.

7) INTEST1NAL METABOLISM OF BILIRUB1N:

According to the following sequence urobilin is formed in the intestine when bilirubin gets reduced to:

Bilirubin glucuronide combines with bacterial enzymes or intestinal beta glucuronidase to form free bilirubin

Free bilirubin is acted upon by bacterial dehydrogenase to form urobiliogen (colourless)

Urobilinogen is in turn acted upon by dehydrogenase and UROBILIN (orange-yellow in colour) is formed.

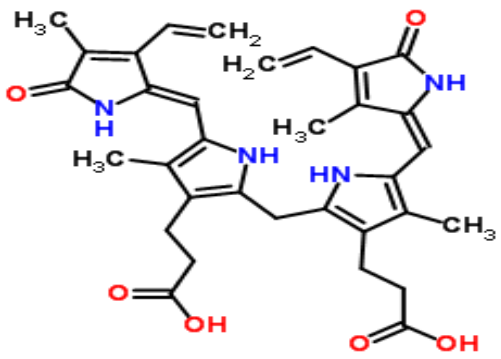
It is through the faeces excretion of the vast quantity of bilirubin, stercobilinogen, stercobilin, urobilinogen and urobilin takes place. Reabsorption of little quantities of bilirubin along with urobilinogen are done through the intestine and it reaches the liver. Reconjugation of bilirubin occurs within the liver and is excreted through the faeces. In the urine there is excretion of urobilinogen which was reabsorbed **(Moershel et al., 2008)**.

8) BILIRUBIN EXCRETION:

Just when the level of conjugated bilirubin in the plasma is greater than the normal it is excreted through the urine. Normal subjects do not contain conjugated bilirubin in urine . In conditions of unconjugated hyperbilirubinemia, as it happens in cases of hemolysis conjugated bilirubin is not excreted through the urine **(Dennery et al., 2001).**

NEONATAL HYPERBILIRUBINEMIA

- **Neonatal icterus or jaundice in Neonates** otherwise **hyperbilirubinemia** in **Neonatal** period (accepted in Greek the same meaning as ἴκτερος), adjective is: **icteric**, which appeares as yellowish discolouration occurring in mucous membrane of a neonate due to elevated serum bilirubin concentration.
- A commonly faced difficulty, neonatal hyperbilirubinemia by definition is rise levels of total serum bilirubin more than 5 mg in one dL or 86 μmol in one Litre.**(Slusher et al., 2004)**
- Tetrapyrrole prosthetic group present in haemoglobin and cytochromes gives rise to biliburin .



- Application of pressure by a finger blanches the skin which detect jaundice in newborn by showing the details of the underlying skin and subcutaneous tissue.
- With skin nature and body area the serum bilirubin level necessary to effect jaundice changes.

- When serum bilirubin reaches a value at two to three mg in one dL or 34 to 51μmol in one litre ; jaundice generally happen to be evident in sclera and in value between 4 and 5 mg in one dL or 68 to 86 μmol in one litre jaundice becomes happens to be in face .

Normal values of serum bilirubin (Stoll and Piazza, 2007).

Age	Preterm	Full term
Cord blood	2mg/dl	2mg/dl
0-1 Day	8mg/dl	6mg/dl
0-2 Day	l2mg/dl	8mg/dl
2-5 Day	16 mg/dl	12 mg/dl

- Jaundice look as if to proceed in a course starting from head and ending in foot, as bilirubin levels rises. When the level increases to 15 mg/dL (258 μmol/L) it becomes apparent upto the level of umbilicus and when the level increases to 20 mg/dL (340 μmol/L) it becomes apparent upto the feet. In the first week of living slightly additional than 50% of all neonates become apparently jaundiced.
- Based on its reason and the degree of increase hyperbilirubinemia may be safe or dangerous . No matter what may be the bilirubin level few reasons of jaundice are very hazardous .
- Once the level is elevated enough hyperbilirubinemia of any cause is a concern. Based on age , level of prematurity and health position the verge

for concern changes. The threshold is taken to be a level > 18 mg/dL (> 308 μmol/L) in term infants.

- All neonates have some hyperbilirubinemia and most have benign outcomes when monitored and treated, if necessary, in a timely manner. Neonatal jaundice may be recognized in about 60% of infants born at full-term during first week subsequent to being born **(Bhutani along with Johnson, 2009)**.

Incidence of Neonatal Hyperbilirubinemia

In the first week of life nearly every newborn has an unconjugated serum bilirubin level above 30μmol/L (1.8 mg/dL) making neonatal hyperbilirubinemia very common **(Schwoebel et al ., 2004).** Visual detection of jaundice by health care providers, which differs extensively. It relies both on notice of the observer and on features of the infant like race and maturity. Infants to be tested are thus recognised. There is elevated incidence in East Asian, American Indians and lesser in blacks. Incidence rate is higher Greeks who are residing in Greece than Greek ancestry existing exterior to Greece **(Ipek and Bozakut, 2008).** People existing at higher altitudes have greater incidence **(Hansen, 2009).**

Phototherapy was suggested by the American Academy of Paediatrics for 4.3% of the total 47,801 infants who had total serum bilirubin levels in the recommended range. It was shown in a 2003 study in the United States**(Atkinson et al.,2003).**10.5% of infants born in term and 25.3% of infants who were born near-term had significant jaundice was the report of a study done in Turkey

(Sarici et al., 2004). In Egypt about 20.4% of newborns develop jaundice yearly. Incidence of jaundice was found to be higher in low birth weight infants (35.6%) compared to normal birth weight infants (16.9%) **(Mansour et al., 2005)**.

Therapeutic interference is necessary for premature babies who have much greater occurrence of neonatal jaundice when compared to term neonates **(Porter and Denim BL 2002).** Most frequent morbidity seems to be hyperbilirubinemia among 65% of 137 very low birth weight neonates who were born in a period of 7 years in AIIMS.

NEONATAL HYPERBILIRUBINEMIA CLASSIFICATION:

A) Classification depending on conjugation of bilirubin

B) Classification based on the onset of jaundice

A) Classification based on conjugation of bilirubin

- Unconjugated (Indirect hyperbilirubinemia)
- Conjugated (Direct hyperbilirubinemia)

B) Classification based on the onset of jaundice

1. Jaundice appears within first 24 hours
2. Jaundice appears on daytime two otherwise three
3. Jaundice appears after first week
4. Persistent jaundice during the first month

I) Unconjugated (Indirect hyperbilirubinemia) is further classified into

a. Physiological jaundice

b. Hemolytic causes – intrinsic, extrinsic

c. Non-hemolytic causes

d. Substances / disorders affecting binding of bilirubin to albumin

a) Physiological jaundice During their first week many infants build up visible jaundice due to rise of unconjugated bilirubin level.

This frequent condition is known as physiological jaundice.

- Mostly in the initial 24 hours it is not present
- Occasionaly rises above 5mg/dl in a day
- Fraction of direct bilirubin is mostlly less than 2 mg/dl.

1. Infants born at term :

- in the initial first week of living 50-60% of neonates are jaundiced
- at 3–5 days level of total serum bilirubin reaches highest range
- serum bilirubin does not exceed 13 mg/dl
- it usually disappears by 14 days

2. Infants born at Preterm:

- elevated occurence of noticeable jaundice is more than in term infants.
- total serum bilirubin reaches highest range at age of 5-7days.
- serum bilirubin does not exceed 15 mg/dl
- It usually disappears by 21 days

Investigation should be carried out in neonates who fail to fulfil the above criteria and managed as pathological jaundice **(Johnson and Terry, 2006).**

Etiology of physiological jaundice

Physiological jaundice is caused by: Usually unconjugated bilirubin is converted to conjugated bilirubin and gets eliminated into the gastrointestinal

tract. This converting action which is carried out by glucuronyl transferase is decreased.

- In the fetus before birth, the enzyme has been keenly kept at low levels, as bilirubin should continue to stay unconjugated so as to pass through the placenta and in view of preventing accumulation.
- Enzyme glucuronyl transferase takes a few days, after birth to regains its function.
- In adults life span of red blood cells 100 to 120 days whereas it is shorter, being just ranging between eighty and ninety days in a infant born at term.
- Increase in absorption of bilirubin back again into the circulation due to little conversion by the intestinal flora of bilirubin to urobilinogen .

  In newborns those who are breastfed two types of jaundice occur. Mostly oboth the types are not dangerous.

  They are

  i. Early - Onset Breastfeeding jaundice
  ii. Late - Onset Breast milk jaundice

Breastfeeding Jaundice - Early Onset

- Sizable energy deficit in the former a small number of days in life makes the neonates who are breast-fed to be prone to bigger jeopardy for early-onset inflated physiologic jaundice
- Delay in passage of meconium and mild dehydration occur due to low volume and number of feedings.

- Moderately jaundiced (value of total serum bilirubin beyond 12 mg per dL) or severely jaundiced (value of total serum bilirubin exceeding 15 mg per dL) occurs in breastfed infants three to six times than formula-fed newborns **(Eneh AU, Uguv 2009).**
- Few newborns those having reduced milk ingestion plus those in whom containing dehydration or decrease in energy ingestion have elevated enterohepatic circulation of bilirubin. Decreased level of intestinal bacteria which converts bilirubin to nonreabsorbed substances could cause the rise in enterohepatic circulation **(John P Cloherty).**

Late-Onset Breast milk jaundice

Breast milk jaundice varies from breastfeeding jaundice. It occurs in otherwise healthy, full term, breastfed babies. It is characterised by indirect hyperbilirubinemia in breast fed newborn. It occurs between five and seven days of life furthermore reaches peak by second week. It persists longer than physiological jaundice. It is caused by the following reasons:

1. At the time of birth, the gut is free from infective organisms and there is delay establishment of normal gut flora. Conjugated bilirubin is converted to stercobilinogen by the bacteria in the adult gut and excreted in the stool.

2. When there is lack of adequate bacteria, brush border β-glucuronidase de-conjugate bilirubin which is then reabsorbed. This route of reabsorption is known as enterohepatic circulation.
3. Augmented levels of substance called epidermal growth factor present in milk of mother causes increased uptake of bilirubin in the intestine (enterohepatic circulation) in babies who are breast fed.
4. Bilirubin deconjugation and enterohepatic recirculation are amplified by glucuronidase present in breast milk **(Gartner and Hershel 2001).**
5. 3-alpha-20-beta pregnanediol which is a metabolic product of progesterone is present in breast-milk of certain women. Activity of uridine diphosphoglucuronic acid glucuronyl transferase predisposed in favor of conjugation and successive elimination of bilirubin is inhibited by pregnanediol.
6. Conjugation of bilirubin is decreased in the infant's liver, since the action of glucuronyl transferase is just 0.1-1 percent of the level of grown person. Elevated values of bilirubin in blood occur due to inhibition of conjugation of bilirubin.
7. Hepatic glucuronyl transferase is inhibited by lipoprotein lipase, an enzyme that is present in breast milk resulting in decrease in conjugation and ensuing excretion of bilirubin.

During month of July in **2004, the American Academy of Peadiatrics** made in print protocols which would decrease beginning of avoidable

circumstances. As per **AAP Subcommittee on Hyperbilirubinemia**, for each baby born by 35 weeks or additional weeks of pregnancy, successful breastfeeding ought to be promoted:

Recommendation 1: Clinicians should give advice mothers to feed their newborn babies atleast 8 to 10 times per day for first numerous days.

Recommendation 1.1: The AAP suggests in opposition to regular supplementation of non dehydrated infants who are breastfed with water or (sugar) dextrose water.

b) Hemolytic causes:

- **Intrinsic**

RBC enzyme defects

- Pyruvate kinase deficiency
- Glucose-6-phosphate dehydrogenase deficiency **(Siberry and Iannone 2000)**

RBC membrane defects

- Hereditary elliptocytosis
- Hereditary spherocytosis

Globin synthesis defect

- Thalassemia
- sickle cell anaemia

Systemic conditions

- Arteriovenous malformation
- Sepsis

Extrinsic

- Kell incompatibility
- ABO incompatibility **(Haque and Rahman 2000)**
- Alloimmunity (The blood from cord or neonate that gives direct Coomb's test positive and maternal blood which gives indirect Coomb's test positive)
- Rhc incompatibility
- Other mismatches in blood group leading to illness of the newborn with hemolysis.
- Rh incompatibility

c) Non-hemolytic etiologies

i) Decreased hepatic uptake and conjugation of bilirubin

- Breast milk Jaundice (pregnanediol inhibits glucuronyl transferase)
- Infants of Diabetic Mothers
- Pyloric stenosis
- Criggler Najjar Syndrome
- Hypothyroidism
- Gilbert Syndrome
- Immaturity of glucuronyl transferase action in all newborns

ii) Increased enterohepatic reabsorption

- Bowel obstruction
- No enteric feedings
- Breast feeding jaundice (due to dehydration from inadequate milk supply)

d) Substances / disorders affecting binding of bilirubin to albumin

- Fatty acids in nutritional products
- Asphyxia
- Acidosis
- Hypothermia
- Hypoglycemia

B) Conjugated (Direct Hyperbilirubinemia)

Whichever of the subsequent aspects illustrates pathological jaundice:

a) Direct bilirubin above 34 μmol/l (2.0 mg/dL).

b) Clinical jaundice which appears within initial twenty four hours .

c) Augmentation in the value of total bilirubin above 8.5 μmol/l (0.5 mg/dL) per hour or (85 μmol/l) 5mg/dL per 24 hours.

d) Total bilirubin above331.5 μmol/l (19.5mg/dL).

II)Classification based on the onset of jaundice

1)Jaundice appears within first 24 hours:

- Pathological jaundice
- Erythroblastosis fetalis.
- Intrauterine infection (TORCH)
- Sepsis
- Extravascular hematoma

2)Jaundice appears on the second or third day:

- Physiological jaundice
- Criggler-Najjar syndrome
- Early onset breast feeding jaundice

3)Jaundice appears after first week:

- Breast milk jaundice
- Extra hepatic biliary atresia
- Hypothyroidism
- G6PD deficiency **(Shahiary 1997)**
- Galactosemia

4) Persistant jaundice during the first month:

- Inspissated bile syndrome
- Hyperalimentation
- Congenital infection **(Stoll and Kligeman, 2004)**

Elevated bilirubin formation and reduction in bilirubin conjugation play a significant part in the pathogenesis of newborn jaundice **(Ogunlensi TA 2007).** There are several risk factors which influence the severity and period of hyperbilirubinemia though physiological jaundice is present in many newborns,.

When thee are mutations in the gene coding UDP-glucuronosyl transferase 1A1 (UGT1A1) present with other risk factors the incidence and rigorousness of neonatal jaundice have been elevated (**Muslu et al,2007).**

Risk Factors for Hyperbilirubinemia (Dennery et al., 2001)

Maternal Factors	Neonatal Factors
1. Drugs: Vitamin K 3, diazepam , oxytocin 2.Inadequate breast feeding 3. Blood type whether Rh or ABO incompatibility 4. Maternal illness **(Oladakun A et al., 2009)** 5. Ethinicity- Asian, Native American	1. Infections: TORCH or sepsis (TORCH- cytomegalovirus , herpes simplex viruses, rubella, toxoplasmosis). 2. Birth trauma: instrumental delivery, cephalohematoma, cutaneous bruising 3. Infrequent feedings 4. Drugs: erythromycin, chloramphenicol 5. Excessive loss of weight after birth 6. Polycythemia. 7. Delayed meconium passage 8. H/o Prematurity 9. H/o Previous sibling with Hyperbilirubinemia. 10. Being male in gender.

Bilirubin Toxicity

The most important effect of neonatal hyperbilirubinemia is **Kernicterus**.

Acute or chronic hyperbilirubinemia giving rise to deposition of unconjugated bilirubin in basal ganglia and brain stem nuclei and producing brain damage is kernicterus **(Soorani- Lusing I et al., 2001).** Kernicterus occurs even till date and can be prevented nearly forever though it is unusual now. **(Steven and Shapiro 2003).**

More care must be taken supposing if bilirubin's value is more than 25 mg per dL (428 μ mol per L)though the jeopardy of bilirubin toxicity is almost unimportant in case of healthy term newborn who is exclusive of hemolysis and in the term newborn who is by way of hemolysis, a bilirubin level more than 20 mg per dL (342 μ mol per L) is a stress.

Inside the intravascular space bilirubin attached to serum albumin is present usually. If injury has happened due to asphyxia, sepsis, hyperosmolality, hypoperfusion, hypoxia or acidosis in the neonate bilirubin crosses the blood-brain barrierand produces kernicterus **(Amin SB 2004).**

The consequences of bilirubin excess has been unalterable in addition frequently overwhelming **(Chang et al ., 2009).** Three to four days later after birth earlier signs of kernicterus which are delicate and imprecise, classically appear. At whatever time all through the neonatal period hyperbilirubinemia may cause kernicterus.

The newborn who is affected starts to show delayed effects of bilirubin toxicity after the initial week of life **(Seoud et al., 2007**). Mildly mental

retardation delays in developmental and motor function, sensorineural hearing loss and are features of chronic bilirubin encephalopathy (apparent by three years) produced if the infant is able to survive after the primary severe neurologic damage **(Newman , T. B., et al. 1990).**

High rational advance to plans used for the analysis of jaundice in the newborn is achieved if an alertness of the risk factors and their possible role to serum bilirubin levels is created **(Maisles, 2006).**

Investigation of jaundice

a) Estimation of bilirubin The diagnosis of jaundice and its severity is substantiated by measuring the level of bilirubin . A sample of blood or by means of a sensor placed over the skin the level can be calculated .

i) Clinical Assessment In light of natural source an inspection visually is carried out.

While the bilirubin level increases, from head to toe the depth of jaundice progresses. Level of serum bilirubin (SBR) along with the intensity of skin discolouration are described by ruleof **Kramer**

Region	Lower body, thighs	Neck and Head	Hands, feet	Chest	Arms,legs below knees
SBR in mol/L	200	100	>250	150	250

Inspecting the infant visually and rule of Kramer, just can be used to assess the intensity of jaundice.

Serum bilirubin assessment should not be done by clinical evaluation of the depth of jaundice as the error a inter-observer is wide. In the infants having pigmented skin the estimation is mostly undependable.

ii) Transcutaneous hand held bilirubinometer:

- This is a transportable, rechargeable and also hand held but expensive and more refined.
- a xenon tube gives rise to a strobe light and that light goes all the way through the subcutaneous tissue when we apply pressure over the photoprobe,.
- By travelling in the second fiber optic bundle to reach the spectrophotometric module the light which gets reflected is returned **(Ebbesen A 1996).**
- After correction is done for hemoglobin the strength of the yellow colour in this light, is calibrated and immediately displayed in arbitrary units.

- To guarantee that total bilirubin levels are securely less than those requiring interference this portable bilirubinometry is sufficient for infants with mild jaundice.
- For individualising babies who need sampling capillary blood or phlebotomy to measure serum bilirubin transcutaneous bilirubinometry may be valuable in the infants with moderate jaundice.

- To select infants to speedy and forceful therapy this hand held bilirubinometry may be a helpful device in infants with extreme jaundice, **(Rubaltelli FF et al., 2001).**

iii) Total serum bilirubin level :

- For a neonate having jaundice moderately and comes on the third or second day of living devoid of physical examination results and history indicative of pathologic progression generally measuring the level total serum bilirubin test alone is needed .
- Earlier assessment of fractions of bilirubin is required for infants in whom jaundice persists after the initial 7-10 days of life and in those with thrombocytopenia hepatosplenomegaly, or other findings suggestive of hepatobiliary disease, petechiae, congenital infection or metabolic disorder .

Additional investigations along with bilirubin may be needed in the situations given below :

- jaundice presented by infants later than third or on the first day of life
- some infants when being born being anemic
- otherwise sick appearing infants
- increase in levels of serum bilirubin in some infants necessary to start management
- persistence in some infants with considerable jaundice further than the primary 2 weeks of life
- pregnancy, family, maternal or the case histories showing the likelihood of a pathologic event in certain infants.

- physical assessment exhibiting features which are not clarified by uncomplicated physiologic hyperbilirubinemia in some of the infants.

The other investigations include:

b) Values of hemoglobin and hematocrit

c) Determination in infant and mother of Rh and blood type.

d) Levels of albumin in serum :

- Since at the initial high-attraction binding site albumin couples bilirubin at a ratio of 1:1 this measurement looks to be a useful accessory in finding the risk of toxicity strength.

e) In the infant direct antiglobulin test (DAT)which is direct Coombs test.

f) In breath measuring carbon monoxide end-tidally:

- a manifestation of production of bilirubin is end-tidal carbon monoxide in breath (ETCO)
- Persons with hike in production of bilirubin and so at an augmented danger of mounting more levels of bilirubin can be noticed by measuring ETCO.
- ETCO is easily measured by an apparatus which has been recently developed.

g) Hour-specific bilirubin values depicted by nomogram : **(Bhutani VK et al, 2001)**

- Infants who are prone to acquire rise in values of serum bilirubin whether before or during the time of discharge from hospital can be judged by this helpful tool.

- Keen follow-up monitoring along with frequent measuring of bilirubin is needed for infants recognized by this manner.
- For both values of bilirubin assessed in the serum and for transcutaneously measured values the ability of prediction has been revealed.
- Beyond that previously got by plotting bilirubin value each hour against the nomogram; result of positive DAT (Direct antiglobulin test) test did not adjoin at all importance for clinically managing of those babies.
- In infants having ABO incompatibility who are DAT (Direct antiglobulin test) - positive nomogram appears to function well

h) Levels of conjugated bilirubin:

In the situations which were described before measuring bilirubin fractions may be needed. Only if frequent measurements assure the occurrence of an high conjugated bilirubin ; measuring direct bilirubin are usually incorrect and are liable to considerable disparity in inter laboratory as well as intra laboratory . So in general it is not a responsive tool in the diagnosis of cholestasis .

i) Erythrocyte morphology identification by peripheral blood film

J) Performing reticulocyte count

k) Viral and/or parasitic infection identification :

For infants with thrombocytopenia or other evidence of hepatocellular disease, petechiae, hepatosplenomegaly these tests may be needed.

l) Examining urine for reducing substance :

If the infant has taken adequate quantities of milk this test is a helpful for screening galactosemia .

m) Tests to assess liver function:

In hepatocellular disease levels of alanine aminotransferase in addition toAspartate aminotransferase are raised. In cholestatic disease levels of gamma-glutamyl transferase along with Alkaline phosphatase are often augmented.

Biliary obstruction is established by A gamma-glutamyl transferase/alanine aminotransferase ratio above 1. But intrahepatic and extrahepatic cholestasis cannot be distinguished **(Haber BA, Lake AM, 1990).**

n) Tests to assess thyroid function

o) Measuring blood gas:

In acidosis, predominantly respiratory acidosis the threat of bilirubin CNS toxicity is augmented.

p) Bilirubin-binding tests:

Unbound bilirubin is among one of numerous factors by which that toxicity of bilirubin can be mediated /modulated even though high levels of unbound ("free") bilirubin are linked with an very high danger of bilirubin encephalopathy,

Treatment

A practical consideration which deals through the treatment in the healthy newborn born at term's hyperbilirubinemia was formed during 1994 October by **the Subcommittee on Hyperbilirubinemia and Provisional Committee for Quality Improvement of the American Academy of Pediatrics (AAP)**.

In three means neonatal hyperbilirubinemia can be managed:

a. Mechanical removal of bilirubin by exchange transfusion **(Forfar JO 1958).**
b. Convertion of bilirubin into substances which can bypass the liver's system of conjugation and their excretion either through the bile or through the urine devoid of metabolism by phototherapy **(Cremer RJ 1958).**
c. Hastening the usual metabolic pathways for clearance of bilirubin or inhibition of enterohepatic circulation for bilirubin by meddling with heme degradation and synthesis of bilirubin through the action of pharmacologic substances **(YaffeSJ, Dorn LD 1990).**

A level of total serum bilirubin above which management of baby is needed is the definition of significant neonatal jaundice .

Phototherapy to be given to term neonates according to age in hours and also level of serum bilirubin (**AAP, 1994; Cashore, 2000**).

Hours of age	(level of serum bilirubin) considering the phototherapy	requiring the phototherapy
twenty four -twevty five hours	-	-
seventy two hours	>15 mg/dl	>18 mg/dl
forty eight -forty nine hours	>12 mg/dl	>15 mg/dl
more than seventy two hours	>17 mg/dl	>20 mg/dl

Having relied upon the age and health condition of the neonate levels of bilirubin for beginning phototherapy differs **(Weinberg 1992).** Phototherapy must be given to newborn having total serum bilirubin in excess of 12 mg/dL .

Phototherapy

Isomerisation in which trans-bilirubin changes into water-soluble cis isomer of bilirubin is the mechanism through phototherapy exerts its action. Since blue light is more successful in the bilirubin break down it is normally used during phototherapy (**Amato, Inaebnit, 1991**).

Exposure to blue light or concentrated green phototherapy was given to two separate groups of neonates having jaundice who were matched. The amount of decrease of serum bilirubin was calculated and it reflects the effectiveness of the treatment.

Blue coloured lamps give a much quick response when compared to the green lamps. Among the babies who were exposed to the green lamps recovery time from phototherapy was lesser. Since to see striking outcome exposure time must be more in green light it is not generally in use **(Dahi Far H).**

The danger of skin moles amidst children is more for treatment with ultraviolet illumination. But which has been used in phototherapy for taking care of neonate's jaundice does not increase the threat of skin malignancy.

Movement of bilirubin in the course of metabolic system of neonate is aided by augmenting feedings **(Gartner L M 2001).** By using overhead lamps the light may be functioned, in this method the eyes of the baby should be covered . The light may be operated by using a device which is known as **Biliblanket,** that should be applied over the skin of the baby and below the clothes **(Schuman AJ 1992).**

Infiltration of tissue by means of light rises strikingly as wavelength is escalating . So absorption of light by bilirubin occurs powerfully close to 460 nm which is occupied by blue area of the colour scale. Under the subsequent conditions 'Biliblankets' plays some task :

- To continue staying in the company of mother in postnatal ward and permit infant to be in an open bed.
- To make available treatment on the way of the part of body which has not been in front of the phototherapy unit being placed above head in the infants who are getting intensive phototherapy.
- Treating as outpatient. **(Costello SA, Nyikal I, Yu VY, et al 1995).**

The strength and wavelengths of the light in usage determines the quantity in which bilirubin photoproducts are developed. Phototherapeutic outcome is achieved by wavelengths that infiltrate tissue and that bilirubin absorbs **(Meberg 1997).**

Considering these influences the most effective source for treating hyperbilirubinemia are most likely lamps that has output chiefly in the range of 460-to-490-nmwhich is occupied by blue area of the colour band.

The powerful output of the light source determines the effectiveness of phototherapy **(Tan KL 1991).** It is expressed as watts per square centimetre per nanometer ($\mu W/cm^2/$ nm) covering a given band of wavelength after being measured by a radiometer or spectroradiometer.

Either standard daylight or conventional phototherapy units have to convey a spectral irradiance of eight to ten μW per square centimeter per nanometer in the

four hundred thirty to four hundred ninety nanometre band, when placed twenty cm on top of the infant, thirty to forty μW per square centimeter per nanometer is delivered by unique blue fluorescent lamps .

Conveying a spectral irradiance of at a rate of thirty μW /cm^2/ nm in the same bandwidth to the entire baby's body surface area as much as possible is the definition of intensive phototherapy in accordance with the **American Academy of Pediatrics**.

In phototherapyblue fluorescent tubes are extensively used **(Seidman DS 2000).** Normal blue fluorescent lights are possibly corresponding with typical white daytime lamps.Narrow-spectrum blue colour lamps which is special blue emerge to work most excellent **(Ennver IF 1990).**

Fixed with the overhead heat origin of few radiant warmers, quartz lamps are also being used in one or two banks having three – four bulbs. The energy output is practically high when compared to spotlights also the energy field conveyed by them is to a great extent is uniform.

The capacity to enhance energy delivery by moving lights near the neonate is restricted since the lamps are attached with the overhead heater component.

In phototherapy units fiberoptic lights too are made use of. **(De Luca G et al 1991).** Elevated energy levels are conveyed by these units, capacity of the smaller "pads" are reduced when compared with bigger wrap-around blanket since spectral power (when we multiply irradiance with the extent of the irradiated region) is related to the extent of the field that is lighted **(Karush G 1992).**

Loud sound from the fan of the light source along with a diminishion of energy delivered due to ageing and/or rupture of the optic fibers are the disadvantages in fiberoptic phototherapy units. Photodiodes are used as light source in some fiberoptic units **(Mills JF, Tudehope D 2001)**.

The following are the advantages in fiberoptic phototherapy:

- home phototherapy easily arranged
- after joining along conventional overhead phototherapy units (double/triple phototherapy) there is likelihood for irradiating a huge surface area
- overheating the newborn is reduced
- eye shields not required
- making the infant lie in a bassinet adjacent to the mother's cot phototherapy is delivered

In many recent phototherapy units light-emitting diode (LED) lights are instituted. **(Kumar P et al 2010).** Little power expenditure, reduced heat production and a good deal prolonged duration of the light-emitting units (20,000 hours) when compared with previous light sources are the advantages .

The absorption range of bilirubin is being overlapped by blue LED lights that have a constricted spectral band of elevated-intensity light. The **Cochrane Collaboration** along with **Tridente and DeLuca 2012had** recently done review in procedures in which LED phototherapy is compared with other light sources**.**

The effectiveness of LED lights in decreasing total serum bilirubin levels is in comparison with conventional light sources like fluorescent or halogen lamps is

the conclusion of those authors of reviews. It is among LEDs in addition to blue fluorescent lamps development of bilirubin photoisomers can be compared.

Special blue fluorescent lamps or light-emitting diode (LED) lights which is established to be valuable for phototherapy is currently advocated by **American Academy of Pediatrics**. Fiber-optic devices within which there is built-in filtered halogen lights too are in usage.

To treat infants with very elevated values of serum bilirubin "double" and "triple" phototherapy, which means the simultaneous usage of two or three phototherapy units in same patient is used

The neonate's space from the light and the region of skin exposed also influence the phototherapy's dose and efficacy. So it is advisable to place the light source underneath the infant. Efficacy of phototherapy can be improved by placing aluminum foil or white cloth on both sides of the infant so that the light gets reflected.

Lowering the levels of bilirubin by increasing its elimination is the objective of phototherapy and it is effectively done by phototherapy. As a method to cure jaundice in neonates sunbathing is not suggested nowadays **(Maisels and McDonagh, 2006).**

The neonate's eyes have to be constantly secured by opaque eye patches as the light can be harmful to the immature retina **(Fok TF, Wong W, Cheung KL. 1997).** When the total serum bilirubin reduces less than the level at which phototherapy was started phototherapy can be safely terminated in infants who were treated **(Meharban Singh 2004).**

Augmenting energy delivery and the accessible surface area are the important facts in the practical implementation of phototherapy. Following points should also be considered:

- To decrease the risk of overheating and if homeostasis of temperature is observed carefully the distance between the baby and the device can be reduced down to ten-twenty cm . For quartz lamps this cannot be applied.
- The inside of the bassinet should be covered with a reflecting substance, white cloth functions good in this condition. A white curtain can be hanged enclosing the bassinet and the phototherapy unit . Energy delivery can improve to several folds by these simple methods.
- Apart from diapers the eyes which has to exist enveloped to lessen possibility of injury to retina and the newborn ought to be left naked.
- The distance from light's origin and the infant's skin should be checked. The distance should not be more than fifty cm or twenty inches when using fluorescent lamps.
- View concerning efficacy of phototherapy have to be customized to the circumstances. A considerable diminution of the rate of rise may be acceptable for infants in whose serum bilirubin concentrations continue to increase.
- Phototherapy should effect in quantifiable reductions in levels of serum bilirubin within some hours for babies whose concentrations of serum bilirubin are nearer to their maximum value.

- The preliminary rate of decrease will be the more striking in infants who had the elevated serum bilirubin concentration in the beginning.
- As photoenergy decline near the circle's border make sure that the infant is positioned at the middle of the light’s circle when spotlights are being used.
- Monitor the infant very much closely to make certain the baby does not shift away as of high-energy region.
- In small premature infants spotlights are possibly more suitable when compared to larger near-term infants.
- Urine specific gravity, weight loss and output of urine, and should be monitored in the infant. Adjustments are made fluid intake consequently.
- Since milk acts like a means of transport for bilirubin away from the gut milk is the ideal fluid particularly for infants those who are fed orally

  (Coglayan, S., et al.1993) .
- Supervising should be done each hour or each other hour for infants who get admitted with severe serum bilirubin values above thirty mg/dL. Individualization is needed for timing the follow-up testing of serum bilirubin **(Kishan 1998).**
- Observing for each 6-12 hours is most likely sufficient in infants having much moderate rise of serum bilirubin. in such conditions diminutions in values of serum bilirubin to five mg per dL per hour or eighty five µmol per Litre per hour have been documented.

- A gadget used to calculate the amount of irradiance delivered through the device that was used should be made prepared at hand wherever phototherapy is given as a means of treatment **(Eggert P, Stick C, Schroeder H 1984).**
- Each time phototherapy is offered and the above mentioned method should be used as a means to make the staff concentrate their attentiveness on increasing the delivery of energy has been suggested regularly by some practitioners. In order to deliver best possible efficiency this helps us to construct phototherapy set-up.
- As the levels of serum bilirubin descends to twenty five – thirty µmol/L (two-three mg/dL) less than the level which caused the commencement of phototherapy, phototherapy is terminated.This is the usual practice**(Bell et al ., 2006)** .
- Later when the management with phototherapy have been stopped, following up tests ought to be done in 6 to 12 hours subsequent to stoppage of treatment since there could be rebounding in the levels of serum bilirubin **(Medhat 2006).** In general phototherapy could have no severe long-term complications in neonates and it is much safer.
- Complications and adverse effects are given below ;
- Within a NICU environment, neonates those who are rendered elevated intensity of ambient luminosity had an enhanced hazard of retinopathy.
- Therefore, enveloping the infant's eyes exposed to phototherapy using eye patches has been regularly done.

- In case the eye patches slide down and making the eyes exposed or blocks one or both nares immediate action should be taken .
- DNA-strand rupture and other complications can occur on genetic material by the combined action phototherapy and hyperbilirubinemia .
- Informations propose insensible water loss might happen, however this problem is not as significant as it was considered earlier. Augmenting fluid intake for all infants who are under phototherapy has minimised this problem .
- Loose stools can occur in phototherapy. Enhancing fluid supply is must to meet out greater faecal loss of water.
- Calculation done through assessment of faecal water loss, weight curves, specific gravity of urine and urinary output directly shows the fluid volume to be supplemented to the needs of that particular infant.
- During the course of intense phototherapy in certain animal models damage of the retina has been noticed **(Ehsanipour et al., 2008).**
- In premature infants who are receiving phototherapy hypocalcemia has been found to be more widespread**(Xiong T 2011).** Changes in melatonin metabolism has been proposeed as the cause for this condition **(Eghbalian and Monsef, 2002).**
- Accidents like burns had been noted due to failure of substitution of UV filters. Hence equipment should be maintained regularly
- Some amino acids in solutions of total parenteral nutrition which are subjected to phototherapy may undergo deterioration in their

concentrations. So as much as possible total parenteral nutrition solutions must be shielded from light.

- In modern servocontrolled incubators increase of blood flow in skin is less pronounced however this effect is increased during phototherapy. In small premature infants blood flow redistribution might occur.
- Due to the above conditions an augmented occurrence of patent ductus arteriosus (PDA) is accounted. The suitable treatment of PDA has been reassessed **(Fanaroff A 2010).**
- **For treating conjugated hyperbilirubinaemia phototherapy is not generally used as this does not produce kernicterus .**

Exchange transfusion

Whenever there are signs suggestive of acute bilirubin encephalopathy in the cases even if total serum bilirubin is falling to lower levels or if there occurs major concerns of neurotoxicity exchange transfusion should be thought about and predicted.

Through an umbilical artery or vein exchange transfusion is made. Cause, gestational age of the baby, clinical well-being, rate of increase in bilirubin are the indications for the usage of exchange transfusion **.**

Suggestions as given by the National Institute for Health Care along with Excellence (NICE):

- Indication on behalf of the need for exchange transfusion depends on total serum bilirubin level which is at or more than the threshold level

- In order to treat babies double-volume exchange transfusion which is the procedure of eliminating twice the estimated volume of total blood and restoring can be used.

DO's and DON'T s

- At the time of exchange transfusion do not:
  - administration of intravenous calcium regularly
  - albumin priming to be used.
  - single-volume exchange being carried out
  - continuous multiple phototherapy stoppage
- After exchange transfusion:
  - Should sustain continuous multiple phototherapy.
  - Treating in concordance with threshold table and management threshold graphs after analysing level of serum bilirubin within a period of two hours.

Neonatal problems like electrolyte and calcium imbalance, apnea, catheter linked complications, infection, complications associated with the usage of blood products, thrombocytopenia, risk of necrotizing enterocolitis, anemia and hemorrhage are the side effects of using exchange transfusion **(Owa and Ogunleni 2009).**

Sick infants exchange transfusion undergoing are possible to suffer from the danger of neonatal mortality **(Jackson JC 1997).**

CALCIUM

In the human body calcium is the most copious trace element. It is present in the volume of one and a half kilograms in average adult male and one kilogram in a woman . The bones and teeth comprise 99% of the body calcium. It is in the cell membrane and also in the cell, lymph, blood and other body fluids the rest of the calcium is present.

In three fractions or forms calcium in serum or plasma occurs :

1. The physiologically active form is free or ionized calcium which is present in the range of fifty percent –sixty percent of the total concentration of calcium.
2. One-third of the total serum concentration of calcium is Protein-bound calcium. It is not of usage to the tissues as it cannot spread through membranes **(John P. Cloherty)**
3. Ten percent of the total concentration of calcium is bound or chelated. Calcium is complexed to bicarbonate, sulphate, phosphate, lactate and citrate.
   - Normal plasma contains 9-11 mg of calcium per 100 ml.
   - In order to have essential health it is important to maintain exact amount of the calcium ion in extracellular fluids. To sustain a steady concentration of calcium, regardless of changes in intake and excretion three major hormones parathormone, calcitonin and vitamin D3 play a major role.
   - Glucagon, thyroxine, adrenal corticosteroids, estrogens and somatotropin are the additional hormones which may also have a role in maintaining of the calcium level **(Venkatraman S 1987) .**

- Calcium has an imperative role in neural excitability, blood coagulation, contraction of muscle, release of hormone, activity of enzyme, membrane permeability, second messengers. An indispensable structural constituent of the skeleton is calcium ion .
- Calcium salts that are not soluble like phytates, phosphates, oxalates and fats which are not degradable are built by the substances that prevent the absorption of calcium. Calcium ingested in diet mostly does not gets absorbed and is being eliminated through the faeces.
- Twenty five to fifty percent of the calcium which is consumed is being absorbed by average adult body. A protein produced in reaction in the direction of the activity of 1,25-dihydroxyvitamin - D3 or1,25-dihydroxycholecalciferol helps in absorption from the duodenum and proximal jejunum after binding with calcium **(Kanis JA 1978) .**

Fetal mineral metabolism : (Tsang R C 1992)

- It has been exclusively modified to get through the particular needs of this intra uterine growth period.
- The fetus gains eighty percent of the needed thirty gram of calcium in the last trimester of gestation hence Mineralization of bones happens quickly in late months of gestation **(Seki K et al 1991).**
- To sustain levels of other minerals and calcium extracellularly so that it is physiologically being suitable for tissues of the fetus.
- To supply adequate calcium and other minerals so as to fully mineralize the skeleton prior to birth fully.

- ❖ A fetus has a considerably elevated concentration of ionized and total calcium when compared to the level in the mother in late gestation which is a constant finding in the fetus **(Givens MH, Macy IG 1993).**
- ❖ Likewise, serum phosphate is notably high and serum magnesium is slightly raised more than the concentration in the maternal blood.

- **Placental Mineral Ion Transport**

  In the later months of gestation massive transfer of calcium and other mineral occurs through the placenta at a speedy rate **(Pikin RM 1985).** for the fetal needs to be fulfilled active placental transport of phosphate, calcium and magnesium is obligatory **(Lester GE1986).**

NEONATE

- ➢ A quick modification in regulating mineral homeostasis happens for hours to days after cutting the umbilical cord and abruptly losing the placental transfer of calcium and placental supply of Parathyroid hormone related peptide **(John P Cloherty).**
- ➢ Skeletal calcium stores, dietary calcium intake, vitamin D status,the parathormone secretion and renal calcium reabsorption determine the levels of serum calcium in newborns following birth**(Bergman L 1972).**
- ➢ Taking place in the day two of life in the healthy term babies calcium levels start to decline and attains a level of seven and a half to eight and a half mg/dL subsequent to delivery **(David L, Anast CS 1974).**
- ➢ End organ unresponsiveness to parathyroid hormone, hypoparathyroidism, hypercalcitonemia which comes about through 12 to 24 hours of age,

abnormalities of vitamin D metabolism, hypomagnesemia and hyperphosphatemia are responsible for the fall in level of serum calcium postnataly **(Holick MF et al., 1983).**

- Levels of parathormone raise slowly during the initial 48 hours of living and get back to standard serum calcium values are typically on their third day of life.
- For each one g/dL drop in the concentration of plasma albumin the plasma calcium decreases by 0.8 mg/dL .
- The effectiveness of the intestinal calcium absorption and renal handling get developed by two to four weeks **(Haeney RP et al 1975).** The augmented threat of hypocalcemia commencing earlier occuring in neonates who are in higher risk is due to this transitional phase**.**

HYPOCALCEMIA

By Definition

Level of total serum calcium below 1.75 mmol/L that is seven mg/dL or ionized calcium below 1 mmol/L which is 4 mg/dL in case of infants being preterm. Level of serum calcium total below 2 mmol/L which is eight mg per dL or ionized calcium below 1.2 mmol/L in term neonates is the definition proposed for hypocalcemia .

Neonatal hypocalcemia - Early onset type (ENH)

This condition is seen commonly and occurs around the initial three to

four days of life. It happens in clinical situations given below:

- Infant of Diabetic mother
- Prematurity
- Perinatal stress or asphyxia
- Preeclampsia
- Iatrogenic (lipid infusions, alkalosis, diuretics, use of blood products, phototherapy)
- Hyperparathyroidism in mother **(Drake TS 1986)**
- intake of anticonvulsants by the mother(phenobarbitone, phenytoin sodium)

Risk neonates for whom screening is suggested is given below **(Koo WWK, 1989).**

1. Infants who are born following harsh perinatal asphyxia and having score of Apgar below four by first minute after birth.
2. Preterm infants who were born prior to 32 weeks
3. Infants born to diabetic mothers those who were on intravenous fluids.

Scheduled time for screening in risk babies –

At twenty four and forty eight hours of age

Clinically presenting as :

1. Early onset neonatal hypocalcemia is frequently asymptomatic when compared tothe late onset type and it is accidentally identified .

2. If by chance the neonate becomes symptomatic:

The symptoms include

- exaggeration of startle reflex
- irritability of neuromuscular system
- convulsions
- jitteriness
- Cardiac association in the form of - decreased contractibility, tachycardia, prolonged QT interval, heart failure .
- Usually the symptoms are non-specific and not connected to its severity. Other symptoms include laryngospasm, tachypnoea, cyanosis, apnea and vomiting **(De Marini, S., et al 1997).**

Hypocalcemia of early onset can be treated as follows :

(Nine mg of elemental calcium is obtained from one ml of calcium gluconate (ten percent))

1. Prophylactic for neonates who are at greater risk of hypocalcemia :

- Four ml/kg/day of ten percent calcium gluconate or forty mg/kg/day of elemental calcium
- Treatment should be maintained for three days.

2. Based on screening neonates identified to be having asymptomatic hypocalcemia :

- Eight ml/kg/day of ten percent calcium gluconate or eighty mg/kg/day elemental calcium or for a period of forty eight hours.

- This may be lessened to fifty percent dose for an additional twenty four hours and then it should be stopped.

3. Neonates who were diagnosed to be having symptomatic hypocalcemia:

- This group of neonates should be given a bolus dosage of two ml/kg/dose to be diluted with five percent dextrose in the ratio of 1:1 for a period of ten minutes with strict cardiac surveillance.
- Calcium chloride twenty mg/kg shall be provided by a central line for a time period of ten to thirty minutes in case of severe hypocalcaemia with reduced cardiac functioning.
- This procedure has to be continued with an uninterrupted intravenous infusion of eighty mg/kg/day calcium in elemental form for a period of 48 hours.
- Infusion given continuously is ideal when compared to intravenous bolus doses at the rate of 1 ml/kg/dose every sixth hourly.
- Infusion of calcium should be brought down to fifty percent for the subsequent 24 hours of the original dosage later terminated.
- The infusion possibly can be substituted by managing with calcium orally scheduled the final day.
- All groups of hypocalcemia must be treated for a minimum of seventy two hours. Symptomatic hypocalcemia be supposed to be taken care of with a flow of continuous infusion for 48 hours period.
- Standard calcium levels must have been recognized by forty eight hours prior to stopping the infusion (**Tricia Lacy Gomella).**

Neonatal hypocalcemia - Late onset vareity (LNH)

- This situation is uncommon when compared with early onset neonatal hypocalcemia .
- The condition is frequently symptomatic presenting as convulsions or neonatal tetany **(Bancroft JD1986).**
- This more often appears by the finish around the earliest week of living.

Hypocalcemia - Late Onset type is caused by :

- Hypomagnesemia **(Mimouni F 1994)**
- Increased phosphate load - renal insufficiency, cow milk
- Parathormone resistance -Transient neonatal pseudohypoparathyroidism
- Iatrogenic - Bicarbonate therapy
    - Diuretics (loop diuretics)
    - Citrated blood products
    - Lipid infusions
    - Alkalosis
    - Phototherapy
    - Glucocorticosteriods
    - Phosphate therapy
- Deficiency of vitamin D - Hepatobiliary disease
    - ❖ Renal insufficiency
    - ❖ Malabsorption
    - ❖ Maternal vitamin D deficiency

- Hypoparathyroidism –(i) Primary - parathyroid glands aplasia - (Di George's syndrome), CATCH 22 syndrome (hypocalcaemia with removal of chromosome 22, cardiac anomaly, thymic aplasia, abnormal facies, cleft palate), Hypoplasia.

(ii) Secondary - Maternal hyperparathyroidism

- Metabolic Syndromes - Kenny-caffey syndrome
    - Long-chain fatty acyl CoA dehydrogenase deficiency
    - Kearns-sayre syndrome

Treatment of Late Onset Hypocalcemia :

1. Hypoparathyroidism

Additional supplementation with 1,25(OH)2 Vitamin D3 in the dose of 0.5-1 μg per day and calcium given as fifty mg/kg/day in three divided dosages is given in these neonates.

2. Vitamin D deficiency states:

They do good to as of supplementation of Vitamin D3 in dosage of 30-60 ng per kg per day.

3. Hypomagnesemia:

The infant should be given 2 dosage containing 0.2 ml/kg of fifty percent magnesium sulphate injection, separated by twelve hours deep intra muscularly. Subsequently maintenance dosage with 0.2 ml/kg/day having 50% magnesium sulphate per oral for 3 days.

4. Elevated phosphate load:

- Avoidance of gels which bind with phosphate .
- Exclusive breast-feeding must be promoted and discouragement should be done for feeding with cow's milk.

HYPERCALCEMIA

When ionized calcium increases beyond limit of normal which is 5.4 mg/dl or 1.35 mmol/l in association with or in the absence of an increase in total calcium more than 2.7 mmol per litre or 10.8 mg per dl it is defined as hypercalcemia **(Mimouni F 1994)**.

Hypercalcemia may be caused by :

a) Hyperparathyroidism
b) Secondary hyperparathyroidism
c) Neonatal severe hyperparathyroidism
d) Familial hypocalciuric hypercalcemia
e) Iatrogenic by calcium salts
f) Parathormone related peptide - tumour
g) Vitamin D intoxication
h) Idiopathic infantile hypercalcemia
i) William's syndrome
j) Parathormone receptor mutation – Jansen's metaphyseal chondrodysplasia
k) Subcutaneous fat necrosis
l) Parathyroid related
m) Granulomatous diseases

n) Miscellaneous - Blue-diaper syndrome

- Idiopathic infantile hypercalcemia

-Hypophosphatasia

- medications – hydrochlorothiazide

- Hypophosphatemia

- Vitamin A intoxication

Treatment of hypercalcemia

The therapy has four main goals: **(De Marini, S., et al 1997)**

a) By inhibiting intestinal absorption or resorption of bone

b) Management of the primary cause

c) Dehydration to be corrected

d) Urinary calcium excretion needed to be improved

In conditions existing between moderate and severe hypercalcemia :

- Extracellular fluid compartment increase by150–250 ml per kg per 24 hours intravenously with normal saline would assist to promote excretion of calcium.
- Afterwards infusing furosemide in the rate of 0.5–1.0 mg per kg by intravenous manner each sixth hourly will additionally support calciuresis.
- It is vital to make certain to continue sufficient hydration throughout this therapy.

Specific therapies :

a) Subcutaneous giving calcitonin each sixth hourly at a dosage of four to eight IU per kg and this should be started immediately. This will quickly diminish the serum calcium.

b) In conditions of severe and unalleviated hypercalcemia and when the newborn is hemodynamically stable hemodialysis can be given. Peritoneal dialysis can also be arranged using low-calcium dialysate. Supplemental phosphorous in the oral form or intravenous infusion can be given to neonates who were treated with peritonal dialysis (**Tricia Lacy Gomella) .**

c) Glucocorticoids given in elevated dose will lessen the calcium absorption in the gut and would lower bone resorption. Methylprednisolone (1mg/kg per 24th hourly intravenously), hydrocortisone (1mg/kg intravenously every 6th hourly) or its equivalent is effective.

d) Biphosphonate treatment is made use in children and also for adults in conditions of vitamin D intoxication and parathormone-mediated hypercalcemia.

Therapy given chronically:

A diet which is less in vitamin D and calcium is the basis of management in newborns who need therapy for more days.

MATERIALS AND METHODS

PLACE OF STUDY

In the Paediatric Department this study was being conducted, Government Rajaji Hospital in co-ordination with the Institute of Physiology, Madurai Medical College, Madurai for a period of one year.

COLLABORATION DEPARTMENT

Department of Biochemistry, Madurai Medical College, Madurai.

ETHICAL COMMITTEE

Approval obtained from the ethical committee of Government Rajaji Hospital, Madurai.

STUDY DESIGN

Prospective study

SAMPLE SIZE

This study is done in 50 term neonates in postnatal ward, Government Rajaji Hospital with unconjugated hyperbilirubinemia receiving phototherapy for jaundice.

Control group consists of blood samples of the neonates in which serum electrolytes and bilirubin were measured before the onset of phototherapy.

Study group consists of blood samples of the neonates in which serum electrolytes and bilirubin were measured after 48 hours of phototherapy.

Inclusion criteria :

Term neonates with indirect hyperbilirubinemia which includes

1. Cephalohematoma

2. Physiological jaundice
3. Idiopathic
4. Large for gestational age
5. Breast feeding jaundice
6. External bruising
7. Breast milk jaundice

Exclusion criteria :

1. Neonatal asphyxia.
2. Preterm infants.
3. Infants of diabetic mothers.
4. Infants undergoing exchange transfusion.
5. Direct hyperbilirubinemia.
6. Hemolytic anaemia/ Rh /ABO incompatability
7. Sepsis.
8. Congenital malformations.
9. Respiratory distress.

MATERIALS USED FOR STUDY

1. Proforma – to record the anthropometric measurements and the clinical findings of the subjects.
2. Weighing machine – to record the body weight in kilograms.
3. Inch tape – to measure the height, head circumference in centimeters.

METHODOLOGY:

The study was initiated with the approval of Institutional ethical committee, Madurai Medical College, Madurai and was carried out after explaining the procedures in detail and getting written informed consent from the subject's mother.

The experimental protocol includes

1) **Recording a detailed history** including mode of delivery, intranatal history, immediate postnatal history, maternal history, history of phototherapy in sibling, death of sibling due to hypocalcemia, family history of seizure disorders and congenital anomalies (as given by the subject's mother) .

2) **Measurement of Anthropometric Indices**:

The following were measured:

- **Weight** (in kilograms) was recorded using a standard weighing machine.
- **Height**, Head circumference (in centimeters) were measured using a inch tape.
- Head to foot examination was done. Icterus, skin changes, anaemia, congenital anomalies were noted and documented.

Blood investigations:

The investigations include indirect bilirubin measured by Diazo method, Serum Calcium measured by Arsenazo III method, Serum electrolytes sodium, potassium, chloride, bicarbonate measured by Ion selective electrodes analyser .

Blood specimens were obtained primarily by heel punctures. The minimally dangerous method to collect blood samples of neonate's is the heel puncturing method . Merely micro amount of serum or plasma is needed for several tests by the analyzers used in new clinical laboratories.

In the heparinized capillary tubes small amounts are easily obtained by heel puncture technique. The deepness of heel pricks must not go beyond 2.4 mm and must be done carefully to prevent underlying bone injury.

Estimation of Serum Bilirubin

Method : Diazo method (**Van den Bergh** 1918)

The Principle of the test:

- Bilirubin is changed to azobilirubin molecules when it is treated along diazotized sulfanilic acid otherwise called as Ehrlich's Reagent. There is formation in the acid of red purplish colour; the strength within that colour is interpreted colorimetrically .
- Purple azobilirubins are formed by conjugated as well as unconjugated bilirubins with diazotized acid.
- Unconjugated needs an accelerator or solubiliser like methanol but conjugated bilirubin can respond to aqueous solution 67 which is known as Direct Reaction.

Name of the reagents used :

1. Methanol 2.Diazo reagent : Solution A consisting 15ml of concentrated Hydrochloric acid per litre in addition to 1gram of sulphanilic acid within water. Solution B consisting in per 100ml 0.5gram of sodium nitrite within

water. Make freshly before use blending 10ml of solution A and 0.3ml of solution B.

2. Diazo Blank : fifteen ml of concentrated Hydrochloric acid per litre mixed in water.
3. Bilirubin standard : Ten mg of bilirubin to be dissolved in a smallest amount (about 5ml) of 0.1N solution of sodium, immediately because it is not stable in a solution kept in alkaline medium and build a quantity by human citrated plasma .

- In order to destroy the bilirubin which is present plasma has to be left in sunlight for few hours prior to use. Since methanol might restore plasma needed to make the volume it should be kept ice-covered in little fractions.

The procedure of the test : The test to be carried out after labelling the test-tubes:

The Reagent used	Standard used in test		Total serum Bilirubin		Conjugated bilirubin	
	Standard	Standard control	Total bilirubin	Total bilirubin Control	Conjugated bilirubin	Conjugated bilirubin control
Serum	-	-	0.2 ml	0.2 ml	0.2 ml	0.2 ml
Standard solution10mg/ dl	0.2 ml	0.2 ml	-	-	-	-
Distilled water	1.8 ml	1.8 ml	1.8 ml	1.8 ml	4.3 ml	4.3 ml
Diazo reagent	0.5 ml	-	0.5 ml	-	0.5 ml	-
Diazo blank	-	0.5 ml	-	0.5 ml	-	0.5 ml
Methanol	2.5 ml	2.5 ml	2.5 ml	2.5 ml	-	-

Permit to position in dark for a period of 30 minutes and mix . After 10 minutes interpret absorbance next to 540 nm with usage of distilled water like blank.

Calculated as follows :

Total

bilirubin= $\frac{\text{Total-Total control}}{\text{Standard-Standard control}} \times \text{Amount of standard} \times \frac{100}{\text{Volume of serum}}$

(mg/dl)

Conjugated

bilirubin= $\frac{\text{Conjugated-Conjugated control}}{\text{Standard-Standard control}} \times \text{Amount of standard} \times \frac{100}{\text{Volume of serum}}$

(mg/dl)

Through reducing the level obtained for conjugated bilirubin as of the value of total bilirubin value of unconjugated bilirubin in serum could be obtained.

Bilirubin value in serum in a newborn :

Upto 5 mg / dl is normal .

Estimation of Serum Calcium

Method : Arsenazo III method

The principle for doing the test:

Arsenazo combining with

Alkaline Calcium → Complex of Calcium-Arsenazo

(purplish in colour)

A purplish tinted complex that takes up at 650 nm is formed when calcium act in response with Arsenazo III within a medium that is faintly alkaline. The concentration of calcium is proportionate to the strength of the colour .

Reagents used

Calcium reagent used: Buffer, arsenazo III more than or equal to 0.15mM, surfactant, eight hydroxyquinoline sulfonate five mM .

Procedure which is done

a. Test tubes labelled as “control”, “standard”, “sample”, “reagent blank”.
b. Within every tube pipetting of 1.0 ml reagent is done .
c. Into the relevant tubes 0.010 ml or 10ul of the sample is added. Allow it to stand at the room temperature as a minimum of one minute after being mixed.
d. Along with the reagent blank at a wavelength of 650 nm adjustment of spectrophotometer for zero is done .
e. Absorbances of every test tube is interpretted and documented.

Calculation:

$$\frac{\text{Absorbance made by sample}}{\text{Absorbance made by the standard}} \times \text{Concentration of the Standard} = \text{Calcium in mg per dl}$$

Normal value of serum calcium :

Newborns: 8.5 -10.5 mg/dl

Estimation of Serum Electrolytes

Method : Ion selective electrodes analyser .

Introduction about the method:

- The anions studied are chloride and bicarbonate.
- The major cations of clinical value are sodium along with potassium .
- Sulphate, organic acids, calcium, proteins, magnesium and phosphate are the other electrolytes which are present in serum

An association exists between the principal ions which could be considered after allowance is applied for those ions:-

(sodium ion + potassium ion) – (chloride ion + bicarbonate ion) = 16 ± 2

Apart from conditions in which there is keen and fast variations in the amount of any one of the ions present in the equation given over the correlation is appropriate in many clinical situations and also if foremost modifications take place in the concentration of further ions present in the serum .

- For assessment of electrolytes in laboratory the above mentioned relationship is a suitable confirmation .

- **Principle**

  Two electrodes are used in the analysis.

  - One electrode contains a known concentration of the ion to be measured and is called the reference electrode.
  - The other electrode which is responsive only to the ion being measured, is exposed to the unknown solution.

- The difference between the concentration of the ion in the reference electrode and the ions in the unknown solution causes an electrical potential to develop.
- This potential across the membrane in the electrode is proportional to the difference between the two concentrations.
- A microprocessor converts this voltage into a number representing the concentration of the ion in the unknown solution.

Procedure:

- To determine levels of potassium, sodium, chlorides and bicarbonates particular electrodes are being used.
- Membrane that is ion selective which would divide a solution of identified movement from that of identifying system is needed .
- The membrane contains unique glass substance, plate of crystalline substance otherwise sometimes an organic ion substituter which would saturate a solvent incapable of being mixed with water that is detained in a plastic or gel.
- Changes in concentration of sodium ion are sensed by the sodium electrode and changes in concentration of potassium ion are sensed through the potassium electrode .

Normal values of serum electrolytes :

Potassium : 3.5 – 4.5 mEq / L
Bicarbonate : 22- 28 mEq / L
Chloride : 95 – 105 mEq / L
Sodium : 135 - 145 mEq / L

RESULTS AND OBSERVATION

The electrolyte changes in term neonates receiving phototherapy for jaundice was analysed (serum calcium, sodium, potassium, chloride and bicarbonate) before and after phototherapy using **Paired t test**. By means of **SPSS (Statistical Package for Social Sciences) software version 16,** analysis of statistics was performed**.**

The **statistical significance** was drawn at **'p' value < 0.05.**

TABLE-1

Distribution of neonates according to age in days (N=50)

Age (in days)	**Number**	**Percent (%)**	**Cumulative (%)**
4	7	14	14
5	13	26	40
6	15	30	70
7	15	30	100
Total	50	100.00	

TABLE-2

Distribution of neonates according to gender (N=50)

Gender	Frequency	Percent (%)
MALE	26	52
FEMALE	24	48
TOTAL	50	100

Comments:

Majority of the neonates (52%) were males.

TABLE-3

Descriptive statistics of anthropometric measurements (N=50)

Measures	Weight (kg)	Length (cms)
Mean	3.16	51.18
Standard Deviation	0.405	1.024

TABLE-4

Analytical statistics of Total serum bilirubin before and after phototherapy (N=50)

Measures	Total serum bilirubin (mg/dl)		p value
	Before Phototherapy	**After Phototherapy**	
Mean	14.04	8.13	**0.001 (significant)**
Standard Deviation	0.71	0.40	

When comparing theTotal serum bilirubin before and after Phototherapy it was found that there was statistical significance in the values between them.

Results analysed using **Paired t test** showed a statistically **significant 'p' value.**

TABLE-5

Analytical statistics of serum calcium before and after phototherapy (N=50)

Measures	Serum calcium(mg/dl)		p value
	Before Phototherapy	After Phototherapy	
Mean	9.51	8.13	**0.014 (significant)**
Standard deviation	0.29	0.40	

When comparing the serum calcium before and after phototherapy it was found that there was statistical significance in the values between them.

Results analysed using **Paired t test** showed a statistically **significant 'p' value.**

TABLE-6

Analytical statistics of serum sodium before and after phototherapy (N=50)

Measures	Serum sodium (mEq/L)		p value
	Before Phototherapy	After Phototherapy	
Mean	141.44	140.54	0.312 (not significant)
Standard deviation	1.75	1.59	

When comparing the serum sodium before and after phototherapy it was found that there was statistical insignificance in the values between them. Results analysed using **Paired t test** showed a statistically **insignificant 'p' value.**

TABLE-7

Analytical statistics of serum potassium before and after phototherapy(N=50)

Measures	Serum potassium (mEq/l)		p value
	Before Phototherapy	After Phototherapy	
Mean	4.030	4.020	0.252 (not significant)
Standard Deviation	0.40	0.37	

When comparing the serum potassium before and after phototherapy it was found that there was statistical insignificance in the values between them. Results analysed using **Paired t test** showed a statistically **insignificant 'p' value.**

TABLE-8

Analytical statistics of Serum chloride before and after phototherapy (N=50)

Measures	Serum chloride (mEq/l)		p value
	Before Phototherapy	After Phototherapy	
Mean	99.32	99.28	0.079(not significant)
Standard deviation	3.61	3.32	

When comparing the Serumchloride before and after phototherapy it was found that there was statistical insignificance in the values between them. Results analysed using **Paired t test** showed a statistically **insignificant 'p' value.**

TABLE-9

Analytical statistics of serum bicarbonate before and after phototherapy (N=50)

Measures	Serum bicarbonate (mEq/l)		p value
	Before Phototherapy	After Phototherapy	
Mean	24.76	24.60	0.472 (not significant)
Standard deviation	1.66	1.49	

When comparing the serum bicarbonate before and after phototherapy it was found that there was statistical insignificance in the values between them. Results analysed using **Paired t test** showed a statistically **insignificant 'p' value.**

TABLE-10

Paired Samples Test

	Phototherapy		Paired Differences					T	df	P value Sig. (2-tailed)
						95% Confidence Interval of the Difference				
	Before	After	Mean	Standard Deviation	Standard Error Mean	Lower	Upper			
Pair 1	Bilirubin1	Bilirubin 2	5.9020	0.8294	0.1173	5.6663	6.1377	50.316	49	**0.001**
Pair 2	Calcium1	Calcium 2	1.1320	0.1743	0.0247	1.0825	1.1815	45.921	49	**0.014**
Pair 3	Sodium1	Sodium 2	0.900	1.693	0.239	0.419	1.381	3.758	49	0.312
Pair 4	Potassium1	Potassium 2	0.00800	0.04882	0.00690	-0.00588	0.02188	1.159	49	0.252
Pair 5	Chloride1	Chloride 2	0.740	1.440	0.204	0.331	1.149	3.634	49	0.079
Pair 6	Bicarbonate1	Bicarbonate 2	0.160	0.548	0.078	0.004	0.316	2.064	49	0.472

- Among the **six pairs**, the mean difference in parameters before and after phototherapy is **statistically significant (p value < 0.05)** in only the **Total bilirubin and Serum calcium pairs.**
- Both the Total bilirubin and Serum calcium **tend to decrease** after phototherapy among the neonates.

TABLE-11

Distribution of neonates according to Hypocalcemia (N=50)

Hypocalcemia	Frequency	Percent (%)
PRESENT	30	60
ABSENT	20	40
TOTAL	50	100

Inference:

60% of neonates showed hypocalcemia

DISCUSSION

The general atypical physical finding in the initial week of life is neonatal hyperbilirubinemia **(Stoll and Piazza, 2007).** A widespread method for reasons of medical, social and economic basis is healthy term newborns being discharged much earlier from the hospital subsequent to delivery.

Recent study suggest that neonates who have a post-delivery hospital stay below 72 hours are at a considerably larger risk for readmissions compared to the neonates those whose stay is above 72 hours.

There is concern regarding early discharge of healthy term newborns due to reports of bilirubin induced brain damage resulting in sequelae like kernicterus **(Maisals, 2006).** The need for early detection of hyperbilirubinemia in the early discharged newborns from the hospital is therefore important.

Phototherapy has emerged as the most widely used form of treatment **(Stokowski, 2006).** In order to diminish the rigorousness of neonatal unconjugated hyperbilirubinemia this is the recent therapy of preference **(Bell et al., 2006).**

As any treatment has, phototherapy also has its side effects**(Ehsanipour et al., 2008).** Unlike other side effects a very few studies are currently available that depicts the adverse effects of phototherapy on serum electrolytes.

A few studies in the recent past have stressed on the incidence of hypocalcemia following phototherapy. The differential effect of other electrolytes with phototherapy has not been studied by other workers except that for **Curtis MD et al (1989)**.

The plan of this study was intended to establish the serum electrolyte changes in neonates receiving phototherapy for neonatal jaundice.

In this present study we have estimated the serum electrolytes in 50 jaundiced term neonates before and after phototherapy. We compared the occurrence of phototherapy induced electrolyte changes in them. We conducted the study for a period of one year.

The study was initiated with the approval of Institutional ethical committee and was carried out after explaining the procedures in detail and getting written informed consent from the neonate's mother.

We included neonates with unconjugated hyperbilirubinemia which comprises of Physiological jaundice, Cephalohematoma, Breast feeding jaundice, External bruising, Breast milk jaundice, Large for gestational age. We excluded Neonatal asphyxia, Preterm infants, Infants of diabetic mothers, Infants

undergoing exchange transfusion, Direct hyperbilirubinemia, Hemolytic anaemia/Rh/ABO incompatability, Sepsis, Congenital malformations and Respiratory distress.

The first table of our study depicts the distribution of neonates according to chronological age. Most of the neonates were 6 and 7 days which is similar to **Taheri PA et al** (2013).The second table shows the gender distribution in which 52% are male.

In the third table anthropometric measurements including weight and length are shown. The mean ± SD weight of the 50 term neonates is 3.16 ± 0.405 kg. The mean ± SD length is 51.18 ± 1.024 cms.

The mean ± SD of total serum bilirubin before phototherapy was 14.04 ± 0.71 mg / dl and after phototherapy was 8.13 ± 0.40 mg / dl. Results analysed using paired t test shows a statistically significant p value.

The mean ± SD of serum calcium before phototherapy was 9.51 ± 0.29mg / dl and after phototherapy it was 8.13 ± 0.40 mg / dl. Levels of serum calcium decreased significantly after phototherapy when compare to values before phototherapy with p value 0.014.

Romagnoli et al in1979 noticed the the relationship in preterm newborns of phototherapy and hypocalcemia. Likewise **Bergstromand Hakanson in** 1981

experimented in newborn rat the same findings. **Odell and Gutcher in** 1983 suggested considerable reduction in levels of serum calcium in rats which were newborn subsequent to keeping them in fluorescent daylight.

Eghbalian et al (2008) in his study found that serum calcium levels declined considerably after neonates with hyperbilirubinemia treated with phototherapy.

There are some studies in the past to observe the hypocalcaemic effect of phototherapy in jaundiced newborn babies which were done by **Bergstrom andHakanson in** 1981,**Tan** in1991, **Sethi** et al, in 1993.

Calcium is essential for several biochemical activities like enzymatic and secretory activity in the cell, coagulation of blood, integrity and function of cell membrane and also excitability of neuromuscular system.

There is a enhanced permeability for sodium ions by the cell and augmented excitabilityof the cell membrane in hypocalcaemia. Hyperreflexia, apnea, seizure, stridor or laryngospasm, increase in extensor tone, jitterness and clonus are general signs which may be non-specific.

Sethi et al in 1990 proposed that after phototherapy 75% of term neonates begin to build up hypocalcaemia. In the same way **Medhat** in 2006 belonging to Cairo University suggested development of hypocalcaemia in 75% of term neonates after phototherapy.

Sourabh dutta (2001) in his study concluded that 75% of fullterm neonates with unconjugated hyperbilirubinemia developed hypocalcemia after phototherapy.

A significant drop in level of calcium was observed after phototherapy among 66.6% of the term neonates which was noted by **Yadav RK and Rajesh KY** in 2011.

Taheri PA et al (2013) in his study found decrease in serum calcium level in 56% babies after 48 hours of phototherapy. **Arora S et al** (2014) in her study found hypocalcemia in 56% of term neonates after 48 hours of phototherapy.

In our study 60% of term neonates developed decrease in serum calcium levels 48 hours after phototherapy. Findings in the present study are in concurrence with the studies mentioned above.

In 1998 **Jain et al** in his study suggested among fullterm neonates with hyperbilirubinemia 30% developed hypocalcemia after 48 hours of phototherapy. **Karamifar et al** (2002) in his study found that prevalance of hypocalcemia was 8.7% in fullterm neonates after 48 hours of phototherapy for hyperbilirubinemia. The observations of both the studies are much lesser when compared to the studies mentioned above**.**

Hunter and Hakinson in 2004 formulated that secretion of melatonin by pineal gland gets inhibited by phototherapy. So effect of corticosterone on bone calcium becomes inhibite. During phototherapy level of corticosterone in serum decreases due to decrease in melatonin. Thus decreased corticosterone has a effect which causes hypocalcemia by a reduction of bone resorption .

Kim (2001)in his study showed of hypocalcemia was caused due to a reduction in parathormone secretion in jaundiced neonates who were treated with phototherapy.

In **Hooman's** study (2005) the significantly higher level of urinary calcium excretion was proposed to be the cause of hypocalcemia in phototherapy treated jaundiced neonates .

Curtis et al (1989) studied diarrhoea in neonates with jaundice who were treated under phototherapy. Drastical reduction in the uptake of potassium, chloride and sodium was shown in the study among neonates who received phototherapy jaundice.

Dee Beresford and Glenys Conolly in the book Neonatal Intensive Care Nursing states that babies under phototherapy can have sodium imbalances due to insufficient fluid replacements.

In our study tables 6 – 9 depicts the analysis among levels of serum bicarbonate, sodium, chloride and potassium in jaundiced neonates before and after phototherapy.

The present study shows no noteworthy alteration in the values of serum bicarbonate, sodium, chloride and potassium in jaundiced neonates after phototherapy which is in contrary to the work of **Curtis et al**.

Table 10 shows the significant decrease in bilirubin and serum calcium in the neonates following phototherapy. Out of the total term neonates who received phototherapy 60% of the neonates developed hypocalcemia .

CONCLUSION

Substantial reduction in the level serum calcium was seen in newborns with icterus which was induced by phototherapy were the observations of current study. There was no signs and symptoms suggestive of hypocalcemia which may present like convulsions, cyanosis and apnea due to diminished calcium in the neonates who received phototherapy.

Proper monitoring of electrolytes after phototherapy in the neonates can prevent dyselectrolytemia and its associated complications. In the newborns who were treated with phototherapy level of calcium need to be measured and should be treated accordingly.

Phototherapy induced hypocalcemia was well evident in our study and although the signs were not remarkable the reduction might proceed to the formation of threshold needed for producing hypocalcemia .

Hence we strongly suggest assessment of serum calcium, sodium, potassium, chloride, bicarbonate along with routine measurement of serum bilirubin in neonates before and after phototherapy. Thus by regular monitoring and maintaining normal serum electrolyte levels we can avoid the development of complications in icteric neonates receiving phototherapy.

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PROFORMA

Name: Age in days: Sex:

Duration of phototherapy:

H/o present complaints:

H/o yellowish discoloration of body
H/o passing high coloured urine
H/o diarrhea, scanty urine
H/o convulsions
H/o skin rashes
H/o irritability
H/o jitteriness

Mode of delivery: Normal vaginal/LSCS/Forceps

Intra natal history:

H/o prolonged labour
H/o meconium aspiration

Immediate Post natal history

H/o prelacteal feed
H/o Jaundice at the time of birth
H/o NICU Admission
Breast feeding: Time of initiation

Maternal history:

H/o consanguinous marriage
H/o Abortions
H/o still birth, Intra uterine death

Past history:

H/o phototherapy in sibling
H/o death of sibling due to hypocalcaemia

Family history:

H/o seizure disorder
H/o congenital anomalies

General examination

Length(cm): Weight(kg): Headcircumference(cm):

Head to foot examination

Icterus Skin changes

Anaemia Congenital anamolies

Systemic examination

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

ABDOMEN

CENTRAL NERVOUS SYSTEM

Investigations:

Haemoglobin(g/dl): Blood grouping, Rh typing:

Blood sugar(mg/dl):

Serum bilirubin-Total(mg/dl):

- Direct(mg/dl):

- Indirect(mg/dl):

Serum calcium(mg/dl):

Serum sodium(mEq/L):

Serum potassium(mEq/L):

Serum chloride(mEq/L):

Serum bicarbonate(mEq/L):

Ultrasound Abdomen

நோயாளி தகவல் மற்றும் ஒப்புதல் படிவம்

இணைப்பு – 3

ஆய்விடத் தகவல் மற்றும் தொடர்பு விவரங்கள்

மஞ்சள் காமாலையிற்காக ஒளிக்கதிர் சிகிச்சை பெறும் நிறைமாத பச்சிளம் குழந்தைகளின் இரத்தத்தின் நீர்த்த பகுதியில் உள்ள மின்பகு கொருள் மாறுதல்களை பற்றிய ஆய்வு.

இந்தப் பக்கத்தை கையொப்பமிடுவதன் மூலமாக, பின்வருவனவற்றை நான் உறுதி செய்கிறேன்.

- மேற்படி ஆய்விற்கான ஜனவரி 2015 தேதியிடப்பட்ட இந்த நோயாளித் தகவல் மற்றும் ஒப்புதல் படிவத்திலுள்ள அனைத்துத் தகவல்களையும் நான் படித்துப் பரிந்து கொண்டிருக்கிறேன் எனவும், அதைப் பற்றி சிந்திக்க எனக்கு கால அவகாசம் இருந்தது எனவும் நான் உறுதியளிக்கிறேன்.
- கேள்விகள் கேட்பதற்கான வாய்ப்பு எனக்கு இருந்தது. மேலும் எனது கேள்விகள் அனைத்தும் எனது திருப்திக்குத் தக்கவாறு பதிலளிக்கப்பட்டிருக்கின்றன.
- இந்த ஆய்வில் என் குழந்தையின் பங்கேற்பு என் தன்னார்வம் சார்ந்தது எனவும், பங்கேற்பை எப்போது வேண்டுமானாலும் எவ்விதக் காரணமும் அளிக்காமல், என் குழந்தையின் மருத்து கவனிப்பு அல்லது சட்ட உரிமைகள் பாதிக்கப்படாமல் விலக்கிக் கொள்ள நான் சுதந்திரமானவர் என்பதை நான் புரிந்து கொள்கிறேன்.
- வேண்டிக் கொள்ளப்பட்டப்படி, ஆய்வு நடைமுறைகளை பின்பற்றவும், மற்றும் மருத்துவர், செவிலிகள், அல்லது மற்ற ஊழிய உறுப்பினர்களுக்கு தேவையான தகவல்களை வழங்கவும் நான் தன்னார்வத்துடன் ஒப்புக் கொள்கிறேன்.

- மருத்துவ சோதனையின் நிதியுதவியளிக்கும் நிறுவனம், நிதியுதவியளிக்கும் நிறுவனத்தின் சார்பில் பணியாற்றும் மற்றவர்கள், நன்னெறிகள் குழு மற்றும் ஒழுங்கு முறை அதிகாரிகள் ஆகியோருக்கு, தற்போதைய ஆய்வு சம்பந்தமாகவும் தரவு பாதுகாப்பு அறிக்கையில் குறிப்பிட்டப்படியும், எனது குழந்தையின் ஆரோக்கியப் பதிவேடுகளைப் பார்வையிடுவதற்கு எனது அனுமதி தேவைப்படாது என்பதை நான் புரிந்து கொள்கிறேன். இந்த அணுகலுக்கு நான் ஒப்புக் கொள்கிறேன். இருந்தாலும், மூன்றாம் நபர்களுக்கு வெளியிடப்படும் அல்லது பிரசுரிக்கப்படம் எந்தவொரு தகவல்களிலும் எனது குழந்தையின் அடையாளமானது வெளிப்படுத்தப்படாது என்பதை நான் புரிந்து கொள்கிறேன்.
- இந்த ஆய்விலிருந்து எழும் எந்தவொரு தரவு அல்லது முடிவுகளின் உபயோகத்தினையும், இது போன்ற உபயோகமானது தரவு பாதுகாப்பு அறிக்கையில் குறிப்பிட்டப்படி மட்டுமாக உபயோகிக்கப்படும் பட்சத்தில் அவைகளைத் தடுக்காமலிருக்க நான் ஒப்புக் கொள்கிறேன்.

  மேற்கண்ட ஆய்வில் என் குழந்தை பங்கெடுக்க நான் ஒப்புக் கொள்கிறேன்.
- எனக்காக வைத்துக் கொள்வதற்காக இந்த நோயாளி தகவல் மற்றும் ஒப்புதல் படிவத்தின் ஓர் நகலை நான் பெற்றுக் கொண்டிருக்கிறேன்.

நோயாளி/சட்டப்பூர்வமாக ஏற்றுக் கொள்ளக்கூடிய பிரதிநிதியின் (எல் ஏ ஆர்) கையொப்பம்

தேதி

(அல்லது நோயாளி அல்லாதவரானால், தாமாகவே பாகுபாடற்ற சாட்சியின் முன்னிலையில் நோயாளி வாய்மூலமாக ஒப்புதல் கொடுத்திருக்கிறார் என்பதை குறிப்பதற்காக பெருவிரல் ரேகை

(நோயாளி/எல்ஏஆர்) தேதியிட வேண்டும்)

ABBREVIATIONS

UDPGT - URIDINE DIPHOSPHATE GLUCURONYL TRANSFERASE

DAT - DIRECT ANTIGLOBIN TEST

ETCO - END -TIDAL CARBON MONOXIDE IN BREATH

LED - LIGHT EMITTING DIODE

NICU - NEONATAL INTENSIVE CARE UNIT

PDA - PATENT DUCTUS ARTERIOSUS

AAP - AMERICAN ACADEMY OF PAEDIATRICS

NICE - NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

ENH - EARLY ONSET NEONATAL HYPOCALCEMIA

LNH - LATE ONSET NEONATAL HYPOCALCEMIA

SBR - SERUM BILIRUBIN

MASTER CHART-BEFORE PHOTOTHERAPY

S.No	Name	Age in days	Gender	Weight (kg)	Length (cms)	Total bilirubin (mg/dl)	Serum Calcium (mg/dl)	Serum Sodium (mEq/l)	Serum Potasium (mEq/l)	Serum Chloride (mEq/l)	Serum Bicarbonate (mEq/l)
1	B/o Jeyanthy	2	F	2.6	52.2	13.1	9.1	139	3.9	95.3	23.66
2	B/o Deepa	3	M	3.1	50.6	14.5	9.56	139.44	4.6	99.66	26.54
3	B/o Lakshmi	4	F	3.8	51.1	13.9	9.66	141.3	4.2	100.99	22.99
4	B/o Jyothy	3	M	2.7	52.1	13.2	9.33	143.6	3.6	96.55	27.65
5	B/oThamarai	5	M	3.5	52	14.2	9.65	143.66	4.6	104.66	25.65
6	B/oKalavathy	5	M	3.6	51.6	13.6	9.8	143.88	4	95	24.86
7	B/oMaharani	3	F	3.6	52.6	13.6	9.4	142.66	4.4	99.56	24.42
8	B/o Seetha	4	M	3.4	51	14	9.1	139	3.8	97.58	25.88
9	B/o Gowri	2	F	3.5	52.7	14.1	9.56	141.66	3.6	95.66	25.91
10	B/o Sathya	3	M	2.6	50	13.5	9.66	142.3	3	99.66	27.94
11	B/o Jeya	2	F	2.9	51.1	13.6	9.33	143.99	4.4	100.99	23.54
12	B/o Vimala	3	M	2.7	51.5	13.5	9.65	142.99	3.7	96.55	22
13	B/o Rajathy	4	F	3.4	50.2	13.1	9.8	139.55	4.7	94	23.58
14	B/o Vinoda	5	M	3.2	50	14.5	9.4	143	3.9	104.88	23.66
15	B/o Selvi	3	F	3.4	51	13.9	9.55	140.66	4.6	99.56	26.54
16	B/o Nagajothi	5	M	3.4	51	14.2	9.15	140.58	4.2	97.58	22.99
17	B/o Karthika	5	F	3.6	50.2	14.6	9.88	140.99	3.6	96.55	27.65
18	B/o Abirami	5	M	3.4	52	14.6	9.95	140.59	4.6	104.66	25.65
19	B/o Mareeshwari	4	F	2.7	52.4	13.6	9.22	139	4	104.88	24.86

20	B/o Sakeela	5	M	3.5	52.3	14.9	9.33	139.44	4.4	99.56	24.42
21	B/o Saranya	2	F	3.6	51	14.1	9.43	141.3	3.8	97.58	25.88
22	B/o Rajalakshmi	3	M	2.9	52.7	13.5	9.41	143.6	3.6	95.66	25.91
23	B/o Valarmathi	4	F	3.4	50.2	13.9	9.6	143.66	3	99.66	27.94
24	B/o Durgaiyammal	5	M	3.5	51.1	13.5	9.4	143.88	4.4	100.99	23.54
25	B/o Sakthi	5	F	2.6	51.5	14.3	9.77	142.66	3.7	96.55	27.64
26	B/o Vimala	3	M	2.9	51.6	14.9	9.95	139	4.7	104.66	23.58
27	B/o Indhira	4	F	2.7	51	14.1	9.55	141.66	4.7	104.66	23.66
28	B/o Nithya	5	M	3.4	50.4	13.5	9.1	142.3	3.9	104.88	26.54
29	B/o Senthamilselvi	3	F	3.2	51.6	13.9	9.5	143.99	4.6	99.56	22.4
30	B/o Saranya	4	M	3.6	50.6	13.5	9.66	142.99	4.2	97.58	22.4
31	B/o Indhu preetha	5	F	3.4	50.8	13.1	9.22	139.55	3.6	96.55	25.65
32	B/o Sengeshwari	2	M	3.5	50.3	14.5	9.84	139	4.6	104.66	24.86
33	B/o Vijayalakshmi	3	F	3.5	52	13.9	9.67	140.66	4	104.88	24.42
34	B/o Renuka	4	M	3.6	50.6	14.2	9.64	140.58	4.4	99.56	25.88
35	B/o Rani	5	F	2.9	50.3	14.6	9.7	141.66	3.8	97.58	25.91
36	B/o Selva meena	3	M	3.4	51.8	14.6	9.5	142	3.6	95.66	22.4
37	B/o Sasikala	4	F	3.5	50.2	13.6	9.6	142.6	3	103.5	23.54
38	B/o Rajeswari	4	M	2.6	52	14.9	9.21	141.66	4.4	96.55	23.8
39	B/o Lakshmi	2	F	3.6	52	14.2	9.65	142.3	3.7	104.66	22.99
40	B/o Chithradevi	4	M	3.2	51	13.9	9.2	143.99	4.7	104.88	22.3
41	B/o Mahalakshmi	2	F	3.4	50.8	13.5	9.33	142.99	4.6	99.56	25.65

42	B/o Jansi	4	M	3.2	50.1	14.5	9.22	142	4	97.58	24.86
43	B/o Santhi devi	4	F	3.5	50.6	14.5	9.84	139	4.4	95.66	25.3
44	B/o Ambiga	3	M	2.5	52	13.9	9.1	141	3.8	94.6	22.58
45	B/o Sri devi	5	F	2.9	50.3	14.2	9.62	139	3.6	94.66	22.8
46	B/o Rekha	5	M	2.7	52	14.6	9.52	141	3	103.6	23.5
47	B/o Latha	4	F	2.5	52	14	9.1	139	4.4	94	23.54
48	B/o Sangeetha	5	M	2.8	50.4	14.8	9.9	143	3.7	94.6	27.65
49	B/o Suganya	3	F	2.6	50	14.9	9.64	139	4.7	94.66	25.65
50	B/o Soniya	4	M	2.5	50	14.2	9.7	141	3.5	103.6	24.86

AFTER PHOTOTHERAPY											
S. No.	Name	Age in days	Gender	Weight (Kgs)	Length (cms)	Total bilirubin (mg/dl)	Serum calcium (mg/dl)	Serum Sodium (mEq/l)	Serum Potasium (mEq/l)	Serum Chloride (mEq/l)	Serum Bicarbonate (mEq/l)
1	B/o Jeyanthy	4	F	2.6	52.2	7.9	7.9	139	3.9	95.3	23.6
2	B/o Deepa	5	M	3.1	50.6	7.9	8.4	139.44	4.2	99.66	26.5
3	B/o Lakshmi	6	F	3.8	51.1	8.5	8.6	141.3	3.6	100.99	22.9
4	B/o Jyothy	5	M	2.7	52.1	8.6	7.9	143.6	4.6	96.55	27.6
5	B/oThamarai	7	M	3.5	52	7.8	7.9	138	3.4	104.66	25.6
6	B/oKalavathy	7	M	3.6	51.6	8.6	7.8	138.7	4.2	95	24.8
7	B/oMaharani	5	F	3.6	52.6	8.2	8.2	142.66	4.5	99.56	24.4
8	B/o Seetha	6	M	3.4	51	8.4	8.4	139	3.6	97.58	25.8
9	B/o Gowri	4	F	3.5	52.7	7.7	8.4	138.9	4.4	95.66	25.9
10	B/o Sathya	5	M	2.6	50	8.4	8.6	142.3	3.9	99.66	27.9
11	B/o Jeya	4	F	2.9	51.1	7.9	8.1	138	3.9	100.99	23.5
12	B/o Vimala	5	M	2.7	51.5	7.9	7.9	142.99	4.2	96.55	22
13	B/o Rajathy	6	F	3.4	50.2	8.5	7.9	139.55	3.6	94	23.5
14	B/o Vinoda	7	M	3.2	50	8.6	8.7	143	4.6	103.88	23.6
15	B/o Selvi	5	F	3.4	51	7.8	8.6	140.66	3.4	99.56	26.5
16	B/o Nagajothi	7	M	3.4	51	8.6	8.5	140.58	4.2	97.58	22.9

17	B/o Karthika	7	F	3.6	50.2	8.2	7.9	140.99	4.5	96.55	27.6
18	B/o Abirami	7	M	3.4	52	8.4	8.7	140.59	3.6	104.66	25.6
19	B/o Mareeshwari	6	F	2.7	52.4	7.6	8.2	139	3.9	94.5	24.8
20	B/o Sakeela	7	M	3.5	52.3	8.6	7.9	139.44	4.2	99.56	24.4
21	B/o Saranya	4	F	3.6	51	8.2	8.4	141.3	3.6	97.58	25.8
22	B/o Rajalakshmi	5	M	2.9	52.7	8.4	8.6	138.6	4.6	95.66	25.9
23	B/o Valarmathi	6	F	3.4	50.2	7.6	8.1	142.5	3.4	99.66	27.9
24	B/o Durgaiyammal	7	M	3.5	51.1	8.4	7.9	138.6	4.2	100.99	23.5
25	B/o Sakthi	7	F	2.6	51.5	7.9	8.8	142.66	4.5	96.55	27.6
26	B/o Vimala	5	M	2.9	51.6	8.8	8.7	139	3.6	94.5	23.5
27	B/o Indhira	6	F	2.7	51	8.5	8.6	141.66	4.4	104.66	23.6
28	B/o Nithya	7	M	3.4	50.4	7.7	8.7	142.3	3.9	102.88	26.5
29	B/o Senthamilselvi	5	F	3.2	51.6	7.8	8.6	143.99	3.9	99.56	22.4
30	B/o Saranya	6	M	3.6	50.6	8.6	8.6	140.3	4.2	97.58	22.4
31	B/o Indhu preetha	7	F	3.4	50.8	8.2	8.2	139.55	3.6	96.55	25.2
32	B/o Sengeshwari	4	M	3.5	50.3	8.4	8.8	139	4.6	104.66	24.2
33	B/o Vijayalakshmi	5	F	3.5	52	7.6	8.4	140.66	3.4	102.8	24.4
34	B/o Renuka	6	M	3.6	50.6	8.2	8.6	139.5	4.2	99.5	25.2
35	B/o Rani	7	F	2.9	50.3	8.4	8.6	140.2	4.5	97.5	25.9
36	B/o Selva meena	5	M	3.4	51.8	7.6	8.6	138.6	4.2	95.6	22.4

37	B/o Sasikala	6	F	3.5	50.2	7.8	7.9	142.6	4.5	103.5	23.5
38	B/o Rajeswari	6	M	2.6	52	7.9	8.7	141.66	3.6	96.55	23.8
39	B/o Lakshmi	4	F	3.6	52	7.9	8.6	142.3	4.4	104.66	22.9
40	B/o Chithradevi	6	M	3.2	51	8.5	8.8	138	3.9	102.88	22.3
41	B/o Mahalakshmi	4	F	3.4	50.8	8.6	7.9	138.7	3.9	99.5	25.6
42	B/o Jansi	6	M	3.2	50.1	7.8	8.4	143.6	4.2	97.5	24.8
43	B/o Santhi devi	6	F	3.5	50.6	7.8	8.6	139	3.6	95.6	25.3
44	B/o Ambiga	5	M	2.5	52	7.9	8.1	143.5	4.6	94.6	22.5
45	B/o Sri devi	7	F	2.9	50.3	7.9	7.9	138.2	3.4	94.6	22.3
46	B/o Rekha	7	M	2.7	52	7.5	8.8	139	4.2	102.1	23.5
47	B/o Latha	6	F	2.5	52	8.6	8.7	139	4.5	94	23.54
48	B/o Sangeetha	7	M	2.8	50.4	7.8	8.6	143	3.2	94.6	27.6
49	B/o Suganya	5	F	2.6	50	8.5	8.4	141.5	4.6	94.1	25.2
50	B/o Soniya	6	M	2.5	50	7.8	8.7	141	3.4	95.6	24.8

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

ETHICS COMMITTEE

CERTIFICATE

Name of the Candidate	:	Dr.M.USHA RANI
Course	:	PG in MD., PHYSIOLOGY
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	**STUDY OF ELECTROLYTE CHANGES IN TERM NEONATES RECEIVING PHOTOTHERAPY FOR JAUNDICE**

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary

Dean / Convenor

Dean
Madurai Medical College
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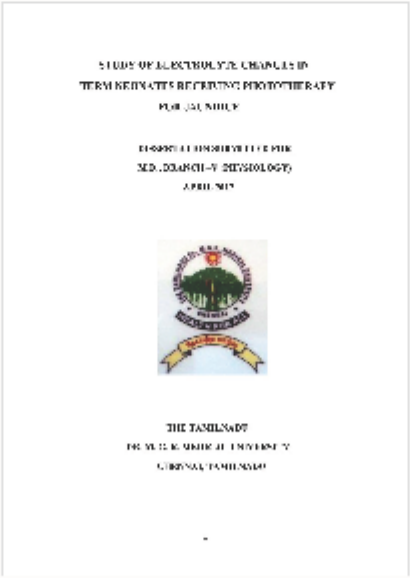


STUDY OF ELECTROLYTE CHANGES IN
TERM NEONATES RECEIVING PHOTOTHERAPY

DISSERTATION SUBMITTED FOR
M.D. (BRANCH – V PHYSIOLOGY)
APRIL 2017

THE TAMILNADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

TERM NEONATES RECEIVING PHOTOTHERAPY

FOR JAUNDICE

DISSERTATION SUBMITTED FOR

M.D., BRANCH –V (PHYSIOLOGY)

APRIL 2017

THE TAMILNADU

DR. M. G. R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

FIGURE - 1

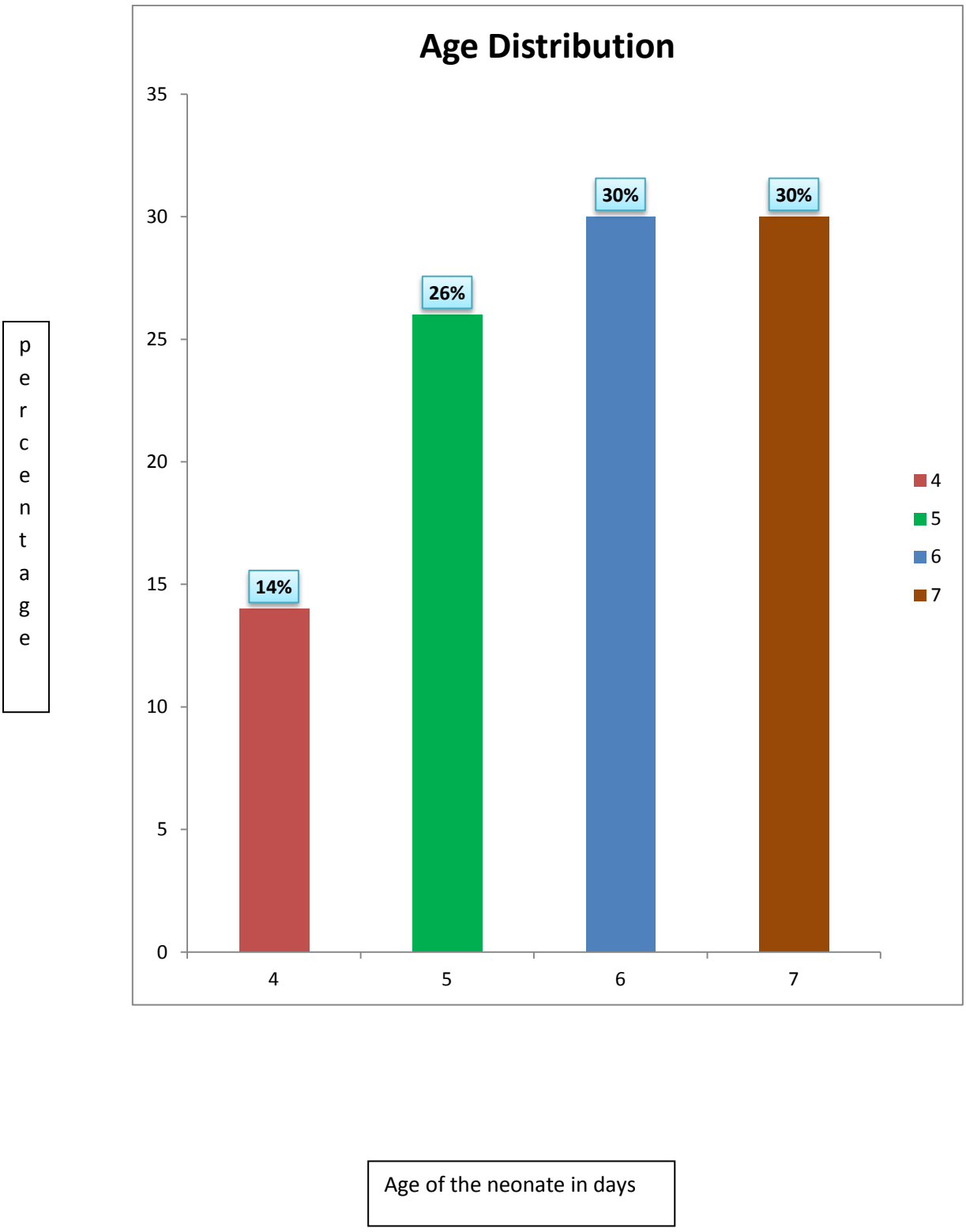

Age Distribution
35
30
25
20
15
10
5
0
14%
26%
30%
30%
4
5
6
7
percentage
Age of the neonate in days

FIGURE - 2

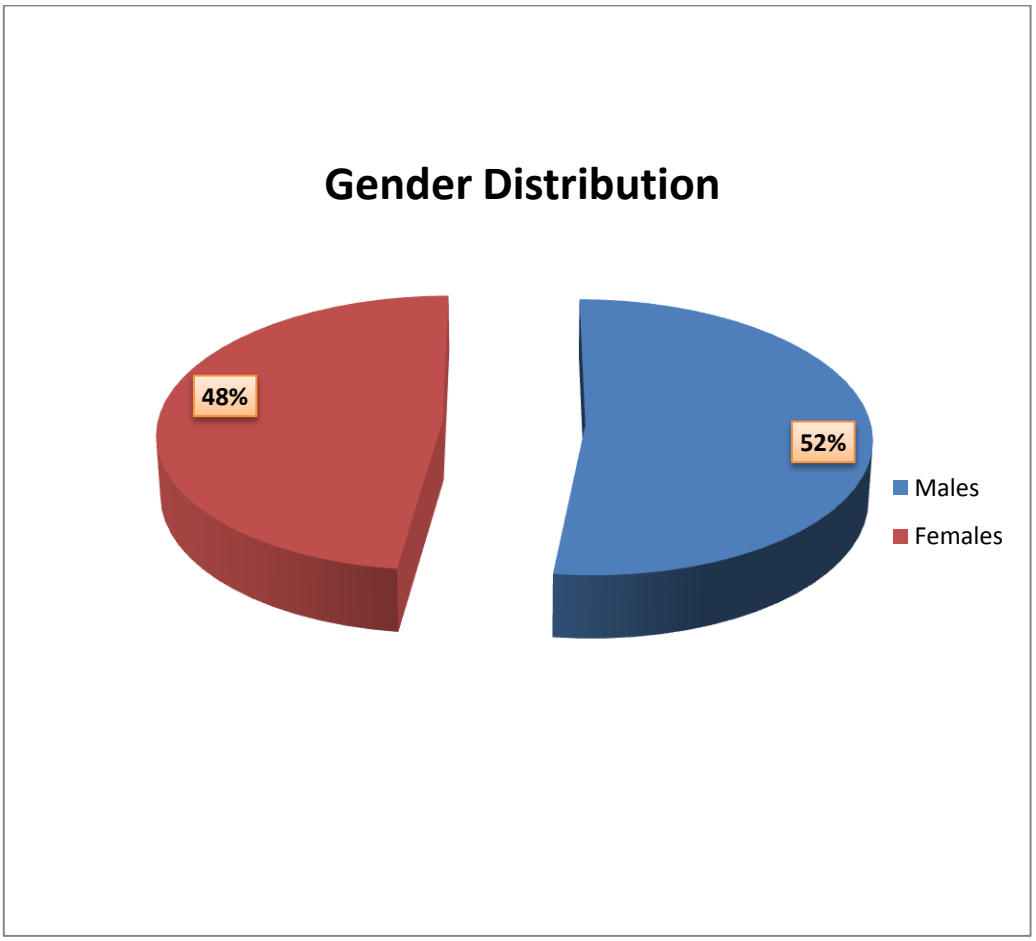


FIGURE - 3

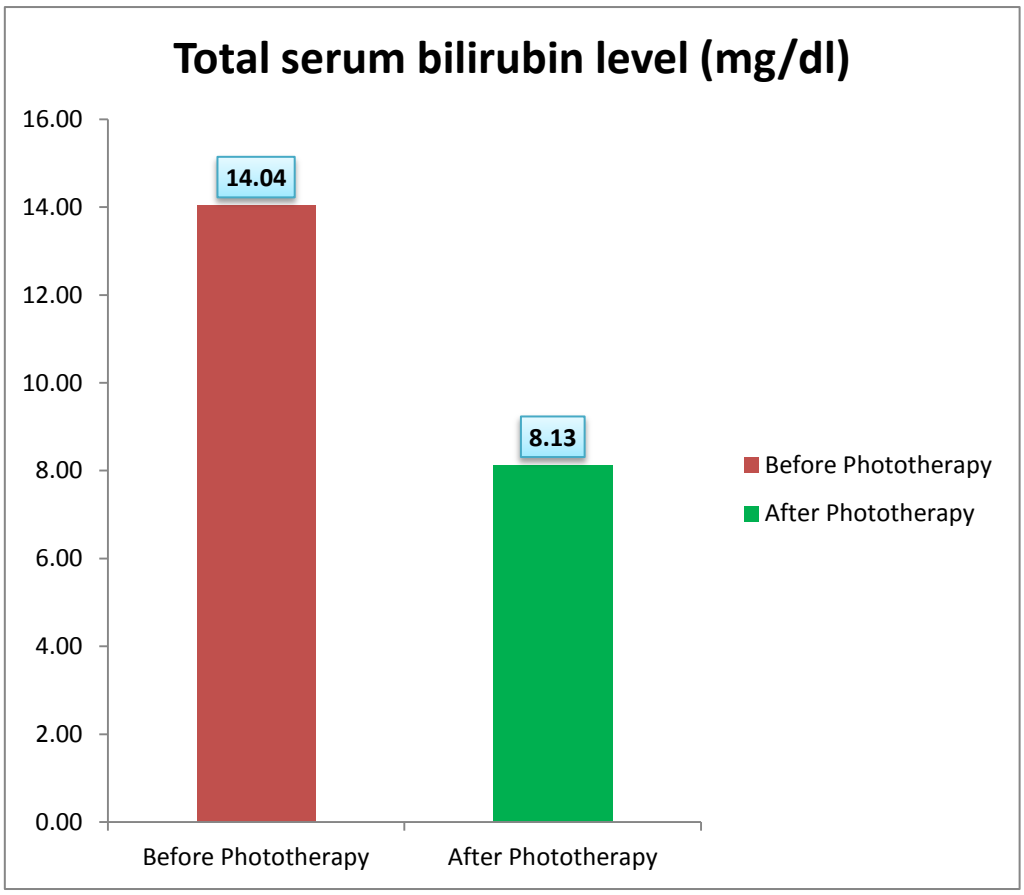

Total serum bilirubin level (mg/dl)
16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
14.04
8.13
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE - 4

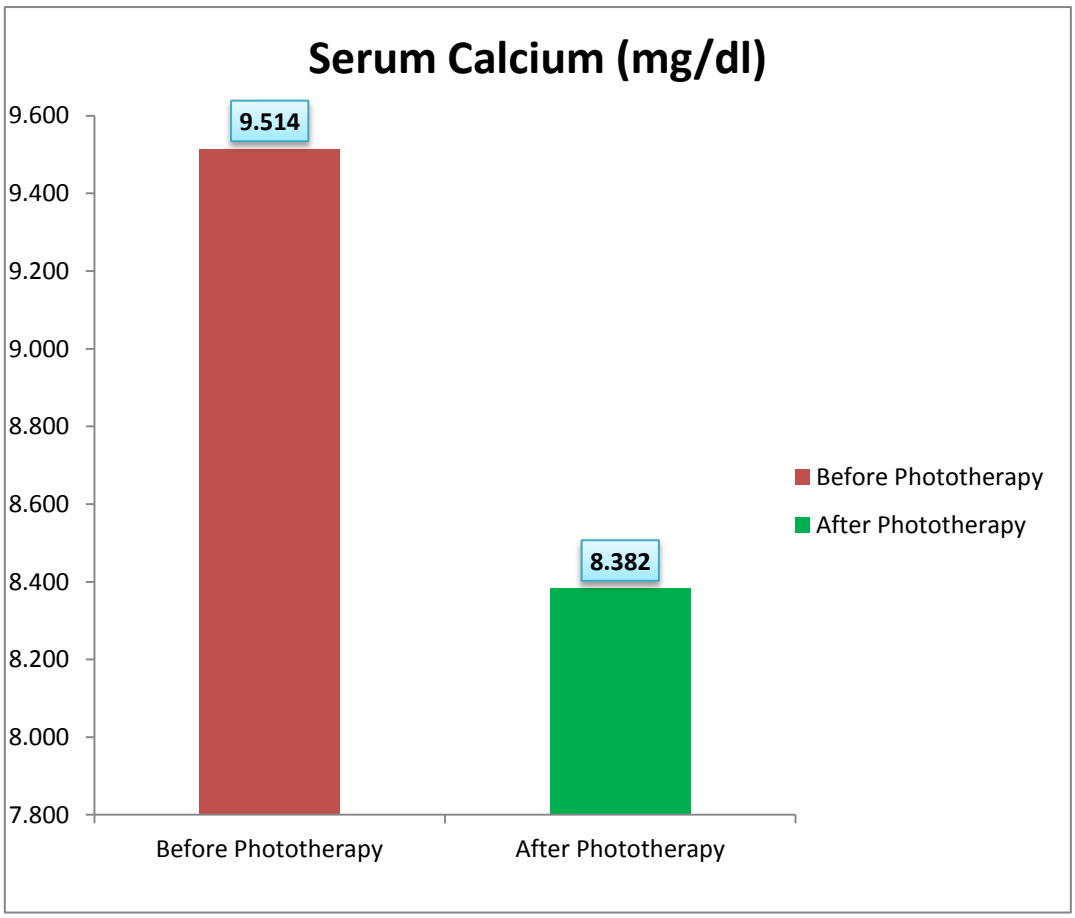

Serum Calcium (mg/dl)
9.600
9.400
9.200
9.000
8.800
8.600
8.400
8.200
8.000
7.800
9.514
8.382
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE-5

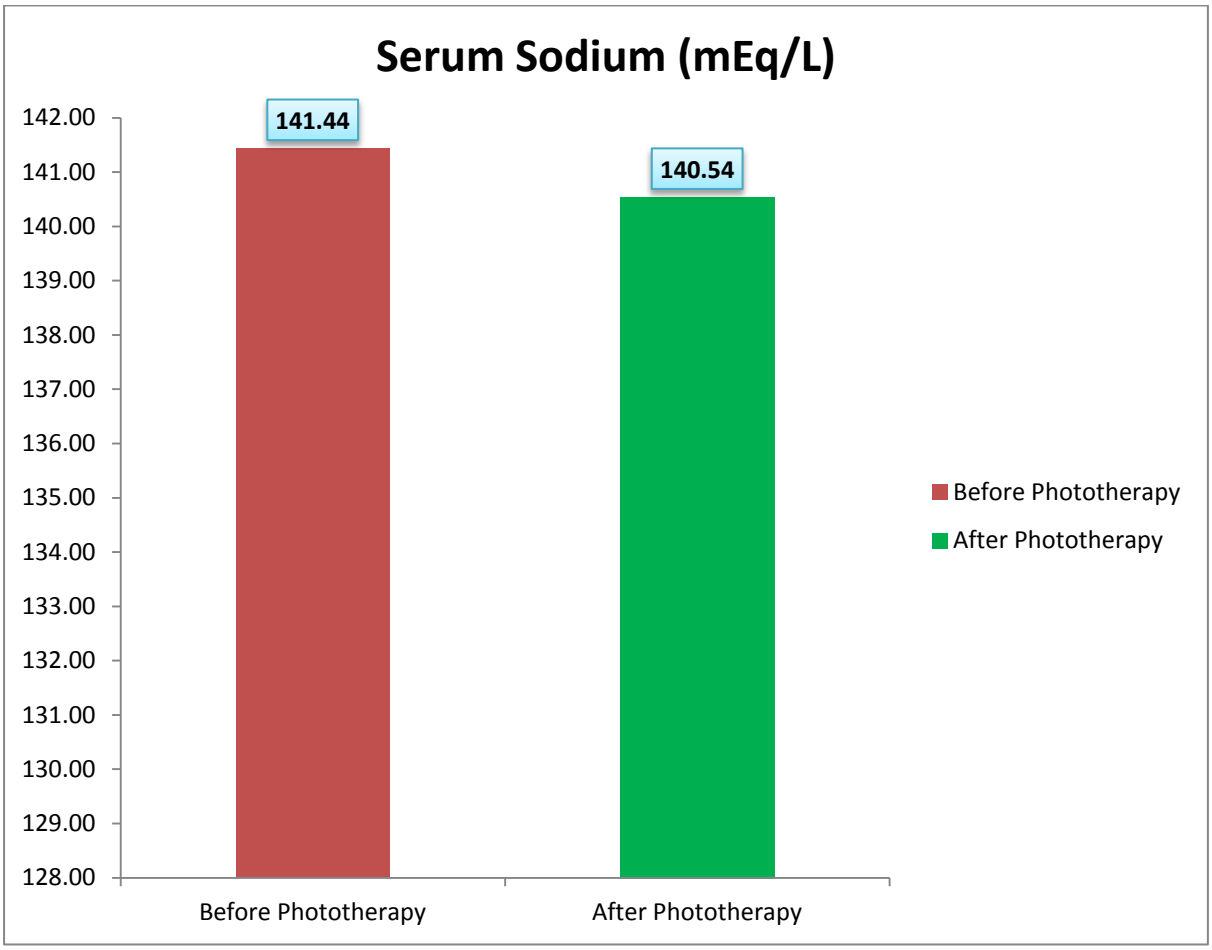

Serum Sodium (mEq/L)
142.00
141.00
140.00
139.00
138.00
137.00
136.00
135.00
134.00
133.00
132.00
131.00
130.00
129.00
128.00
141.44
140.54
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE - 6

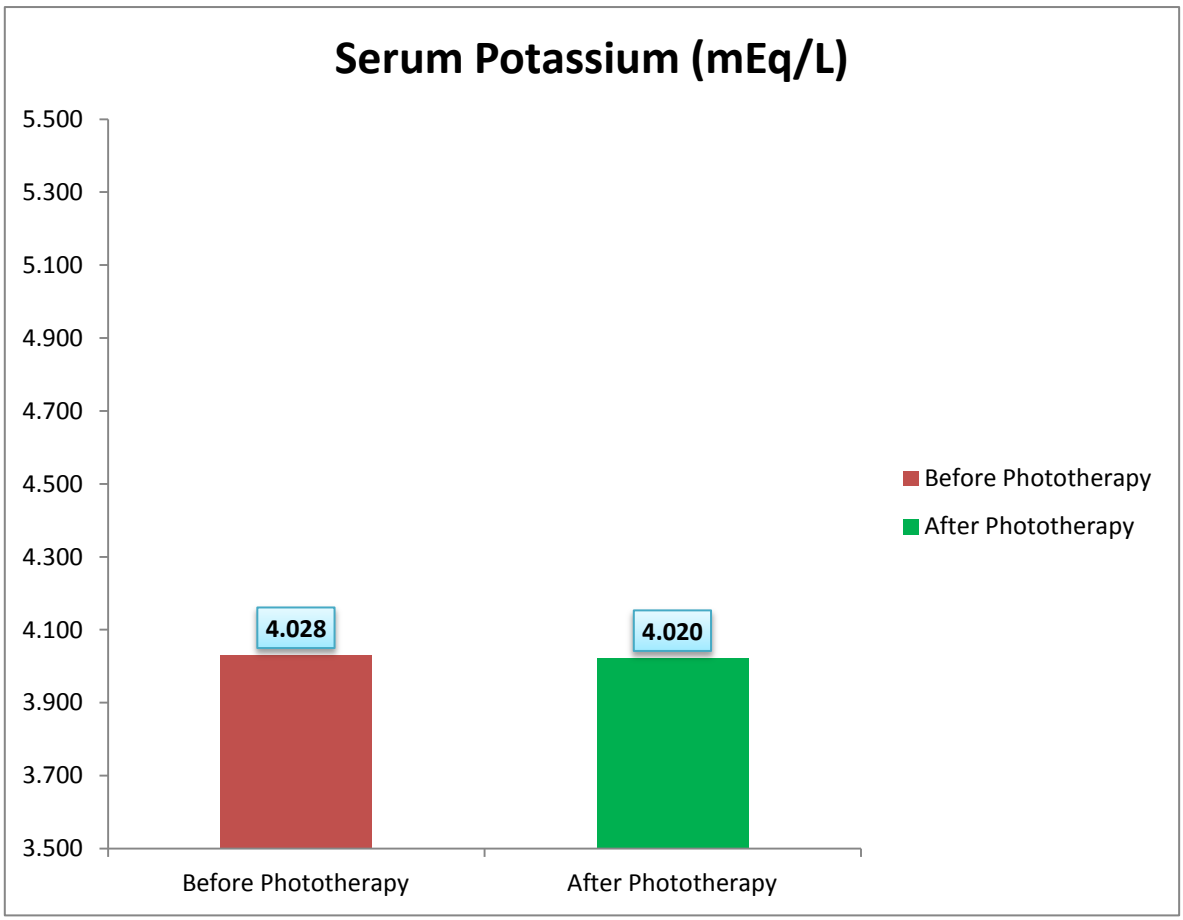

Serum Potassium (mEq/L)
5.500
5.300
5.100
4.900
4.700
4.500
4.300
4.100
3.900
3.700
3.500
4.028
4.020
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE - 7

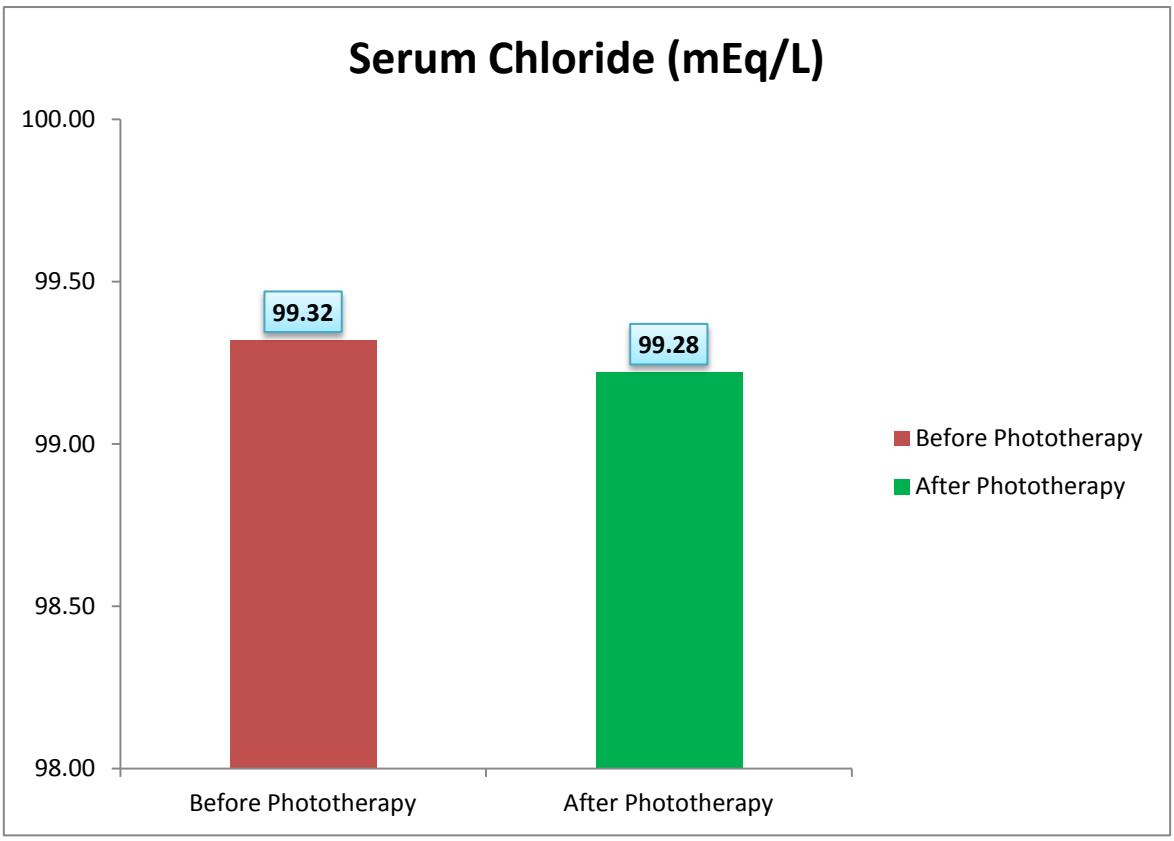

Serum Chloride (mEq/L)
100.00
99.50
99.00
98.50
98.00
99.32
99.28
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE - 8

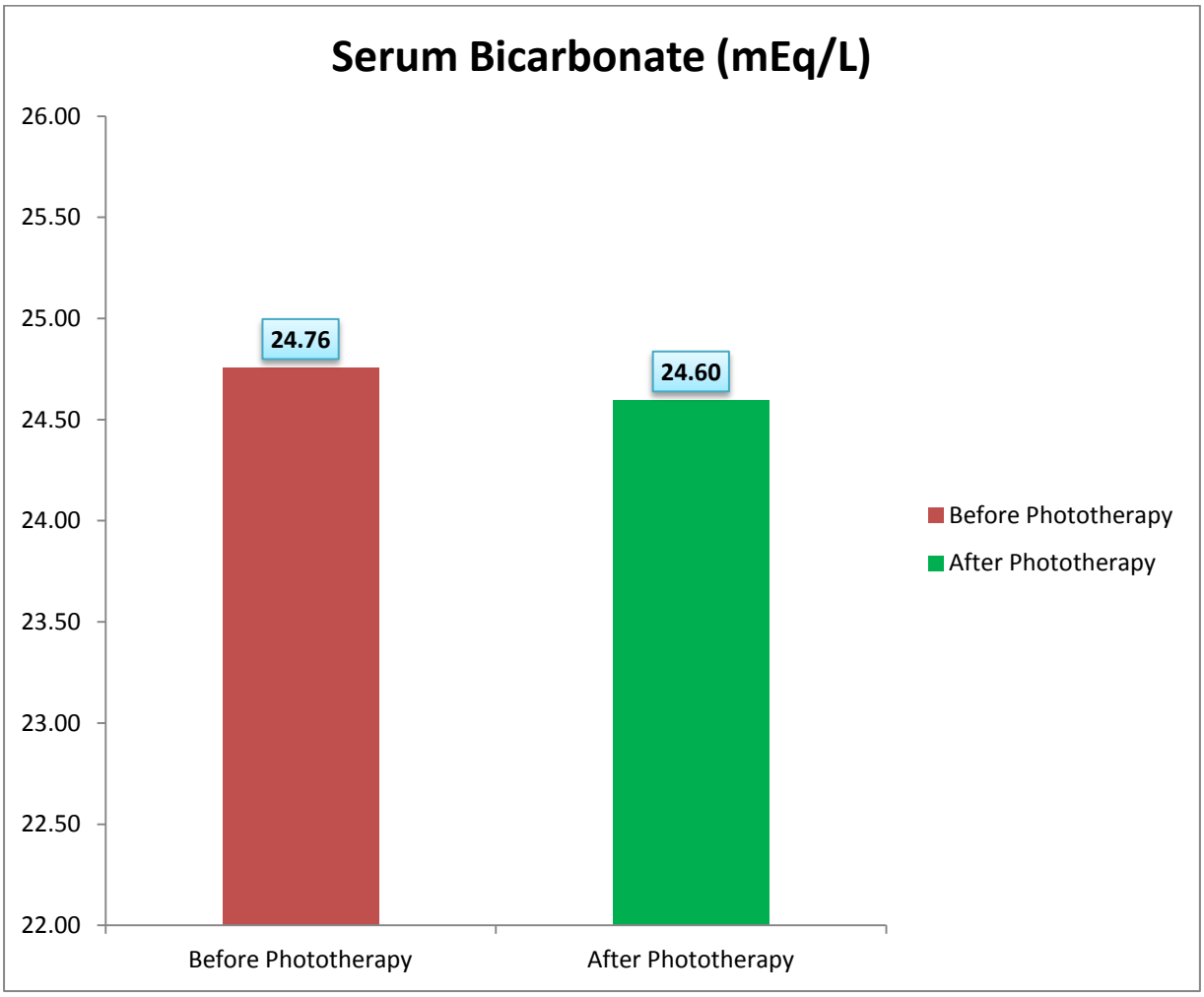
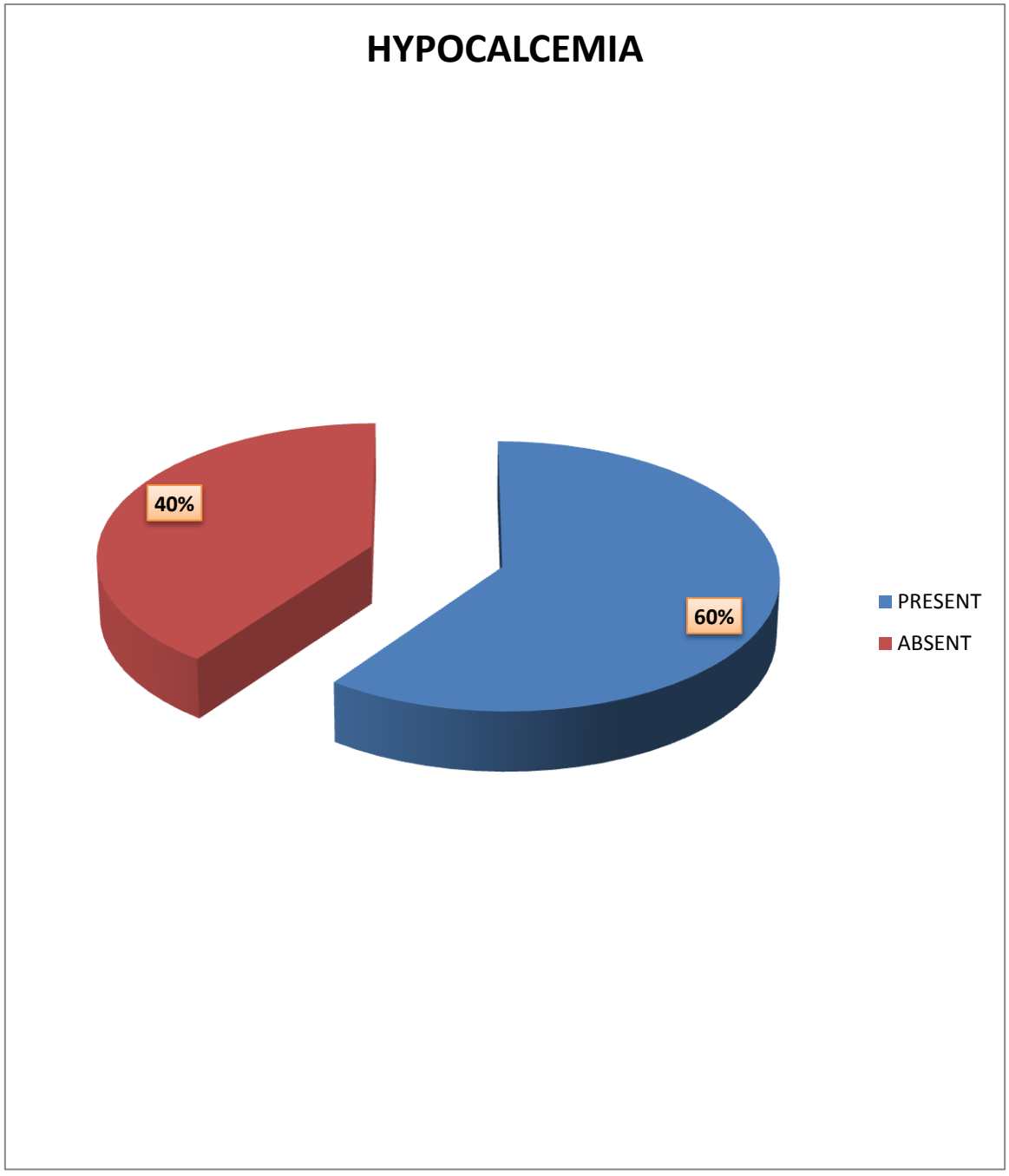

Serum Bicarbonate (mEq/L)
26.00
25.50
25.00
24.50
24.00
23.50
23.00
22.50
22.00
24.76
24.60
Before Phototherapy
After Phototherapy
Before Phototherapy
After Phototherapy

FIGURE - 9

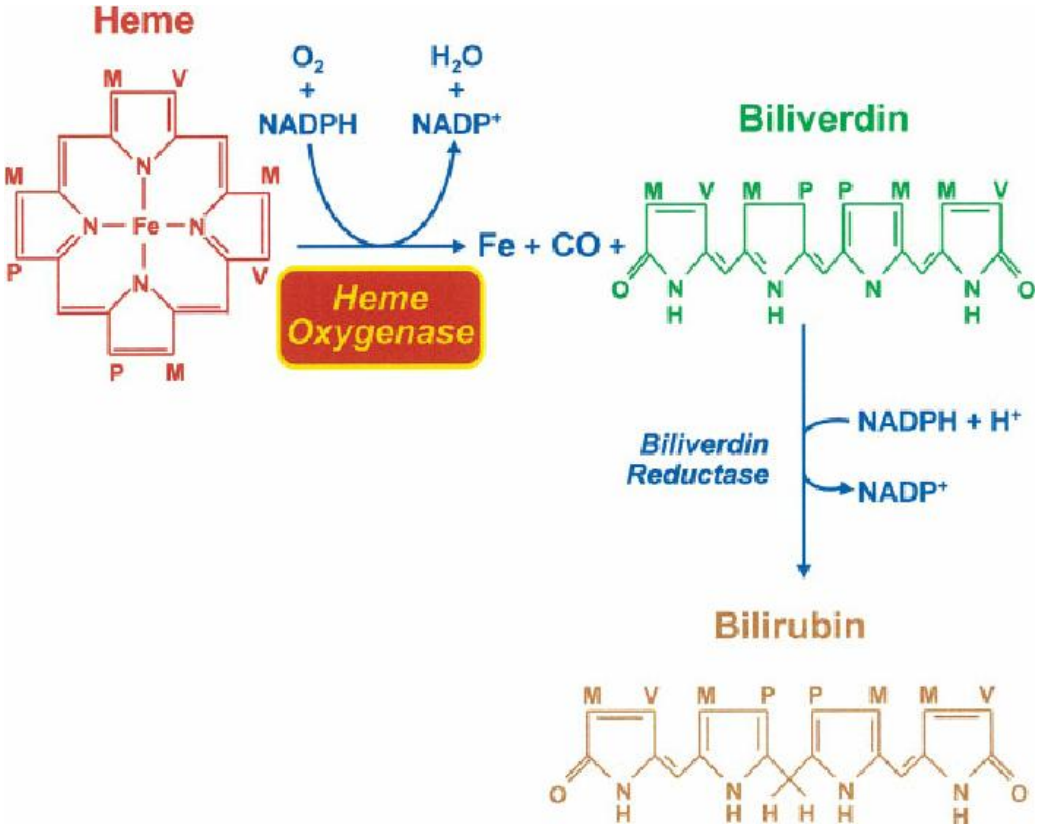


RICHARD JOHN CREMER PAEDIATRICIAN

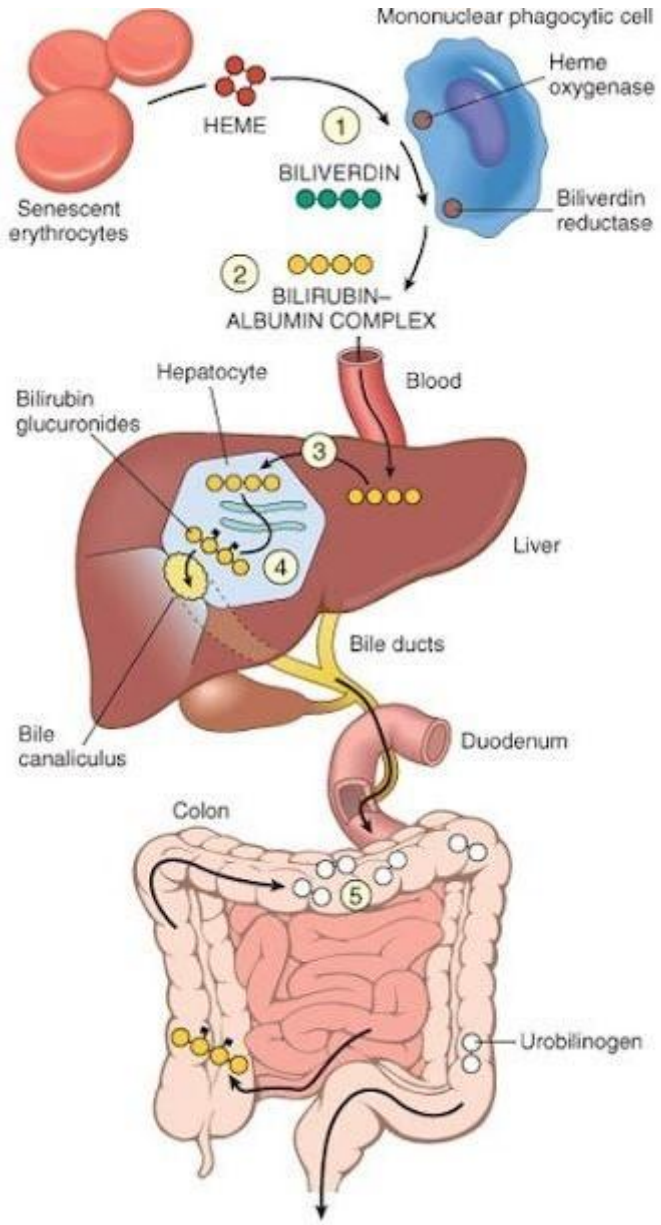
WARD NURSE – ROCHFORD HOSPITAL ENGLAND

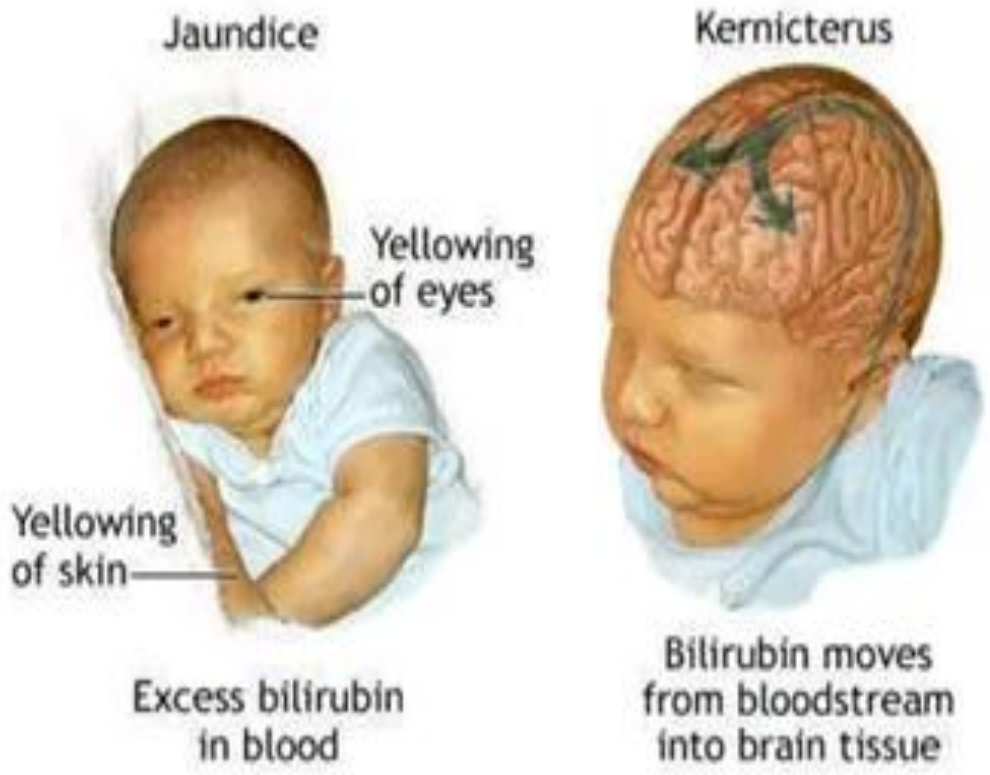
Fig.—Miss J. Ward, S.R.N., in 1956, with one of the earliest of the infants given phototherapy at Rochford General Hospital.

HEME METABOLISM



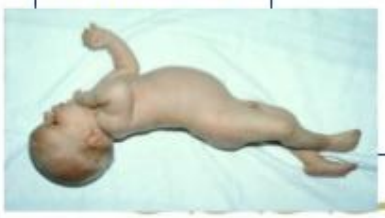
BILIRUBIN METABOLISM




Jaundice
Yellowing of eyes
Yellowing of skin
Excess bilirubin in blood
Kernicterus
Bilirubin moves from bloodstream into brain tissue

Kernicterus Signs

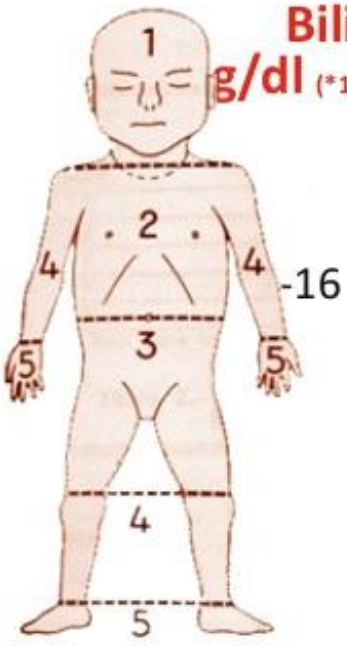
Early (3-4d)	Late (>1 wk)	Chronic (by 3 years of age)
●Lethargy ●Poor feeding ●High-pitched cry ●Hypotonia	●Irritability ●Seizures ●Apnea ●Hypertonia ●Fever	●Athetoid cerebral palsy ●High-frequency hearing loss ●Paralysis of upward gaze ●Dental dysplasia ●Mild mental retardation



Clinical assessment of jaundice (Kramer's staging)

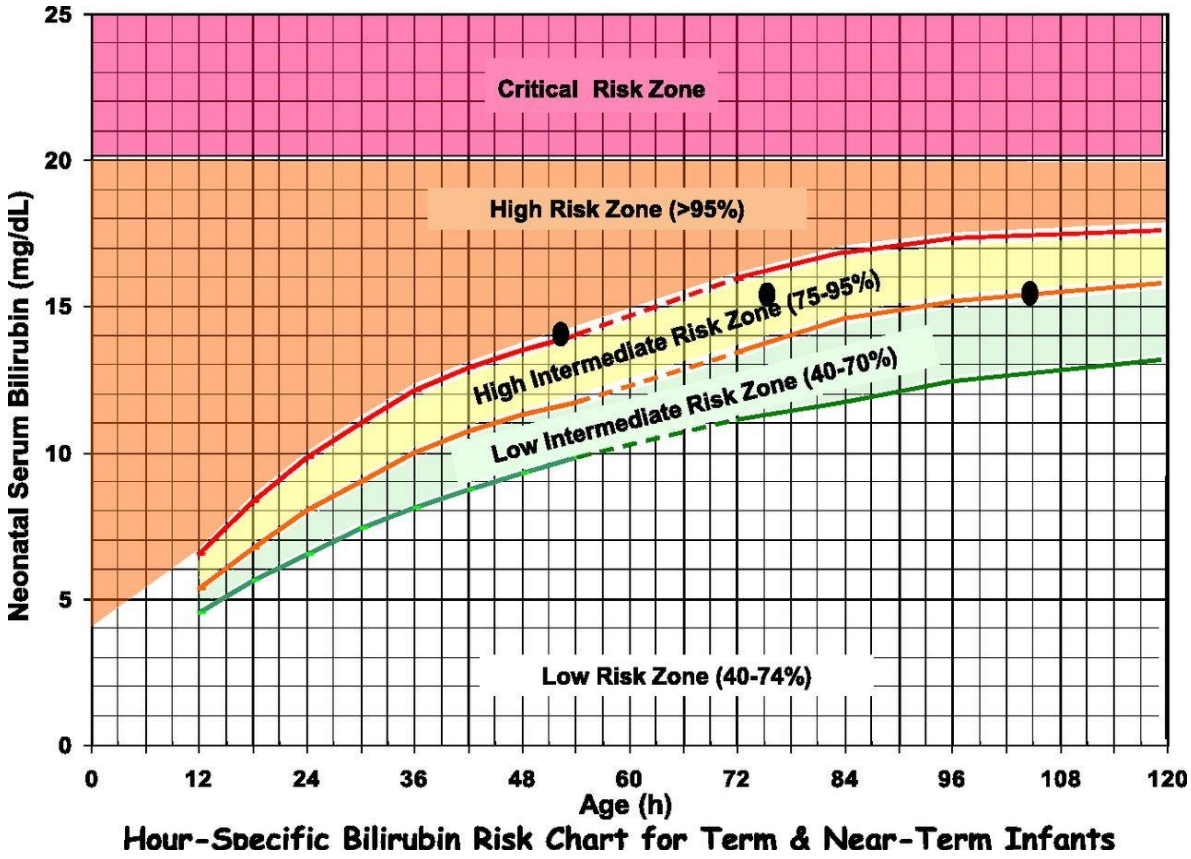
Area of body

Face
Upper trunk
Lower trunk & thighs
Arms and lower legs
Palms & soles



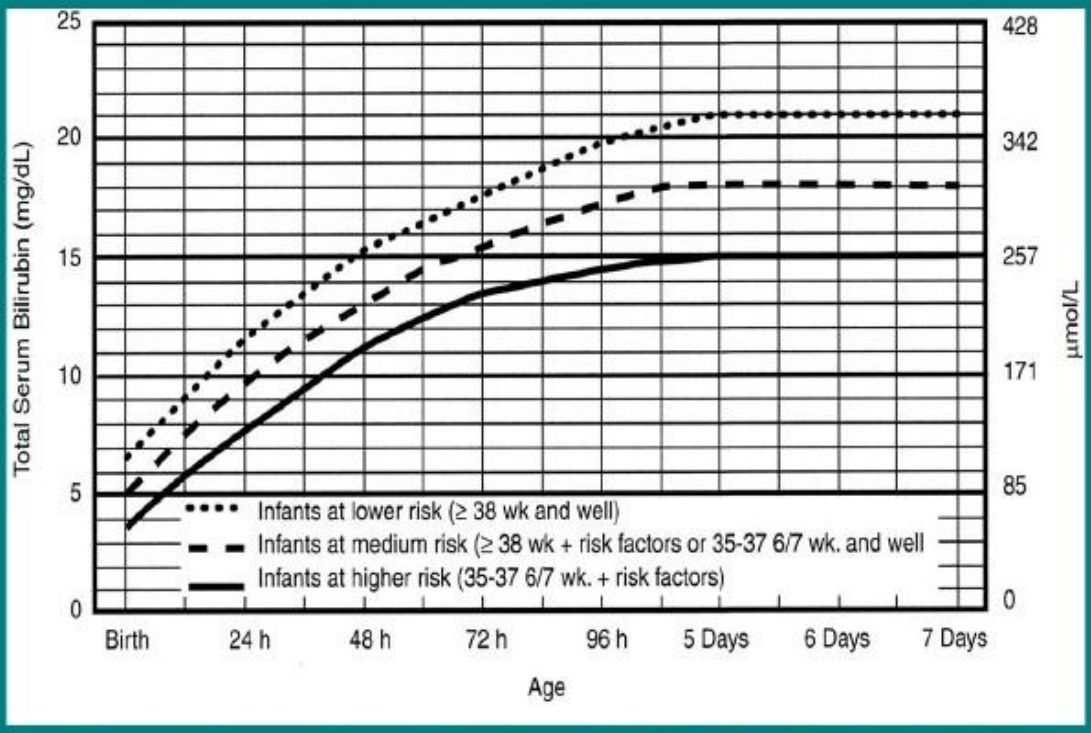
Bilirubin levels
g/dl (*17=umol)

Zone-1: 4-6
Zone-2: 6-8
-16
Zone-3: 8-12
Zone-4 :12-14
Zone-5 :>15



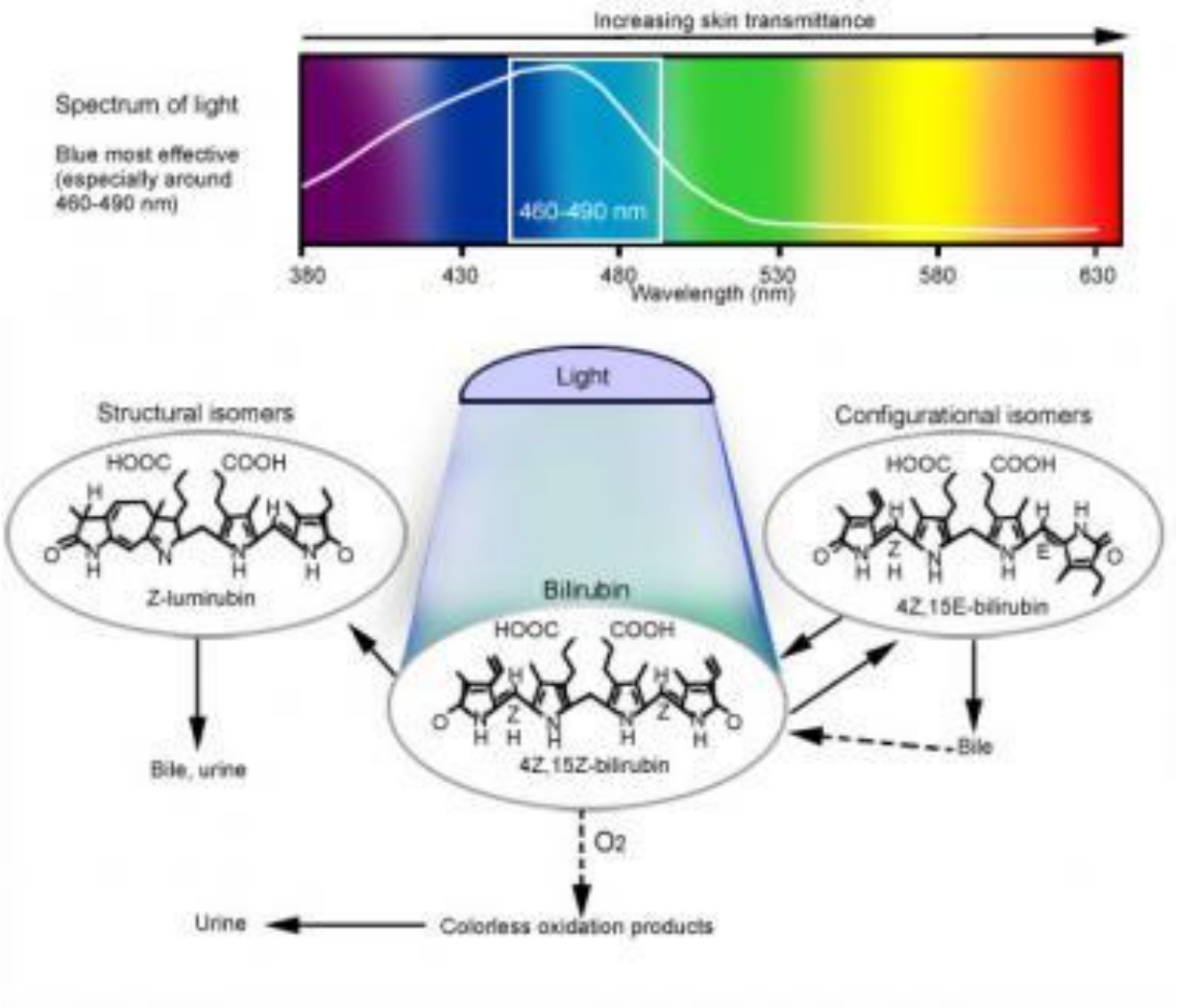
Hour-Specific Bilirubin Risk Chart for Term & Near-Term Infants

Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation



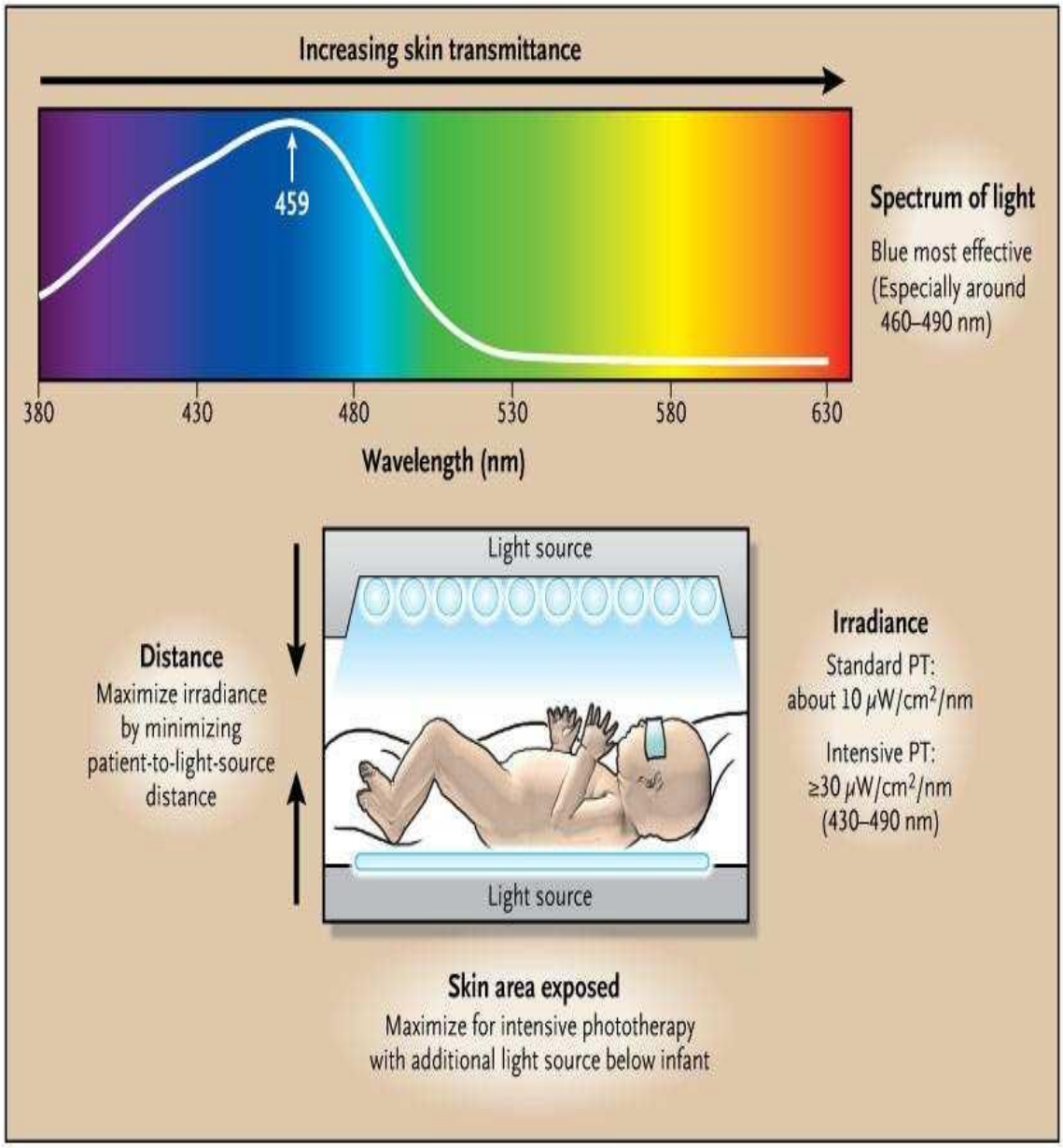
Subcommittee on Hyperbilirubinemia, Pediatrics 2004;114:297-316

ISOMERISATION OF BILIRUBIN TO LUMIRUBIN



BILIBLANKET

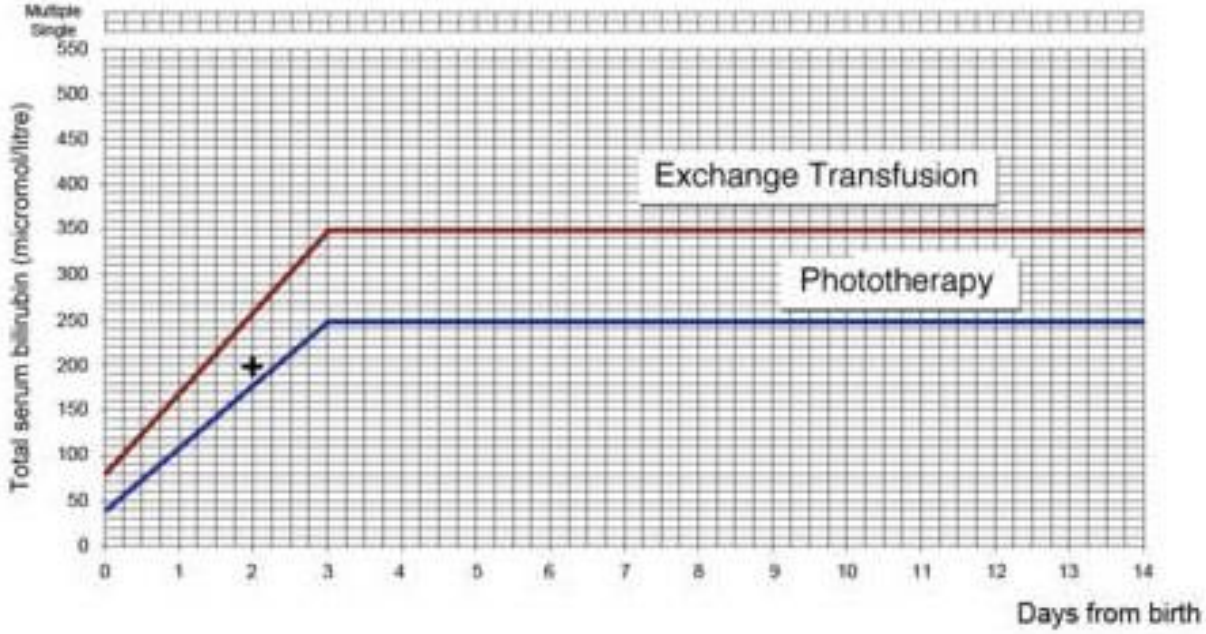
CRITERIAS OF PHOTOTHERAPY

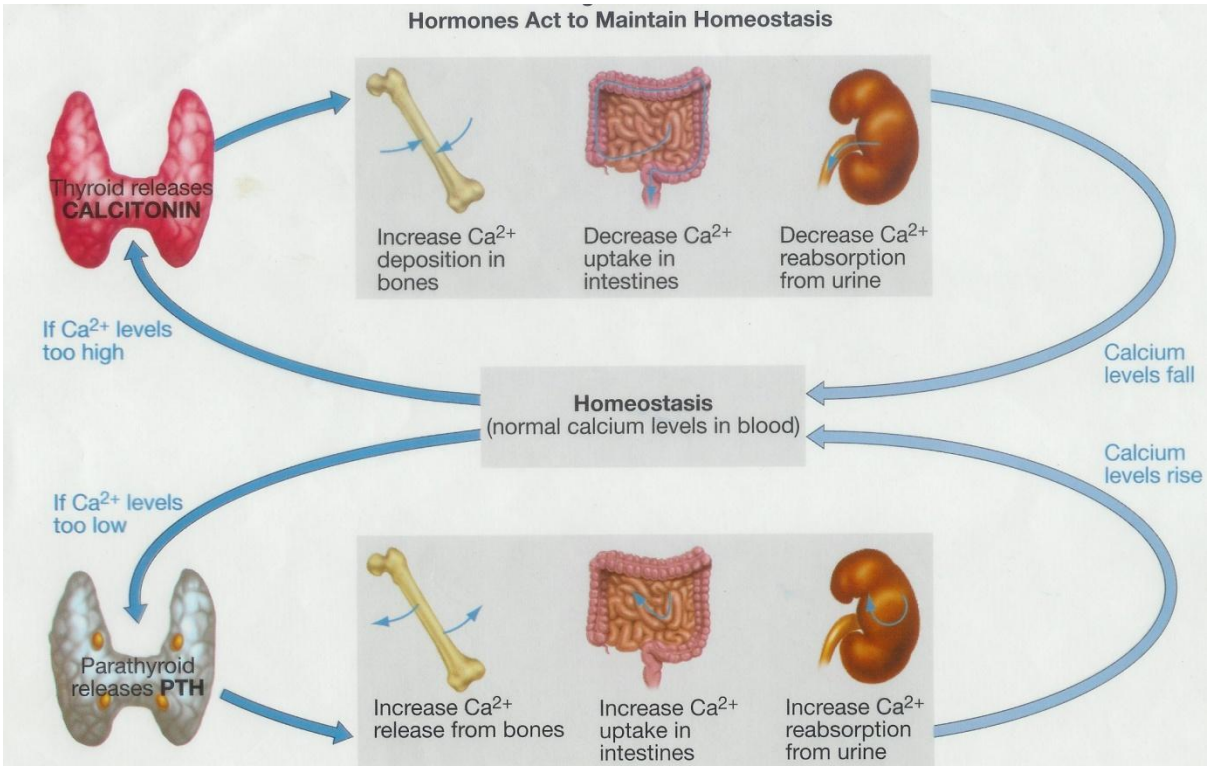


Baby with mild jaundice

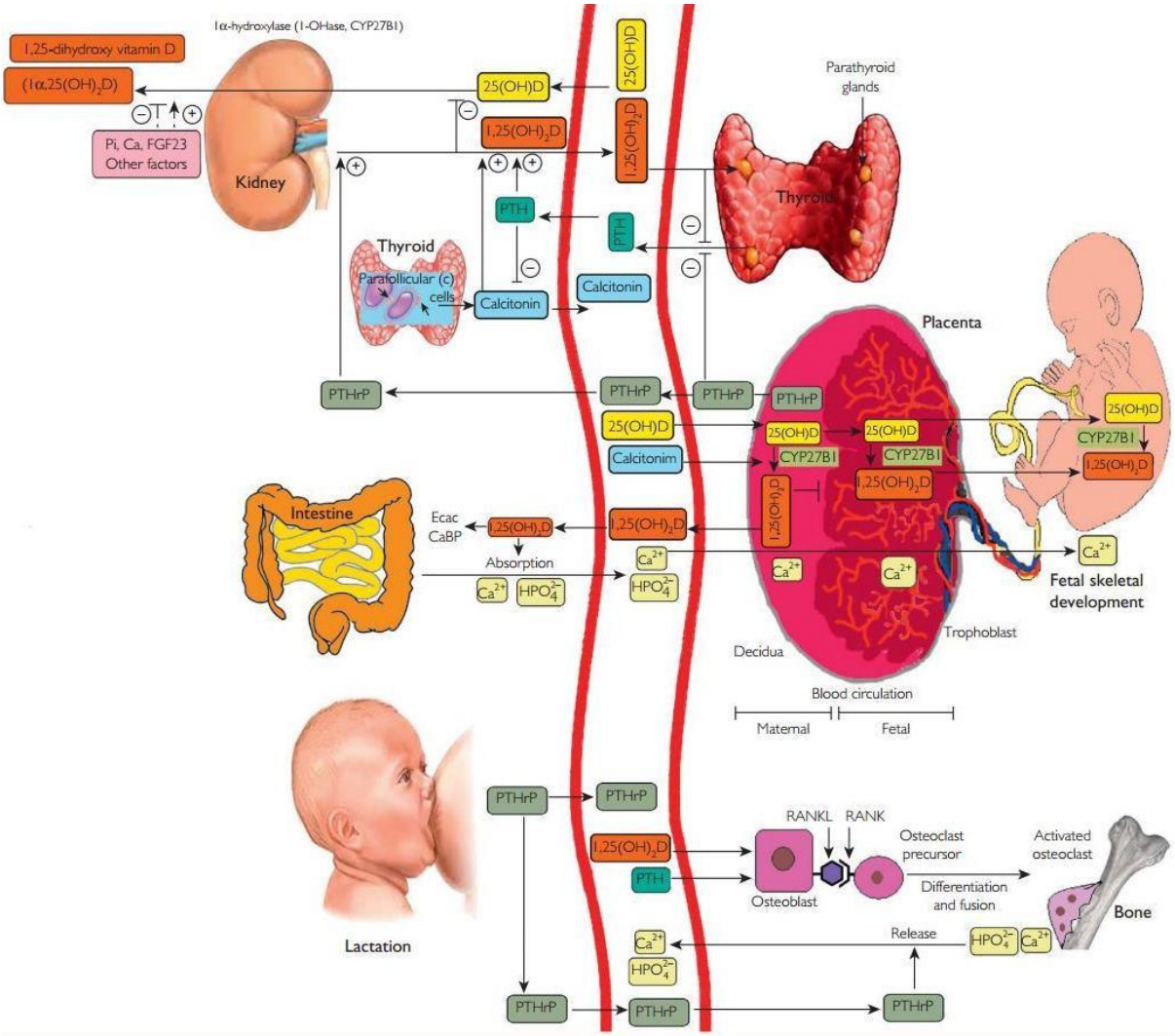
PHOTOTHERAPY DONE WITH EYE SHEILDING

NICE Treatment Threshold Graph




Hormones Act to Maintain Homeostasis
Thyroid releases CALCITONIN
Increase Ca^{2+} deposition in bones
Decrease Ca^{2+} uptake in intestines
Decrease Ca^{2+} reabsorption from urine
If Ca^{2+} levels too high
Calcium levels fall
Homeostasis
(normal calcium levels in blood)
Calcium levels rise
If Ca^{2+} levels too low
Parathyroid releases PTH
Increase Ca^{2+} release from bones
Increase Ca^{2+} uptake in intestines
Increase Ca^{2+} reabsorption from urine

CALCIUM METABOLISM IN FETUS AND IN NEONATE



ARSENAZO III METHOD