"COMPARISON BETWEEN TRANSCUTANEOUS BILIRUBIN MEASUREMENTS AND SERUM TOTAL BILIRUBIN LEVELS IN NEONATES WITH CLINICAL JAUNDICE: AN OBSERVATIONAL STUDY"

By

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Under the Guidance of

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**COMPARISON BETWEEN TRANSCUTANEOUS BILIRUBIN MEASUREMENTS AND SERUM TOTAL BILIRUBIN LEVELS IN NEONATES WITH CLINICAL JAUNDICE: AN OBSERVATIONAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. SUDHA REDDY V. R.**, Professor & Head, Department of Paediatrics, and co-guidance of **Dr. SUMATHI M. E.,** Professor & Head, Department of Biochemistry, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award of "**M.D. DEGREE IN PAEDIATRICS**", the examination to be held in November, 2019 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

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Dr. SAHIL CHAUDHARY

LIST OF ABBREVIATIONS

AAP – American Academy of Pediatrics

AGA - Appropriate for Gestational age

CPD - Cephalo Pelvic Dislocation

CS - Caesarean Section

FFP - Fresh Frozen Plasma

G6PD - Glucose-6-Phosphate Dehydrogenase

GA - Gestational Age

Hb - Haemoglobin

HBR - Hyperbilirubinemia

HDN - Haemolytic Disease of Newborn

IAP NNF – Indian Academy of Pediatrics National Neonatolgy Forum

IVIG - Intravenous Immunoglobulin

LBW - Low Birth Weight

NPV - Negative Predictive Value

NVD – Normal vaginal delivery

PDA - Patent Ductus Arteriosis

PIH - Pregnancy Induced Hypertension

PPV - Positive Predictive Value

SBR - Serum Bilirubin

T/ID - Total/ Indirect Bilirubin

TcB - Transcutaneous Bilirubinometer

TSB - Total Serum Bilirubin

UDPGT - Uridine Di Phosphate Glucuronosyl Transferase

ABSTRACT

Background: Total serum bilirubin (TSB) estimation is traditionally done on serum sample drawn by venipuncture, which is invasive and painful to the neonate. This has led to search for non-invasive, reliable techniques for bilirubin estimation such as transcutaneous bilirubinometry (TcB).

Aims and Objectives:. This study was performed to measure TSB by using lab method, to measure TcB by using JM 105 bilirubinometer, to compare the values of both methods and to establish cut off values using JM-105.

Methodology: The cross sectional observational study was conducted for a period of one year in neonates with clinical jaundice. Study subjects were divided into 4 groups based on weight and gestational age as follows: term appropriate for gestational age (AGA), term small for gestational age (SGA), late preterm AGA and late preterm SGA. TcB measurements were made with a Tc bilirubinometer "JM-105" over forehead and sternum. TSB was estimated in the laboratory by diazotized sulfanilic test. Correlation between TSB values and TcB measurements at the two sites were performed. Cut-off points for "JM-105" with desirable sensitivity and specificity values for detecting need of treatment were determined.

Results: The gestational age ranged from 35 to 42 weeks (mean 38.36 ± 1.3 weeks) with bodyweight ranging from 2100 g to 3920 g (mean 2825 g ± 477 g). The TSB

levels ranged between 5.20 mg/dl to 21.40 mg/dl (mean 12.35 ± 2.47 mg/dl). The range of TcB values at forehead 1 was 6.2 to 22.40 mg/dl, forehead 2 was 6 to 22.2 mg/dl, sternum 1 was 5.5 to 21.8 mg/dl and sternum 2 was 5.4 to 21.5 mg/dl.

Limbs were the commonest site of appearance associated with hyperbilirubinemia in 102 babies (67.55%) followed by palms/soles (n = 39; 25.8%), abdomen (n = 9; 6%), and lastly chest (n = 1; 0.7 %).

In our study, jaundice was more common in term/AGA babies (84.11%) followed by late preterm/AGA babies (8.61%), term/SGA babies (5.96%) and lastly late preterm/SGA babies (1.32%).

The mean TSB level was 12.3523 mg/dl with a standard deviation of 2.47302 mg/dl. The mean TcB forehead value was 13.0285 mg/dl with a standard deviation of 2.66756 mg/dl. Mean TcB level over sternum was 12.7576 mg/dl with a standard deviation of 2.60471 mg/dl. The difference between TSB and TcB (forehead) levels was statistically significant (P = 0.23). However, the difference between TSB and TcB (sternum) levels was not statistically significant (P = 0.167). This shows that TcB sternum correlates closely with TSB.

Mean TcB levels at forehead 1 and 2 were 13.0172 ± 2.67112 mg/dl (mean ± SD) and 13.0397 ± 2.6849 mg/dl (mean ± SD), which was not significant (*P* = 0.559). Mean

TcB levels at sternum 1 and 2 were 12.7834 ± 2.635 mg/dl (mean ± SD) and 12.7318 ± 2.596 mg/dl (mean ± SD), the difference was not significant (P = 0.196). There was significant correlation between TSB levels and TcB levels at individual sites (forehead 1, forehead 2, sternum 1 and sternum 2).

Average TcB level ≥ 12.00 mg/dl at forehead showed sensitivity of 91% and specificity of 66.7% beyond which phototherapy is indicated, while TSB level ≥ 11.35 mg/dl showed sensitivity of 94% and specificity of 66.5% for the same. Similarly average TcB level ≥ 11.975 mg/dl at sternum showed sensitivity of 92.5% and specificity of 77.4% beyond which phototherapy is indicated and TSB level of ≥ 11.75 mg/dl showed sensitivity of 92.5% and specificity of 81% for the same. It was concluded that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is high sensitive and specific for diagnosis of neonatal jaundice, beyond which phototherapy is indicated and is comparable to TSB levels.

Conclusion: We conclude that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of hyperbilirubinemia and is comparable to TSB. TcB at the level of sternum and forehead can be considered as an accurate non-invasive tool for diagnosis and estimation of neonatal hyperbilirubinemia. Furthermore, it is easy to perform and presents little clinical challenge in day-to-day practice.

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INTRODUCTION

Neonatal hyperbilirubinemia (jaundice) is a common problem encountered in approximately 60% of term infants and 80% of preterm infants during the first week of life[1]. Jaundice is defined as the yellowish discoloration of the mucous membranes skin, and conjunctival membranes caused by excess of bilirubin in the blood. Bilirubin formation in newborns is 2 to 3 times greater than in adults owing to the shorter life span of fetal hemoglobin compared to adult hemoglobin. The developmentally immature liver and gastrointestinal tracts of newborns are unable to excrete bilirubin as quickly as it is produced. When bilirubin accumulates in blood and body tissues, skin and eyes exhibit the yellow color characteristic of jaundice[1]. Discoloration is most noticeable in the face and descends cephalocaudally, with clearance of yellowish hue occurring in the opposite direction. Adults appear jaundiced when serum bilirubin levels are greater than 2 mg/dl while newborns appear jaundiced when the levels are greater than 7 mg/dl[2].The major risk factors for hyperbilirubinemia are prematurity (gestation 38 weeks), breastfeeding, family history of significant jaundice in a sibling, Rh/ABO incompatibility, or glucose-6-phosphate dehydrogenase (G6PD) deficiency[3].

Neonatal hyperbilirubinemia is usually a benign condition that peaks between the second and fourth day of life[4]. However, when a pathological process interferes with the normal functioning of the metabolism and excretion of bilirubin, severe hyperbilirubinemia occurs and immediate treatment with phototherapy and/or exchange blood transfusions is required[5,6].

Kernicterus is defined as increased levels of unconjugated bilirubin that deposits in the brainstem nuclei and cerebellum. Although preventable, Kernicterus is associated with significant neonatal morbidity such as cognitive impairment, cerebral palsy and neurosensory hearing loss[2].In 2010, severe neonatal jaundice (NNJ) was estimated to be about 480,700 in late preterm and term neonates with 1,14,000 dying and >63000 surviving with moderate to severe long term neurological sequalae[7]. In 2016 Neonatal jaundice (NNJ) was estimated to account for ~8 under 5 children deaths per 100000 (95% uncertainty level [UI] 7-9) globally. From more than 100 possible causes of under 5 mortality, NNJ ranked 16th consistently since 1990. The burden is high in sub Saharan Africa and south asia[8].

For the better treatment of neonatal jaundice, measuring bilirubin levels is vital. Different methods of measuring bilirubin levels are currently used which is usually done by visual, cutaneous, and serum evaluations[9,10]. Although visual assessment is simple, it has two major shortcomings; it is dependent on the physician's experience with no accurate and reliable criteria, and possible estimations in this method are based on the cephalocaudal trend of jaundice. Moreover, the color of skin and clothes as well as the lighting affect visual estimation[10].

Total serum bilirubin (TSB) estimation is traditionally done on serum sample drawn by venipuncture. This technique requires drawing of blood which is invasive and painful to the neonate[11]. This problem has led to search for non-invasive, reliable techniques for bilirubin estimation such as transcutaneous bilirubinometry (TcB)[12].

Although the use of transcutaneous bilirubin (TcB) measurement is a valid method for determination of the severity of jaundice and is used in increasing frequency, its use is still not widespread worldwide yet[13]. One reason of non-application of TcB may be the assumption that in sick neonates TcB is less useful, because in these neonates blood sampling is often done for other indications and serum bilirubin (SB) measurement is simultaneously measured. Furthermore, in low-income countries, TcB is not widely applied, although this may be of great value due to feasibility of TcB in community settings with low resources[14,15]. Most published data on the use of TcB originate from validation studies, comparing SB with TcB[16,17]. Recently, it has been shown that the use of TcB can be applied reliably in preterm infants with gestational age of 32 to 35 weeks as well, deriving the question of what methods can cause reduction in blood draws, which can be achieved in this group of neonates[18].

AIMS AND OBJECTIVE

1. To measure TSB by using lab method.
2. To measure TcB by using JM -105 bilirubinometer.
3. To compare the values of both methods.
4. To establish cut off values using JM-105 beyond which TSB is needed.

REVIEW OF LITERATURE

Jaundice is the most common condition that requires medical attention. In order to develop a diagnostic as well management of jaundice in newborns, we need to have a clear back ground idea about pathological and non-pathological factors as well as their bilirubin levels.

BILIRUBIN METABOLISM

A normal newborn produces 6-10 mg of bilirubin/kg/day. Red blood cells(RBC) contain heme and globin. The senescent RBCs release heme in reticuloendothelial system, which is the major source of bilirubin (~75%). One g of haemoglobin produces 34 mg of bilirubin. It is found in the blood stream as two forms indirect (unconjugated) bilirubin and direct (conjugated) bilirubin. Accelerated release of bilirubin produces hyperbilirubinemia. The remaining 25% of bilirubin is called early-labelled bilirubin, which is derived from haemoglobin released by ineffective erythropoiesis in bone marrow from other heme containing proteins in tissue and from free heme[19].

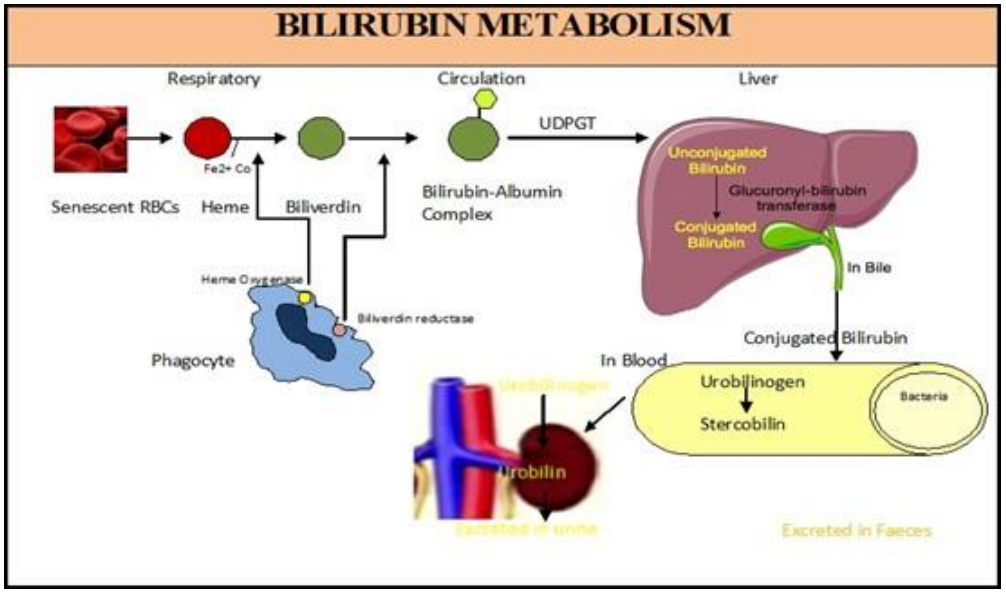

Figure 1. Bilirubin metabolism.

The conversion of heme to bilirubin requires two closely linked enzymatic steps.

1. 1st step is conversion of heme to linear tetrapyrolebiliverdin. One molecule of ferrous ion and one molecule of carbon monoxide are released by enzyme hemeoxygenase. It is the rate limiting step and upregulated during hemolysis[20].
2. 2nd step involves synthesis of biliverdin found in cytosol of most of cells. Biliverdin is then converted to bilirubin (Figure 1)[20].

BILIRUBIN TRANSPORT IN THE PLASMA

Bilirubin in plasma is tightly bound to serum albumin, usually does not enter the central nervous system and is thought to be nontoxic[19].

Bilirubin uptake

Non-polar fat-soluble bilirubin (dissociated from albumin) crosses the hepatocyte plasma membrane and is bound mainly to cytoplasmic ligandin (Y protein) for transport to the smooth endoplasmic reticulum. Phenobarbitone increases the concentration of ligandin[19].

Bilirubin conjugation

Unconjugated bilirubin (UCB) is converted to water soluble conjugated bilirubin (CB) in the smooth endoplasmic reticulum by uridine diphosphate glucuronyltransferase (UDPG-T). This enzyme is inducible by phenobarbitone and catalyzes the formation of bilirubin monoglucuronide. Both mono and diglucuronide forms of conjugated bilirubin are able to be excreted into the bile canaliculi against a concentration gradient[19].

Bilirubin excretion

Conjugated bilirubin in the biliary tree enters the gastrointestinal tract and is thus eliminated from the body in the stool, which contains large amount of bilirubin. Excretion is considered to be the rate limiting step of overall bilirubin clearance from the plasma[19].

Enterohepatic circulation of bilirubin

Conjugated bilirubin is not normally reabsorbed from the bowel unless it is converted back to unconjugated bilirubin by the intestinal enzyme beta-glucuronidase[19].

Fetal bilirubin metabolism

Most unconjugated bilirubin formed by the fetus is cleared by the placenta into the maternal circulation. Formation of conjugated bilirubin is limited in the fetus due to decreased fetal hepatic blood flow, decreased hepatic ligandin and decreased UDPG-T activity. The small amount of conjugated bilirubin excreted is usually hydrolyzed by beta-glucuronidase and reabsorbed[19].

Bilirubin is normally found in the amniotic fluid by 12 weeks gestation. Increased amniotic fluid bilirubin is found in hemolytic disease of the newborn and in fetal intestinal obstruction below the bile ducts[19].

ETIOLOGY OF HYPERBILIRUBINEMIA IN NEWBORN

Any process that increases the production or impairs the elimination of bilirubin can exacerbate the normally occurring physiologic jaundice in newborn[19].

1. Physiological (normal) jaundice

Most newborns have this mild jaundice because their liver is still in the phase of maturing. It appears when a baby is 2 to 4 days old and disappears by 1 to 2 weeks of age (≥ 2 mg/dl). In full term infants, peak occurs (6-8mg/dl) by 3 to 5 days of age and then falls (≥ 12mg/dl). In premature infants the rise may be (10-12mg/dl) by3 to 5th day of life and then rise (≥ 15mg/dl). In newborns unconjugated bilirubin is not excreted much, whereas the conjugated bilirubin excretion is also limited. As a result, high serum bilirubin concentration leads to physiological jaundice[19].

Various factors that bring about physiological jaundice are:

- Increased RBC volume/kg and reduced RBCs survival (90 days versus 120 days in newborns) [19]:
- Increased ineffective erythropoiesis and increased turnover of non haemoglobin heme proteins
- Increased enterohepatic circulation due to increased intestinal β-glucuronidase enzyme.
- Decreased intestinal bacteria
- Decreased gut motility.
- Defective uptake of bilirubin from plasma due to decreased ligandin and binding of ligandin by other anions
- Defective conjugation due to decreased UDPGT activity
- Decreased excretion of bilirubin by liver

Criterion for physiological jaundice[21]

The various criteria for diagnosis of physiological jaundice are as follows[21]:

- Type of bilirubin – indirect bilirubin
- Direct bilirubin not more than 2 mg/dl or less than 15% of total bilirubin.
- Appearance- after 36 hours of age
- Rate of rise of bilirubin- less than 5 mg/dl/day
- Severity of jaundice- usually does not exceed 15 mg/dl
- Natural course – Peak TSB levels seen between 3 -5 day of life and 3-7 day in preterm and disappears by 2 weeks
- Clinical condition- Healthy newborn

2. Non physiological (pathological) jaundice

Non-physiological jaundice is referred to as jaundice developing in ≤ 24 hours of age, rise of serum bilirubin ≥ 0.2 mg/dl/hour, ≥ 5 mg/dl/day, direct serum bilirubin level > 2 mg/dl or 15% of total bilirubin or rise of serum bilirubin that requires phototherapy. It may be associated with features of sepsis. Jaundice of more than eight days in term newborn or more than 14days in preterm newborn is also pathological in nature[19].

Causes are as follows[19]:

- **Over production**
    - Fetomaternal blood group incompatibility
    - Hereditary spherocytosis, elliptocytosis, stomatocytosis.

- Nonspherocytic hemolytic anemias
- Glucose 6-phosphate dehydrogenase deficiency (G6PD) and drugs
- Pyruvate kinase deficiency
- Other red cell enzyme deficiencies
- Alpha thalassemia
- Beta thalassemia
- Acquired hemolysis due to vitamin K, nitrofurantoin, sulfonamides, antimalarials, penicillin, oxytocin, bupivacaine or infection
- Extra vascular blood: petechial hemorrhage, hematomas, pulmonary, cerebral or occult hemorrhage.
- Polycythemia: Fetomaternal or fetofetal transfusion. Delayed clamping of the umbilical cord.
- Increased enterohepatic circulation
- Pyloric stenosis
- Intestinal atresia or stenosis including annular pancreas
- Hirschsprung disease
- Meconium ileus or Meconium plus syndrome,
- Swallowed blood

- **Undersecretion**
  - Metabolic or endocrine conditions
  - Galactosemia
  - Familial nonhemolytic jaundice (Crigler-Najjar syndrome and Gilbert syndrome)
  - Hypothyroidism
  - Tyrosinemia

- Hypermethioninemia
- Drugs and hormones – Novobiocin, Pregnanediol
- Lucy- Driscoll syndrome
- Infant of diabetic mothers
- Prematurity, hypopituitarism and anencephaly
- Obstructive disorders
- Biliary atresia
- Dubin Johnson and Rotor syndrome
- Choledochal cyst
- Cystic fibrosis (inspissated bile)
- Tumor or band (extrinsic compression)
- Parental nutrition
- Alpha 1- antitrypsin deficiency

- **Mixed**
  - Sepsis
  - Intrauterine infections
  - Toxoplasmosis
  - Rubella
  - Herpes simplex
  - Syphilis, Hepatitis
  - Respiratory distress syndrome
  - Asphyxia
  - Infant of diabetic mother
  - Severe erythroblastosis fetalis
- **Uncertain mechanism**

- Breast milk jaundice
- Chinese, Japanese, Korean and American Indian infants

Breastfeeding Jaundice:

Jaundice occurs when breastfeeding babies do not get enough breast milk from their mother or difficulty in breast feeding persists. It occurs after day 3 of life and usually the peak level is more than 12mg/dl in 12 to 13% of breast feeding babies. The main factor responsible for breast feeding jaundice is decreased intake of breast milk leading to late bilirubin elimination and increased enterohepatic circulation[19,22].

Breastmilk Jaundice:

This jaundice usually has a late on set and the incident varies form 2-4%. The serum bilirubin level may rise to 20-30mg/dl by 14days. This may return to normal by 4 to 12 weeks of age. The various mechanisms responsible for this are unidentified factors that interferes with bilirubin metabolism, increased enterohepatic circulation (increased β- glucuronidase) and decreased intestinal bacteria that converts conjugated bilirubin to urobilinoids[19,22].

RISK FACTORS OF HYPERBILIRUBINEMIA

Major risk factors[19,21]

1. Jaundice observed in first 24 hours of life

2. Blood group incompatibility with positive direct Coomb's test (DCT) or elevated end tidal carbon monoxide (ETCOc)
3. Gestational age 35-36 weeks
4. Previous sibling received phototherapy
5. Cephalohematoma or significant bruising
6. Exclusive breast feeding, particularly if nursing is not going well and weight loss is excessive.
7. East Asian race

Minor risk factors[19,21]

1. Pre discharge TSB level on the high intermediate risk zone
2. Gestational age 37-38 weeks
3. Jaundice observed before discharge
4. Previous sibling with jaundice
5. Infant of diabetic mother
6. Maternal age >25 years
7. Male gender

Decreased risk factors for jaundice[19,21]

1. TSB level in low risk zone
2. Gestational age>41 weeks
3. Exclusive bottle feeding
4. Black race
5. Discharge from hospital after 72 hours.

Causes of jaundice on the basis of onset

Within 24 hours: Rh and ABO incompatibility, G6PD and pyruvate kinase deficiency[19,21].

Infections: Bacterial, Malaria, Toxoplasmosis, Other Agents, Rubella, Cytomegalovirus, and Herpes Simplex (TORCH) group of infections, RBC Membrane defects(hereditary spherocytosis), alpha thalassemia, administration of large amount of drugs (such as vitamin K, salicylates, sulfisoxazole, etc.) to the mother[19,21].

24-72 hours after birth: Physiological jaundice, blood group incompatibility, polycythemia, extra vascular bleed such as cephalohaematoma and subgaleal hemorrhage, breast feeding jaundice, neonatal sepsis, increased enterohepatic circulation, intestinal obstruction[19,21].

After 72 hours of birth: Neonatal sepsis, cephalohaematoma, neonatal hepatitis, biliary atresia, breast milk jaundice[19,21].

Metabolic: Hypothyroidism, hypopituitarism, galactosemia, tyrosinemia, cystic fibrosis, hereditary fructosemia, Crigler – Najjar syndrome, Gilbert disease[19,21].

CLINICAL ASSESMENT OF NEONATAL JAUNDICE

Clinicians should ensure that all infants are routinely monitored for the development of jaundice, and nurseries should have established protocols for the assessment of jaundice. Jaundice should be assessed whenever the infant's vital

signs are measured but no less than every eight to12 hours. In new born infants, jaundice can be detected by blanching the skin with digital pressure, revealing the underlying colour of the skin and subcutaneous tissue. The assessment of jaundice must be performed in a well-lit room or, preferably, in day light near a window. Jaundice is usually seen first in the face and progresses caudally to the trunk and extremities, but visual estimation of bilirubin levels for the degree of jaundice can lead to errors[10].

Approach to a Jaundiced Newborn

The approach in assessment of jaundiced newborn is as follows[21]:

1. Identify "high risk" newborns at delivery, likely to develop jaundice.
2. Ensure appropriate follow up for jaundice.
3. Emphasize need for early, exclusive breast feeds and ensure adequacy of breast feeding.
4. Assess clinical condition (well or ill)
5. Ascertain birth weight and gestation
6. Evaluate jaundice with post-natal age in hours
7. Perform systematic evaluation – history and physical examination.
8. Decide whether jaundice is physiological or pathological
9. If physiological and baby well, only observation is required
10. If deeply jaundiced, look for signs of bilirubin encephalopathy (lethargy, poor, feeding, shrill cry, asymmetric Moro reflex, hypertonia, opisthotonus or convulsions)

11. If jaundice is pathological perform lab tests.

12. Initiate appropriate measures to reduce elevated bilirubin

13. Counsel parents

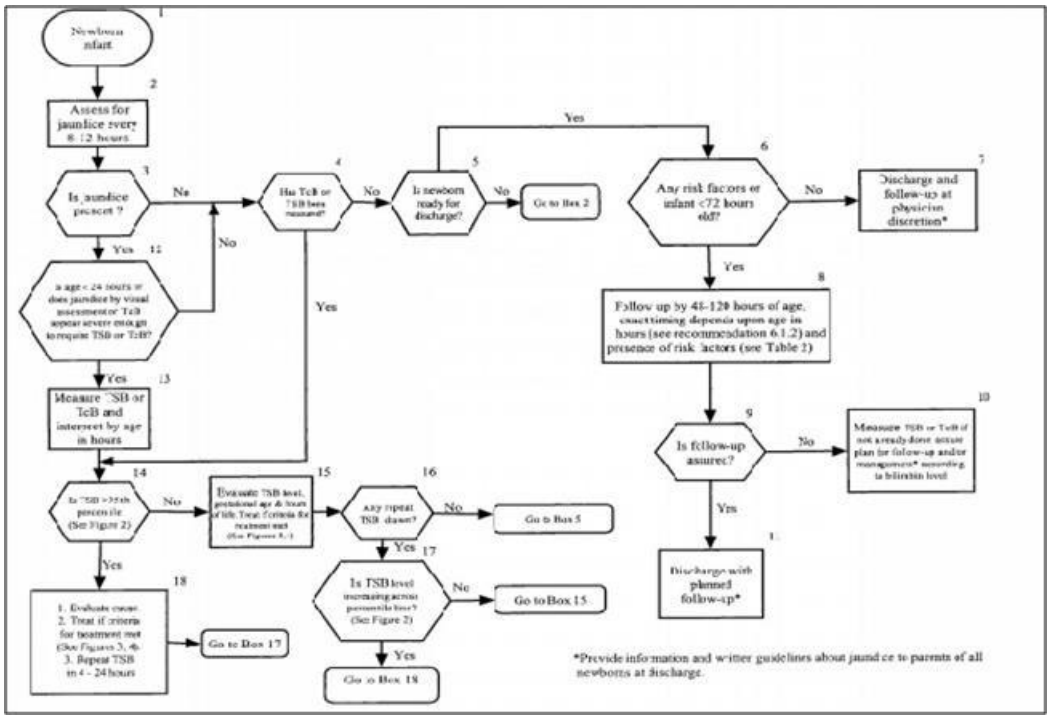

Figure 2. Algorithm for the management of jaundice in newborn[10,19,21]

COMPLICATIONS OF NEONATAL JAUNDICE

The precise blood level above which indirect-reacting bilirubin or free bilirubin will be toxic for an individual infant is unpredictable. Kernicterus is rare in healthy term infants in the absence of hemolysis or if the serum level is <25 mg/dl. In previously healthy, predominantly breast-fed term infants, kernicterus has developed when bilirubin levels exceeded 30mg/dl. The duration of

exposure needed to produce toxic effects is unknown. Little evidence suggests that a level of indirect bilirubin of <25mg/dl affects the intelligent quotient (IQ) of healthy term infants without hemolytic disease[22].

Although originally pathological jaundice diagnosis is characterized by bilirubin staining of the brainstem nuclei and cerebellum, the term "kernicterus" has come to be used interchangeably with both the acute and chronic findings of bilirubin encephalopathy. Bilirubin encephalopathy describes the clinical central nervous system findings caused by bilirubin toxicity to the basal ganglia and various brainstem nuclei[19].

To avoid confusion and encourage greater consistency in the literature, the American Academy of Pediatrics (AAP) committee recommends that in infants the term "acute bilirubin encephalopathy" be used to describe the acute manifestations of bilirubin toxicity seen in the first weeks after birth and that the term "kernicterus" be reserved for the chronic and permanent clinical sequelae of bilirubin toxicity[10].

CLINICAL FEATURES OF BILIRUBIN ENCEPHALOPATHY

Signs and symptoms of kernicterus usually appear 2–5days after birth in term infants and as late as the 7th day in premature infants, but hyperbilirubinemia may lead to encephalopathy at any time during the neonatal period (Table 1). The early signs may be subtle and indistinguishable from those of sepsis, asphyxia, hypoglycemia, intracranial hemorrhage, and other acute systemic illnesses in a neonate[22].

Table 1. Clinical Features of Bilirubin Encephalopathy[19,22]

ACUTE FORM
Phase 1 (1st 1–2 days): Poor sucking, stupor, hypotonia, seizures **Phase2 (middle of 1stweek)**: Hypertonia of extensor muscles, opisthotonos, retrocollis, fever **Phase 3 (after the 1st week)**: Hypertonia
CHRONIC FORM
First year: Hypotonia, active deep tendon reflexes, obligatory tonic neck reflexes, delayed motor skills **After 1st year**: Movement disorders (choreoathetosis, ballismus, tremor), limitation of upward gaze, sensorineural hearing loss, dental dysplasia and intellectual deficits.

TREATMENT

The aim of therapy is to ensure that serum bilirubin is kept at a safe level and neurological damage is prevented. Reduction of TSB levels and prevention of neurotoxicity can be achieved by phototherapy, pharmacotherapy and exchange transfusion[19,22]. Algorithm for management of jaundice in the newborn is depicted in Figure 2.

Principles of treatment in jaundiced infants according to 2006 Indian Academy of Pediatrics National Neonatology Forum (IAP NNF) guidelines are[21]

1. Treatment decisions are based on total serum bilirubin.
2. Gestation is more important than birth weight of the baby. A higher cut off can be used for a small for date baby.
3. Postnatal age in hours should be considered when deciding treatment.
4. Sick baby refers to presence of asphyxia, hypothermia, sepsis, acidosis, hypoxia, hypercapnia and evidence of hemolysis.

Phototherapy

The goal of therapy is to lower the concentration of circulating bilirubin or keep it from increasing. Phototherapy achieves this by using light energy to change the shape and structure of bilirubin, converting it to molecules that can be excreted even when normal conjugation is deficient[19,21,22] Bilirubin absorbs light most

strongly in the blue region of the spectrum near460 nm (Figure 3), a region in which penetration of tissue by light increases markedly with increasing wavelength. The rate of formation of bilirubin photo products is highly dependent on the intensity and wavelengths of the light used. Taking these factors into account, lamps with output predominantly in the 460 to 490 nm blue region of the spectrum are probably the most effective for treating hyperbilirubinemia[15].

Combination of two special blue and 4-6 white fluorescent tubes to be used. The blue tubes must have the serial number F20T12/BB to be a special phototherapy light. This combination would deliver 12mw/cm^2/nm[15].

The absorption of light by the native form of bilirubin (4*Z*,15*Z*-bilirubin) generates transient excited-state bilirubin molecules. These fleeting intermediates can react with oxygen to produce colourless products of lower molecular weight, or they can undergo rearrangement to become structural isomers (lumirubins) or isomers in which the configuration of at least one of the two *Z*-configuration double bonds has changed to an *E* configuration. Configurational isomerization is reversible and much faster than structural isomerization, which is irreversible. Both occur much more quickly than photooxidation. The photoisomers are less lipophilic than the 4*Z*,15*Z* form of bilirubin and can be excreted unchanged in bile without undergoing glucuronidation. Lumirubin isomers can also be excreted in urine. Photo-oxidation products are excreted mainly in urine. Once in bile, configurational isomers revert spontaneously to the natural 4*Z*,15*Z* form of bilirubin[15,23].

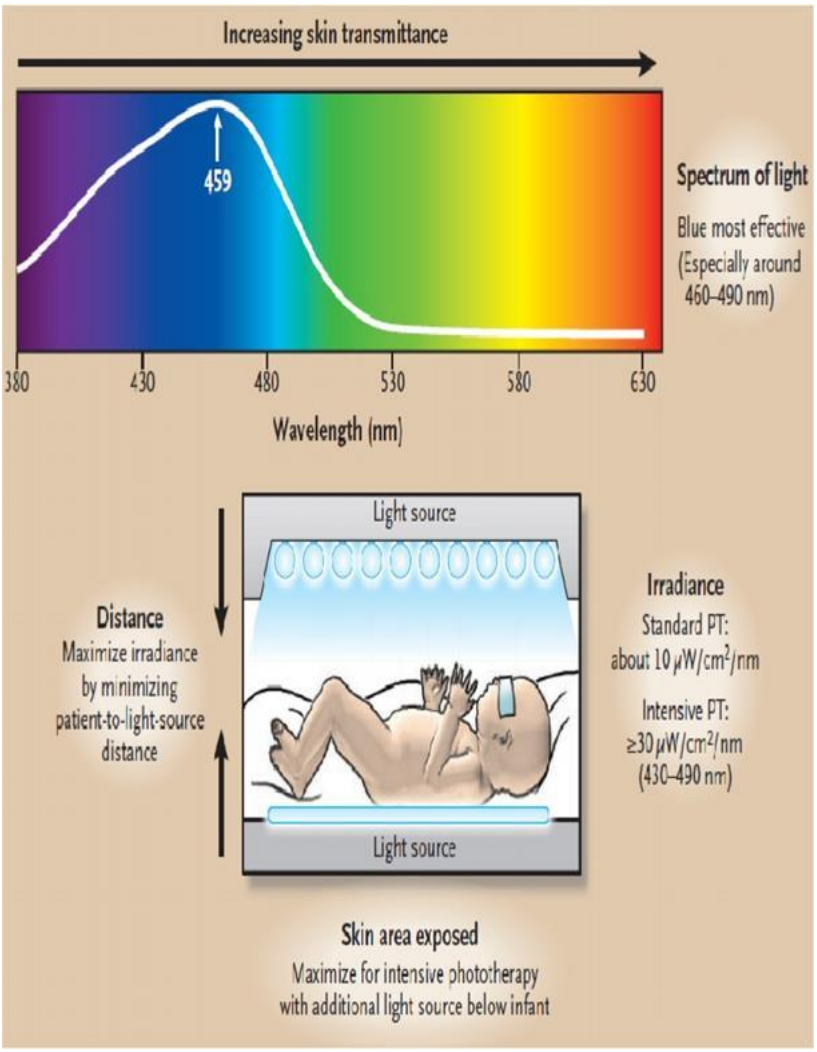

Figure 3. Important factors in the efficacy of phototherapy

Distance of the phototherapy unit should be as close to the baby as possible ensuring normothermia. Hyperthermia makes the phototherapy less effective[10,24].

On an average, for infants of more than 35 weeks' gestation readmitted for phototherapy, intensive phototherapy can produce a decrement of 30% to 40% in the initial bilirubin level by 24 hours after initiation of phototherapy. The most significant decline will occur in the first 4 to 6 hours. With standard phototherapy

systems, a decrease of 6% to 20% of the initial bilirubin level can be expected in the first 24 hours[10,24].

Care of a newborn receiving phototherapy

The following steps are involved in care of a new born receiving phototherapy[19,22,25]:

1. The eyes should be covered during phototherapy.
2. Breast feeding on demand is continued. More frequent breast feeds or 10-20% extra IV fluids are provided.
3. Adequacy of hydration is checked by urine colour and frequency, skin turgor, mucous membrane and weight.
4. Assess and record urine and stool pattern.
5. Frequent change of posture is necessary.
6. Temperature is monitored every 3-4 hrs. Avoid hypo or hyperthermia.
7. Weighing of neonate daily.
8. TSB is measured every 12 hours or 4-6 hourly if severe jaundiced.
9. Monitor for adverse effects of phototherapy: Dehydration, loose stools, hyperthermia/hypothermia, erythematous rash and bronze baby syndrome.

Side effects of phototherapy

The following are adverse effects of phototherapy[19,22,25]:

1. Retinal damage
2. Passage of loose green stools
3. Hyperthermia
4. Dehydration
5. Hypocalcemia
6. Bronze baby
7. Flea-bite rash
8. Opening up of PDA in preterm
9. Increase in mean cerebral blood flow velocity.
10. Decrease in renal blood flow velocity.
11. Increase in renal vascular resistance.

EXCHANGE TRANSFUSION

Exchange transfusion is the most rapid method for lowering serum bilirubin concentrations. This treatment is rarely needed when intensive phototherapy is effective. The procedure removes partially hemolysed and antibody-coated erythrocytes and replaces them with uncoated donor red blood cells that lack the sensitizing antigen[19,22].

The appearance of clinical signs suggesting bilirubin encephalopathy is an indication for exchange transfusion at any level of serum bilirubin. Double volume exchange transfusion (170 ml/ kg) is performed if intensive phototherapy has failed to reduce bilirubin levels to a safe range and if the risk of kernicterus exceeds the risk of the procedure[19,22].

Blood for exchange transfusion is modified whole blood (red cells and plasma) crossmatched against the mother and compatible with the infant[19]. Exchange transfusion should be done in small aliquots of 5 – 10 ml[19,22,25].

Exchange transfusion

Exchange transfusion is done by two methods[19,22]:

1. Push and pull technique: Central access usually through umbilical venous catheter
2. Isovolumetric exchange with simultaneous infusion of donor blood through venous line and removal of baby blood through arterial line

Potential complications from exchange transfusion

The potential complications from exchange transfusion are as follows[19,22]:

1. Metabolic

a. Hypocalcemia
b. Hypoglycemia
c. Hyperglycemia
d. Hyperkalemia

2. Cardiorespiratory
    a. Apnea
    b. Bradycardia
    c. Hypotension
    d. Hypertension
    e. Hematologic
    f. Thrombocytopenia
    g. Dilutional coagulopathy
    h. Neutropenia
    i. Disseminated Intravascular coagulation
3. Vascular Catheter Related
    a. Vasospasm
    b. Thrombosis
    c. Embolization
4. Gastrointestinal
    a. Feeding intolerance
    b. Ischemic injury
    c. Necrotizing enterocolitis
5. Infection
    a. Omphalitis
    b. Septicemia

Choice of blood for exchange transfusion

Rh isoimmunisation: In emergency situation use O Rh negative cells. It is ideal to use O Rh negative blood suspended in AB plasma. Cross matched baby's blood group but Rh negative can also be used. ABO incompatibility: Blood group O types (Rh compatible) with baby. Ideal is to use blood group O (Rh compatible) suspended in AB plasma. Other situations: Cross-matched baby's blood group and give accordingly[19,22].

PHARMACOTHERAPY

Prevention of hemolysis by intravenous immunoglobulin

The administration of intravenous immunoglobulin is an adjunctive treatment for hyperbilirubinemia due to isoimmune hemolytic disease. Its use is recommended when serum bilirubin is approaching exchange levels despite maximal interventions including phototherapy. Intravenous immunoglobulin (0.5–1.0g/kg/dose; repeat in 12 h has been shown to reduce the need for exchange transfusion in both ABO and Rh hemolytic disease, presumably by reducing hemolysis[19,22].

Inhibitors of bilirubin formation: Metalloporphyrins

These are structural anologues of the heme molecule in which the central iron molecule has been replaced with other metallic ions including tin, zinc, manganese and chromium. The metalloporphyrin Sn-mesoporphyrin (SnMP) offers promise as a drug candidate. The proposed mechanism of action is by competitive enzymatic inhibition of the rate limiting conversion of heme-protein to biliverdin (an intermediate metabolite to the production of unconjugated bilirubin) by heme-oxygenase. A single intramuscular dose of 6mg/kg on the 1st day of life may reduce the need for phototherapy. Complications from metalloporphyrins include transient erythema if the infant is receiving phototherapy[19,22].

Bilirubin transport: Albumin infusion

Bilirubin bound to albumin is relatively not harmful, as it cannot diffuse across the blood brain barrier. The amount of free bilirubin (unbound) doubles when TSB level reaches 15-20mg/dl, quadruples at 25mg/dl and increases 8 folds at 30mg/dl. Before an exchange transfusion, one may consider an albumin infusion (1g/kg)[19,22].

Inducers of liver enzymes: phenobarbitone

Phenobarbitone enhances bilirubin clearance by liver by increasing its uptake, increasing the intracellular concentration of ligandin, increasing its conjugation by UDPGT and increasing the excretion of conjugated bilirubin by increasing bile flow[19,22].

The dose is 2.5 to 5 mg/ kg/ day in two divided doses. The main drawback with the use of phenobarbitone is its latent period. It exerts its effect after 1- 3 days and adjuvant therapy in the form of phototherapy is usually required in the first 48 to 72 hours[19,22].

Principle of TcB bilirubinometry

The transcutaneous bilirubin absorbs blue and green light. The Jaundice meter determines the yellowness of the subcutaneous tissue by measuring the difference in the optical densities for light in the blue (450 nm) and green (550 nm) wavelength regions. When the measuring probe is pressed against the sternum or forehead of the infant, the built-in xenon lamp flashes. The light from the xenon lamp passes through the glass fiber and illuminates the skin. The light scatters and is absorbed in the skin and subcutaneous tissue repeatedly, and then finally returns to the sensor side of the glass fiber. The denser the transcutaneous bilirubin, the weaker the reflected blue light. The reflected green light remains unchanged regardless of the density of the bilirubin.

CLINICAL STUDIES

In the study done by Kurnianto et al, 2016 on 150 babies, it was observed that TcB values >5mg/dl correlated with TSB level > 5mg/dl, with 100% sensitivity and 83.3% specificity using JM 105. This cut-off point was obtained from a receiver-operator characteristic (ROC) curve with AUC 99.3% (95%CI 97.9to 100%; $p<0.001$). The correlation coefficient (r) for TSB and TcB measurements on the forehead were 0.897($p< 0.001$).Thus it was concluded that TSB is useful in clinical practice for hyperbilirubinemia as it is a non-invasive method[26].

Varughese et al performed a study on 396 babies in South India comparing the reliability of TcB in different skin colored babies using JM 105. The authors used colour-coded scales to evaluate reliability of TcB in various skin colours. It was observed that the mean TcB was uniformly higher than TSB for all the variables evaluated, which included sex, gestational age, birth weight, and growth of the baby with an excellent correlation (r = 0.698-0.932). Furthermore, it was also observed that TcB had better correlation in light skin tone babies (color code 3) when compared with dark skin tone babies (color code 4) with r= 0.874 and r= 0.856 respectively. The authors concluded that while TcB overestimated the bilirubin levels, it had a good correlation with TSB in lighter skin tone babies[27].

Pendse et al performed a study in 30 preterm neonates with jaundice and compared transcutaneous bilirubin with total serum bilirubin prior to and 12 hours

after initiation of phototherapy. TcB was performed using JM 105 at the level of sternum. The authors reported that TcB had good correlation with TSB following phototherapy (r=0.918, P<0.001). Furthermore, it was also seen that TcB at 28 to 32 weeks of gestation (r = 0.97) had better correlated with TSB than those at 32 to 37 weeks (r =0.88). Similarly, the correlation between TcB and TSB was better for neonates <72 hours old (r =0.96) when compared with those >72 hours of age (r = 0.82). The authors concluded that TcB at the level of sternum has significant correlation with TSB in preterm neonates[28].

Surana et al conducted a study in 160 newborns comparing TcB and TSB levels in neonates. The mean gestational age in the study was 38.23±2.01 weeks; mean birth weight was 2.403±0.61 kg; mean TSB levels were 11.65±4.58 mg/dl and mean TcB levels were 11.73±3.53 mg/dl. The study showed positive and significant correlation between TcB and TSB measurements (r=0.836, r2=0.69, *P*<0.001). The average error in evaluating hyperbilirubinemia with TcB as compared to TSB was 0.856 with limits of agreement between -3.41 to +5.48. The AUC at three TSB levels (>10mg/dl, >12 mg/dl, >15 mg/dl) of TcB were 0.899, 0.937 and 0.963 respectively. ROC analysis showed good sensitivity for all. It was observed that specificity reduced with increasing TSB concentration. The authors concluded that TcB levels correlated significantly with TSB levels with good sensitivity and satisfactory specificity. Thus, TcB can be used as a screening tool for evaluation of hyperbilirubinemia in newborns[29].

A 4-year prospective observational study was conducted by Olusanya et al in 2015 which included 1553 infants with 2107 TcB and TSB measurements to compare discrepancies between TcB and TSB measurements. They also compared the two models of bilirubunometers (Bilicheck and JM 103) in black African population. The authors evaluated the observed divergence of these two bilirubinometers amongst black African population. Divergence of findings provided by BiliChek and JM-103 were further explored through linear regression and Bland-Altman analysis. It was observed that TSB was overestimated by ≥2 mg/dl in 64.5% babies, ≥3 mg/dl in 42.7% babies, and ≥4 mg/dl in 25.7% of babies. Additionally, it was also observed that TSB was underestimated by ≥2 mg/dl in 1.1% of babies, ≥3 mg/dl in0.5% of babies, and ≥4 mg/dl of babies in 0.3% recording. It was observed that amongst other things the type of TcB instrument used was predictive of overestimation of TSB level. The JM-103 was found to have greater imprecision than BiliChek at all TSB levels. The authors concluded that BiliChek and JM-103 bilirubinometers significantly overestimated TSB levels in black African neonates. This may translate to unnecessary or excessive treatment of babies. Therefore, there was need to develop additional bilirubin determination devices especially for Africans[30].

Chimhini et al conducted a study in Zimbabwe involving 283 babies in 2015 to evaluate accuracy of JM 103 for estimating TSB. The authors reported significant correlation between TcB (sternum) and TSB (correlation coefficient, r = 0.77) and between TcB (forehead) and TSB (r = 0.72). The overall sensitivity for TcB sternum was 76%, specificity was 90%, Positive Predictive Value (PPV) was 70% and Negative Predictive Value (NPV) was 92%. Similarly, the overall

sensitivity for TcB (forehead)was 62%, specificity was 95%,PPV was 80% and NPV was 90%. The ROC curves showed that both TcB (sternum) and TcB (forehead) had good correlation without any statistical difference among them (*P*=0.2954). The authors concluded that there is strong positive correlation for both TcB sternum and TcB forehead with serum TSB; however, sternum can be considered a better site when compared with forehead[31].

Leite et al conducted a study to compare TcB values using Bilicheck with capillary plasma bilirubin levels (Unistat bilirubinometer; Leica) in 200 assays. The study evaluated the correlation and agreement between TcB and capillary plasma bilirubin levels. The authors also evaluated the effect of gestational age, birth weight, postnatal age, skin color, and phototherapy for correlation between TcB and capillary plasma bilirubin level. The authors reported a linear correlation coefficient of 0.92. ROC curves showed that TcB values of 14 mg/dl had sensitivity of 88.2%, specificity of 97.8%, PPV of 78.9%, and NPV of 98.9%. The authors concluded that use of TcB using Bilicheck can be considered for capillary plasma bilirubin levels up to 14 mg/dl. In values above 14 mg/dl, Bilicheck was suggested only for screening purpose[32].

In the study on Tc bilirubinometer in assessment of neonatal jaundice, a good correlation was found between TSB levels and TcB over forehead and sternum in infants not exposed to phototherapy. The determined action levels for TcB over forehead and sternum had a sensitivity of 77.8 to 100% in assessing the need for serum bilirubin estimation[33].

A strong correlation between plasma and transcutaneous bilirubin assays measured in the frontal and sternal regions before phototherapy with narrow 95% and 99% confidence intervals was reported by Povaluk et al. It was also reported that the covered sternal areas presented the strongest correlation index 24 hours after phototherapy ($r= 0.86$; $p < 0.001$). The conclusion of the study was that TcB measurement of frontal and sternal areas closely correlated with plasma bilirubin levels before starting phototherapy in jaundiced infants, while after 24 hours of phototherapy, TcB(sternum) measurement showed better correlation[34].

In a study on Turkish newborns, a good correlation between TcB and high pressure liquid chromatography bilirubin (HPLC-B) – ($r=0.85$; 95% CI: 0.76-0.91) was observed. However, with a mean error (HPLC-B minus TcB) of 1.845 mg/dl, TcB measurements underestimated true serum bilirubin levels as estimated by HPLC. Despite having good correlation with HPLC, TcB showed worse performance than bilirubinometer and diazo methods at various clinically relevant HPLC-B cut off values. The cut-off limits providing a sensitivity of 100% for TcB measurements were as follows: TcB ≥9mg/dl for HPLC-B >17, TcB ≥8mg/dl for HPLC-B >15 and HPLC-B >13.The conclusion was that TcB could not be recommended as a complete substitute for TSB measurements since TcB required relatively lower thresholds with false positive results for having a sensitivity of 100%[35].

In a systematic review by Nagar et al on the reliability of TcB devices in preterm infants, it was reported that 2 TcB devices namely, JM103 and BiliCheck

were commonly used. The results were comparable to the forehead site, although JM103 device exhibited better correlation at the sternum. Analysis of Bland Altman plots in 13 studies revealed negligible bias in measurement at the forehead or sternum site by using either of the devices. However, the JM103 device exhibited better precision than the BiliCheck (SD for TcB-TSB differences of 24.3 and 31.98 μmol/L respectively)[36].

In an update on the use of TcB estimation in neonatal hyperbilirubinemia by Kaur et al, it was concluded that implementation of universal bilirubin screening definitely lowered the incidence of hyperbilirubinemia but was also associated with increasing use of phototherapy. While the use of TcB as a non-invasive, painless and bloodless method of screening was accepted in term and near term neonates, its value in preterm neonates needed to be established. It was further commented that TcB cannot be used for making decisions about exchange transfusion and phototherapy as the validity of TcB is accepted till 15mg/dl only[37].

Miguel et al reported a statistically significant correlation between TcB and TSB ($r= 0.81$; $p< 0.001$). The authors found that, with the use of ROC curve, TcB level of 13 mg/dl was the optimal cut-off point for detecting need of treatment, with a sensitivity of 92.9%, specificity of 62.1%, positive predictive value (PPV) of 39% and negative predictive value (NPV) of 97%[38].

A comparison between TcB and TSB measurements in term neonates was studied and the authors found a high correlation (r= 0.89) between the two measurements. The sensitivity and specificity of TcB measurement was 95.1% and 68% respectively for detection of hyperbilirubinemia[39].

A study done by Sadik et al on the comparison between TSB levels and TcB concentration in neonates with jaundice showed that there were no significant differences in TSB and TcB before and after phototherapy. The mean TSB levels and TcB index before phototherapy was 13.40±2.83 mg/dl and 13.49±3.00 mg/dl respectively (P = 0.539). After phototherapy, the mean TSB levels and TCB index was 13.00 ±4.40 and 13.06±2.57 mg/dl respectively (P = 0.769). The study revealed that TcB estimation was comparable to TSB levels before and after phototherapy[40].

METHODOLOGY

This study was conducted in Department of Pediatrics at R. L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College. Eligible newborns (n = 151) who fulfilled inclusion and exclusion criteria and those who came to this hospital during 1-year period (Jan 1st 2017 to December 31st 2017) were prospectively enrolled in the study. The study was approved by the Institutional Ethics Committee of Sri Devaraj Urs Medical College.

INCLUSION CRITERIA

The following were the inclusion criteria:

1. All term and late preterm neonates referred to the neonatal unit with history of jaundice.
2. All term and late preterm neonates in post-natal wards and NICU with evidence of clinical jaundice.

Term neonate is defined as neonate with gestational age ≥ 37 weeks and late preterm neonate is defined as neonate with gestational age of 35 to <37 weeks[22].

EXCLUSION CRITERIA:

The following were the exclusion criteria:

1. Neonates with major congenital anomalies
2. Sick neonates (sepsis, shock, birth asphyxia)
3. Neonates with evidence of liver disease
4. Neonates receiving phototherapy

5. Neonates who had received blood transfusion/ exchange transfusion
6. Neonates with skin disorders

METHOD OF COLLECTION OF DATA

TcB measurements were made with a Tc bilirubinometer “JM-105” by gently pressing against the skin (free of bruises, hair, birth marks and hematoma) over forehead and upper end of sternum. The transcutaneous bilirubin absorbs blue and green light. The Jaundice meter determines the yellowness of the subcutaneous tissue by measuring the difference in the optical densities for light in the blue (450 nm) and green (550 nm) wavelength regions. When the measuring probe is pressed against the sternum or forehead of the infant, the built-in xenon lamp flashes. The light from the xenon lamp passes through the glass fiber and illuminates the skin. The light scatters and is absorbed in the skin and subcutaneous tissue repeatedly, and then finally returns to the sensor side of the glass fiber. The denser the transcutaneous bilirubin, the weaker the reflected blue light. The reflected green light remains unchanged regardless of the density of the bilirubin. Bilirubin concentration displayed digitally on the device screen in mg/dl was taken as TcB level. A total of four TcB measurements were taken (two over the forehead; two over the sternum) and the mean value of each site was recorded. Within 30 minutes of TcB determination, blood sample was drawn in a plain vial for TSB estimation and sent to the laboratory. Precautions were taken to keep the vials away from sunlight to prevent photocoagulation. TSB was estimated in the laboratory by diazotized sulfanilic test.

Correlation between TSB values and TcB measurements at the two sites in the above mentioned groups was determined by applying the SPSS version 21 for statistical analysis. Area under the curve and ROC curves were used to compare the two methods. Cut-off points for "JM-105" in the study group with desirable sensitivity and specificity values for detecting need of treatment was determined. Usefulness of "JM-105" as a diagnostic tool was evaluated by sensitivity and specificity.

STATISTICAL ANALYSIS

The measurable variables were analyzed and interpreted between them by the student's t test and the ordinal and categorical variables between them were interpreted by Chi- square (χ^2) test. The risk factors were interpreted by binary logistic regression. The predictive value of incidence was estimated by the ROC curve. The statistical procedures were performed with the help of an SPSS statistical package (ver 21). *P* value less than 0.05 ($P<0.05$) was considered as statistically significant

RESULTS

This observational clinical study consisted of 151 newborns with jaundice. Table 2 gives gender wise distribution of jaundice. There were 58 females (38.4%) and 93 males (61.6%) with a male-to-female ratio of 1.6:1 (Figure 4).

Table 2. Gender-wise Distribution of Cases with Neonatal Jaundice

Gender	Frequency	Percent
Female	58	38.4
Male	93	61.6
Total	151	100.0

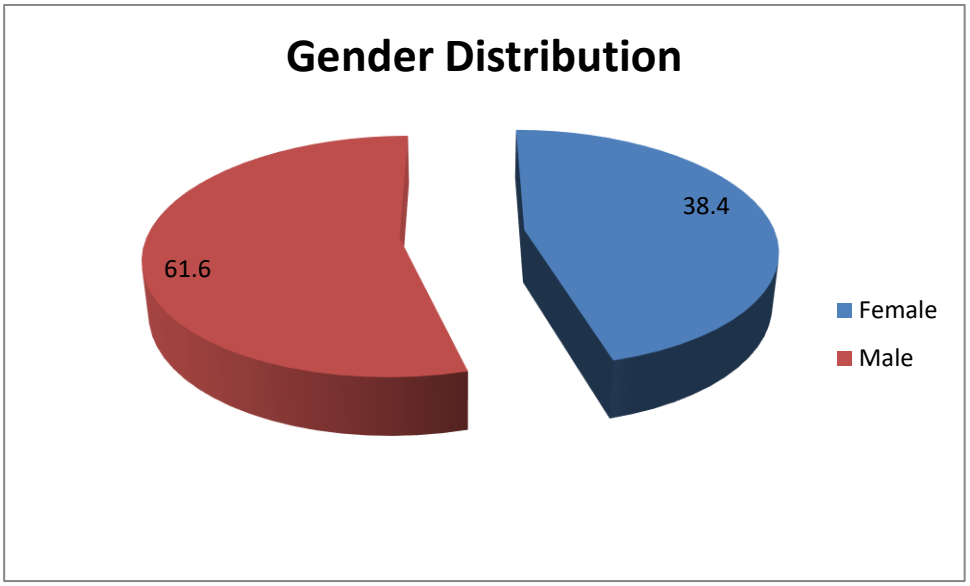

Figure 4. Pie chart depicting gender-wise distribution of cases with neonatal jaundice.

The gestational age ranged from 34 to 42 weeks (mean 38.36 ± 1.3 weeks) with bodyweight ranging from 2100 g to 3920 g (mean 2825 g ± 477 g). The TSB levels ranged between 5.20 mg/dl to 21.40 mg/dl (mean 12.35 ± 2.47 mg/dl). The range for various TcB readings at forehead and sternum are shown in Table 3with forehead 1 depicting 1stTcB value and forehead 2 depicting second TcB value at forehead. Similarly, 1st sternum measurement was depicted as sternum 1 and 2nd sternal measurement as sternum 2. The range of TcB values at forehead 1 was 6.2 to 22.40 mg/dl, forehead 2 was 6 to 22.2 mg/dl, sternum 1 was 5.5 to 21.8 mg/dl and sternum 2 was 5.4 to 21.5 mg/dl.

Table 3. Baseline Characteristics in Newborns.

Parameters	**N**	**Minimum**	**Maximum**	**Mean**	**SD**
Weight	151	2.10	3.92	2.8254	.47716
Gestational Age	151	34.00	42.00	38.3642	1.31394
TSB level (in mg/dl)	151	5.20	21.40	12.3523	2.47302
TCB level forehead 1 (mg/dl)	151	6.20	22.40	13.0172	2.67112
TCB level forehead 2(mg/dl)	151	6.00	22.20	13.0397	2.68490
TCB level sternum 1(mg/dl)	151	5.50	21.80	12.7834	2.63582
TCB level sternum 2(mg/dl)	151	5.40	21.50	12.7318	2.59637
N = no of patients; SD = standard deviation; TCB = transcutaneous bilirubin; TSB = total serum bilirubin; TCB forehead 1 = first reading at forehead by TCB; TCB forehead 2 = second reading at forehead by TCB; TCB sternum 1 = first reading at sternum by TCB; TCB 2 = second reading at sternum by TCB					

Table 4. Frequency of Neonates with Jaundice in Relation to Maternal Blood Group.

Maternal Blood Group	Frequency	Percent
A Positive	29	19.2
AB Positive	8	5.3
B Negative	6	4.0
B Positive	48	31.8
O Positive	60	39.7
Total	151	100.0

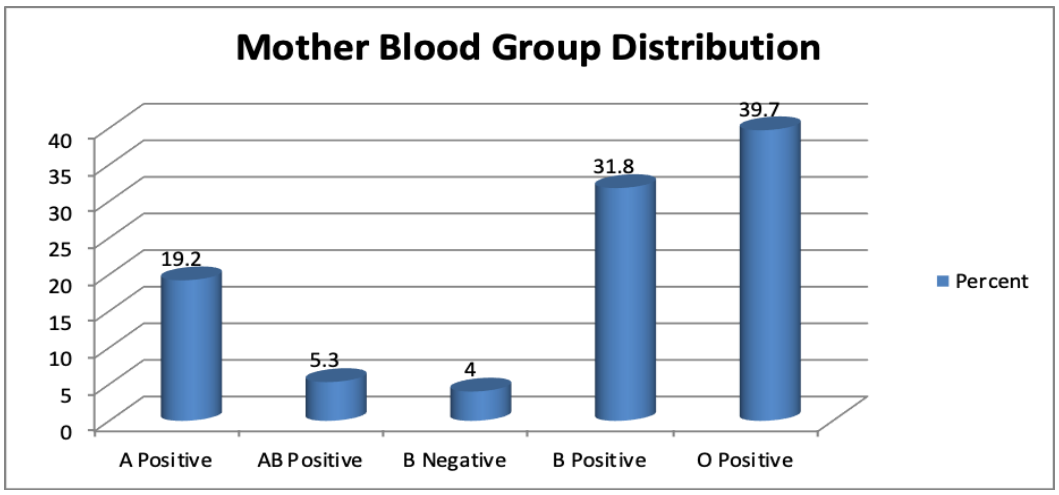

Figure 5. Percentage of neonates with jaundice in relation to maternal blood group.

It can be seen from Table 4 and Figure 5 that O positive was the commonest maternal blood group associated with jaundice in 60 babies (39.7%) followed by B positive in 31.8% (n = 48), A positive in 19.2% (n = 29), AB positive in 5.3% (n = 8) and lastly B negative in 4% (n = 6).

Table 5. Distribution of Neonates with Jaundice in Relation to Neonatal Blood Group.

Baby Blood Group	Frequency	Percent
A Negative	1	0.7
A Positive	29	19.2
AB Positive	8	5.3
B Negative	2	1.3
B Positive	43	28.5
O Negative	2	1.3
O Positive	66	43.7
Total	**151**	**100.0**

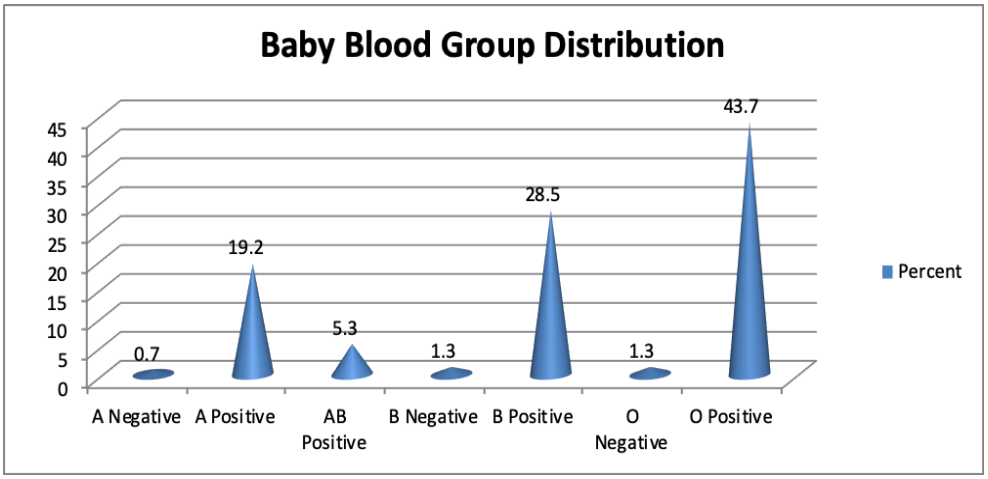

Figure 6. Distribution of neonates with jaundice in relation to neonatal blood group.

Table 5 and Figure 6 depict the relationship between jaundice and neonatal blood group. The commonest neonatal blood group associated with jaundice was O positive (43.7%) followed by B positive (28.5%), A positive (19.2%), AB positive (5.3%),O negative (1.3%), B negative (1.3%) and A negative (0.7%)

Table 6. Distribution of Cases with Neonatal Jaundice Based on Site of Appearance

Site of appearance	**Frequency**	**Percent**
Abdomen	9	6.0
Chest	1	0.7
Limbs	102	67.55
Palms/soles	39	25.83
Total	**151**	**100.0**

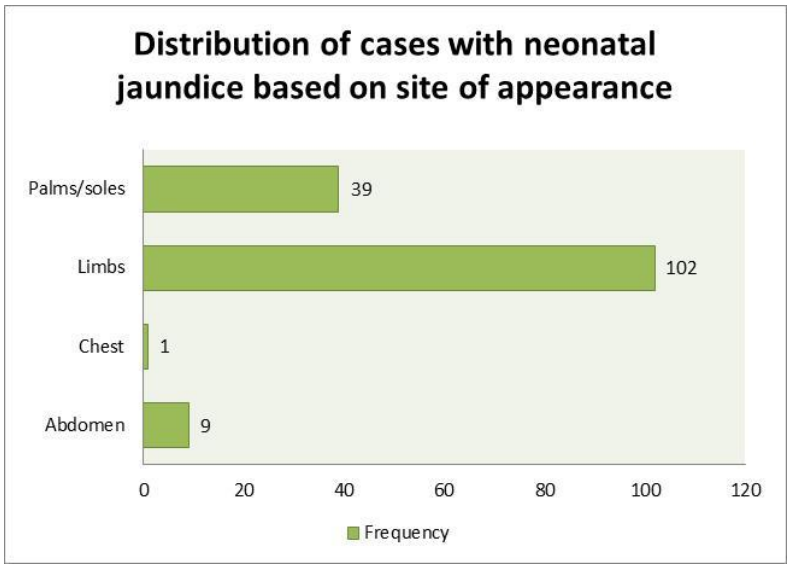

Figure 7. Distribution of cases with neonatal jaundice based on site of appearance.

It can be seen from Table 6 and Figure 7 that limbs were the commonest site for appearance of jaundice in 102 babies (67.55%) followed by palms/soles (n = 39; 25.8%), abdomen (n = 9; 6%), and chest (n = 1;0.7 %).

Table 7. Distribution of Cases of Neonatal Jaundice According to Gestation and Birth Weight

Study group	Frequency	Percent
Late Preterm AGA	13	8.61
Late Preterm SGA	2	1.32
Term AGA	127	84.11
Term SGA	9	5.96
Total	151	100.0

AGA = appropriate for gestational age; SGA = small for gestational age

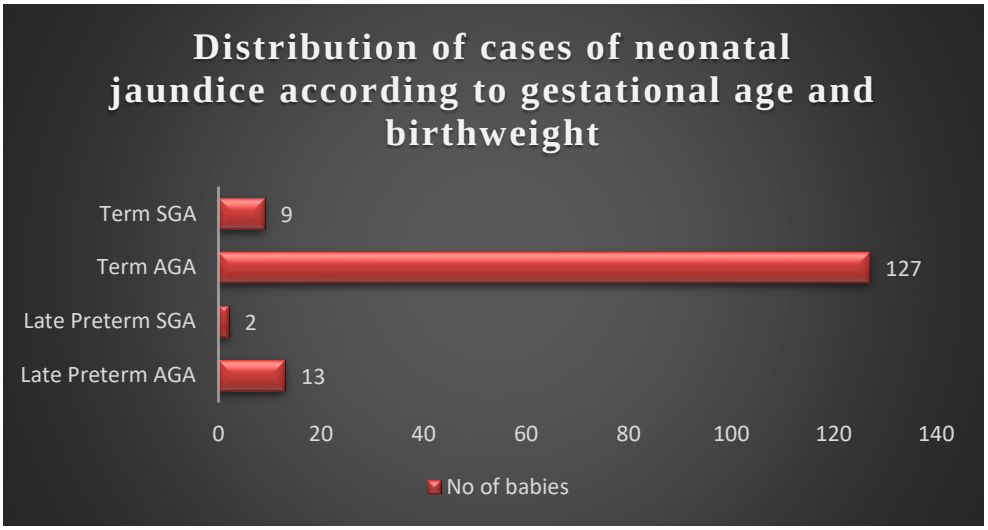

Figure 8. Distribution of cases of neonatal jaundice according to gestation and birth weight.

Table 7 and Figure 8 depict the distribution of cases of neonatal jaundice according to gestation and birth weight. Term/AGA (appropriate for gestational age) was the commonest group associated with neonatal jaundice in 127 babies (84.1%) followed by Late Preterm/AGA (n = 13; 8.61%), Term/SGA (n = 9; 5.96%) and Late Preterm/SGA (n = 2; 1.32%).

Table 8. Comparison between TSB Levels and TcB Levels on Forehead and Sternum

Group Statistics						
	Group	N	Mean	SD	t-statistic	*P* value
Score	TSB	151	12.3523	2.47302	-2.283	0.023 (S)
	TcB Forehead	151	13.0285	2.66756		
Score	TSB	151	12.3523	2.47302	-1.387	0.167 (NS)
	TcB Sternum	151	12.7576	2.60471		

N = number of patients, NS = not significant; S = significant; TcB = transcutaneous bilirubin; TSB = total serum bilirubin; all values in mg/dl

Table 8 shows the mean serum bilirubin with TSB levels and TcB levels (over forehead and sternum). The mean TSB level was 12.3523 mg/dl with a standard deviation of 2.47302 mg/dl. The mean TcB forehead value was 13.0285 mg/dl with a standard deviation of 2.66756 mg/dl. Mean TcB level over sternum was 12.7576 mg/dl with a standard deviation of 2.60471 mg/dl. The difference between TSB and TcB (forehead) levels was statistically significant (P = 0.23). However, the difference between TSB and TcB (sternum) levels was not statistically significant (P = 0.167). This shows that TcB sternum correlates closely with TSB. Although the difference between TcB forehead and TSB was significant, numerically, the values were similar.

Table 9. Comparison between TcB Values Over Forehead and Sternum

Paired Samples Statistics		N	Mean	SD	Paired t-test statistic	*P*-value
Pair 1	TcB level forehead 1	151	13.0172	2.67112	-0.585	0.559 (NS)
	TcB level forehead 2	151	13.0397	2.68490		
Pair 2	TcB level sternum 1	151	12.7834	2.63582	1.298	0.196 (NS)
	TcB level sternum2	151	12.7318	2.59637		
N = No of patients; NS = not significant; SD = standard deviation; TcB transcutaneous bilirubin; all values in mg/dl						

Table 9 shows comparison between TcB levels over forehead 1 and forehead 2 and TcB levels between sternum 1 and sternum 2. The mean TcB levels at forehead 1 and 2 were 13.0172 ± 2.67112 mg/dl (mean ± SD) and 13.0397 ± 2.6849 mg/dl (mean ± SD), which was not statistically different ($P = 0.559$). Similarly, the mean TcB levels at sternum 1 and 2 were 12.7834 ± 2.635 mg/dl (mean ± SD) and 12.7318 ± 2.596 mg/dl (mean ± SD), again the difference was not statistically significant ($P = 0.196$).This suggests that there is no significant difference between the various TcB values taken over forehead and various TcB values taken over sternum. This could also indicate that a single TcB reading at sternum or forehead may be sufficient.

Table 10. Karl Pearson's Correlation Coefficient between TSB level and TcB levels

TCB Levels 2 sides	TSB level		
	N	Pearson's Coefficient	*P* value
TCB level forehead 1	151	.922	.000*
TCB level forehead 2	151	.927	.000*
TCB level sternum 1	151	.935	.000*
TCB level sternum 2	151	.946	.000*
*Correlation is significant at the 0.01 level (2-tailed).			

Table 10 shows the Karl Pearson's correlation coefficients between TSB levels with two set of TcB levels over forehead and sternum. It can be seen that there is a strong correlation between TSB levels and that of TcB levels over forehead and TcB levels over sternum. The *P*-value is significantly correlated at 99 percent level of significance. This suggests that TcB levels at individual sites correlate with TSB levels. Figure 9 shows the scatter diagrams showing significant correlation between TSB levels and TcB levels at individual sites (forehead 1, forehead 2, sternum 1 and sternum 2).

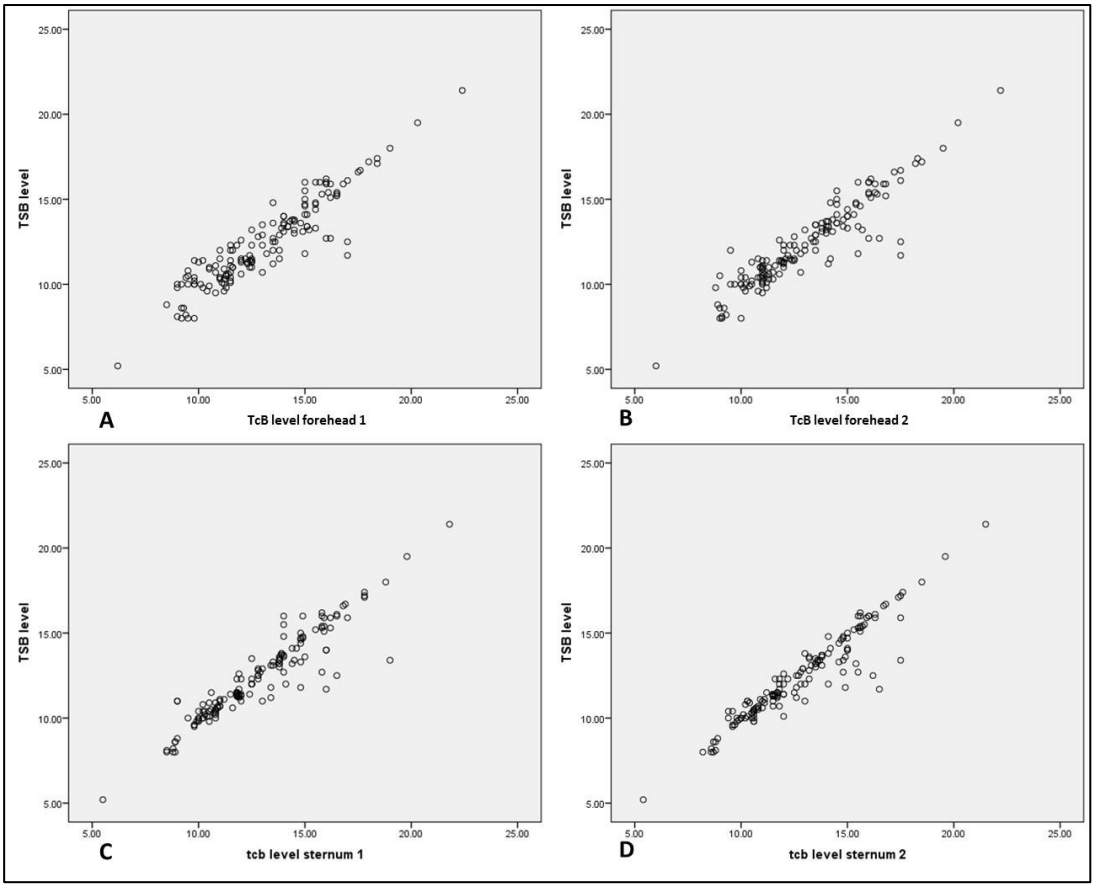

Figure 9. Scatter diagrams showing correlation between TSB level and individual TcB levels. A) Correlation between TSB level and TcB level forehead 1. B) Correlation between TSB level and TcB level forehead 2. C) Correlation between TSB level and TcB level sternum 1. D) Correlation between TSB level and TcB levels over sternum 2.

Figure 9 shows correlation TSB levels and individual TcB levels. There was strong linear correlation of approximately 92.2% between TSB level and TcB level forehead 1 (Figure 9-A). There was also strong linear correlation of approximately 92.7% between TSB level and TcB level forehead 2 (Figure 9-B). Similarly, there was strong linear correlation of approximately 93.5% between TSB level and TcB level sternum 1 (Figure 9-C). Lastly, a strong linear correlation of approximately 94.6% was found between TSB level and TcB levels over sternum 2 (Figure 9-D). It can be inferred

from the ROC curves that individual TcB measurements over sternum and forehead correlate well with TSB values. Thus, any single value of TcB can be considered significant.

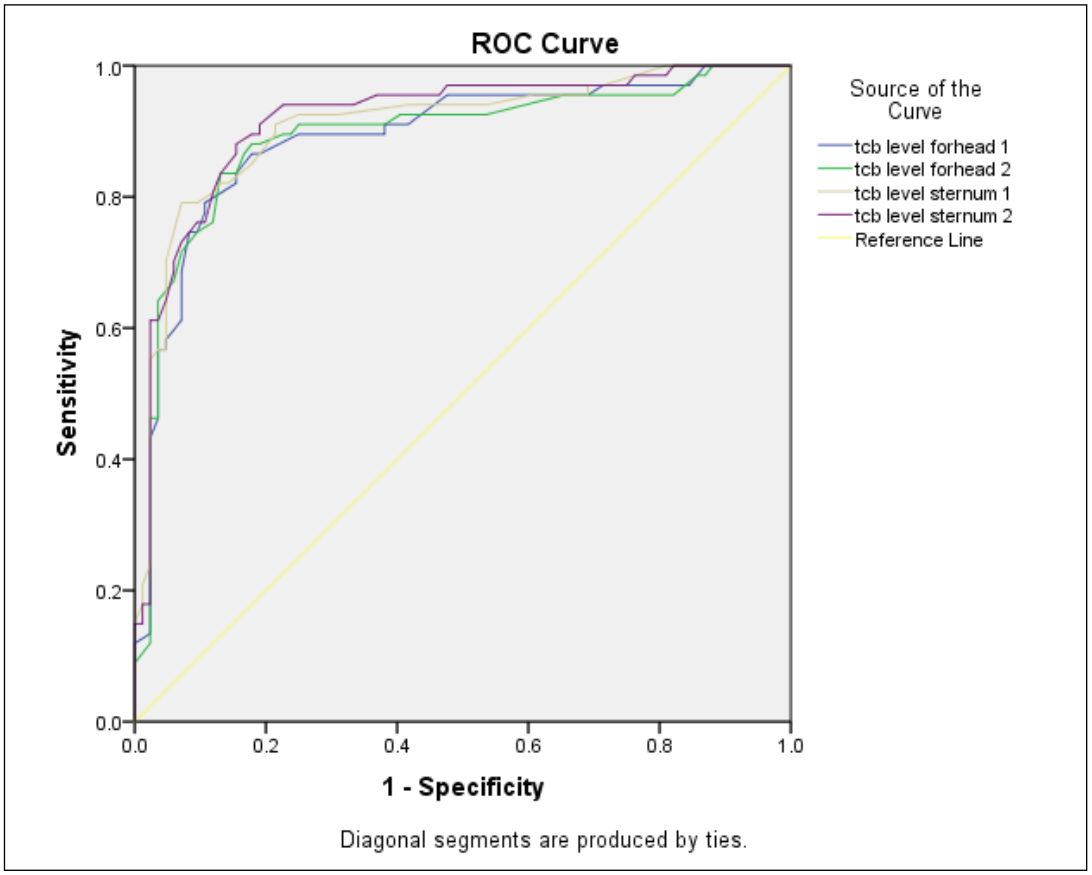

Figure 10. ROC curves for TcB levels at forehead 1, forehead 2, sternum 1 and sternum 2.

Table 11. Area Under Curve Statistics for TcB Level at Forehead 1, Forehead 2, Sternum 1 and Sternum 2.

Test Result Variable(s)	**Area**	**Std. Error[a]**	**Asymptotic Sig.[b]**	**Asymptotic 95% CI**	
				Lower Bound	**Upper Bound**
TcB level forehead 1	.892	.028	.000	.836	.947
TcB level forehead 2	.891	.029	.000	.834	.949
TcB level sternum 1	.909	.026	.000	.858	.959
TcB level sternum 2	.918	.024	.000	.870	.965
The test result variable(s): TcB level forehead 1, TcB level forehead 2, TcB level sternum 1, and TcB level sternum 2 has at least one tie between the positive actual state group and the negative actual state group. [a]Under the nonparametric assumption [b]Null hypothesis: true area = 0.5					

Table 11 shows area under curve statistics for the TcB measurements done at different sites viz. forehead 1, forehead 2, sternum 1 and sternum 2. The AUC for forehead 1 was 0.892 (95% CI: 0.836 to 0.947), AUC for forehead 2 was 0.891 (95% CI: 0.834 to 0.949), AUC for sternum 1 was 0.909 (95% CI: 0.858 to 0.959) and AUC for sternum 2 was 0.918 (95% CI: 0.870 to 0.965).

Table 12. Co-ordinates of Curve Representing optimum values of two set of TCB forehead and two set of TCB sternum

Test Result Variable(s)	Positive if ≥ To[a]	Sensitivity	1 - Specificity
TCB level forehead 1	12.9000	.866	.179
TCB level forehead 2	13.4500	.836	.131
TCB level sternum 1	13.2000	.806	.119
TCB level sternum 2	12.8500	.851	.143

The test result variable(s): TCB level forehead 2, TCB level sternum 1, TCB level sternum 2 has at least one tie between the positive actual state group and the negative actual state group.

[a]The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

All values in mg/dl

Table 12 shows the optimal cut off values for individual TcB measurements at forehead 1, forehead 2, sternum 1 and sternum 2, which show high sensitivity and specificity. ROC curves (Figure 10) suggested the cutoff values of sensitivity and specificity for two TcB level of forehead and two TcB level of sternum. It was found the that sensitivity for TcB level of first forehead was approximately 86.6% and specificity with 82.1% (cut off value 12.9 mg/dl) and for TcB level of second forehead is approximately 83.6% and specificity with 87.9% (cut off value 13.45 mg/dl). The sensitivity and specificity for TcB level of sternum first was 80.6% and 88.1% respectively (cut off value 13.2 mg/dl). The sensitivity and specificity for TCB level of sternum second was 85.1% and 85.7% respectively (cut off value 12.85 mg/dl). This suggests that TcB measurement at sternum and forehead have high sensitivity and specificity comparable with TSB measurements for diagnosis of neonatal jaundice.

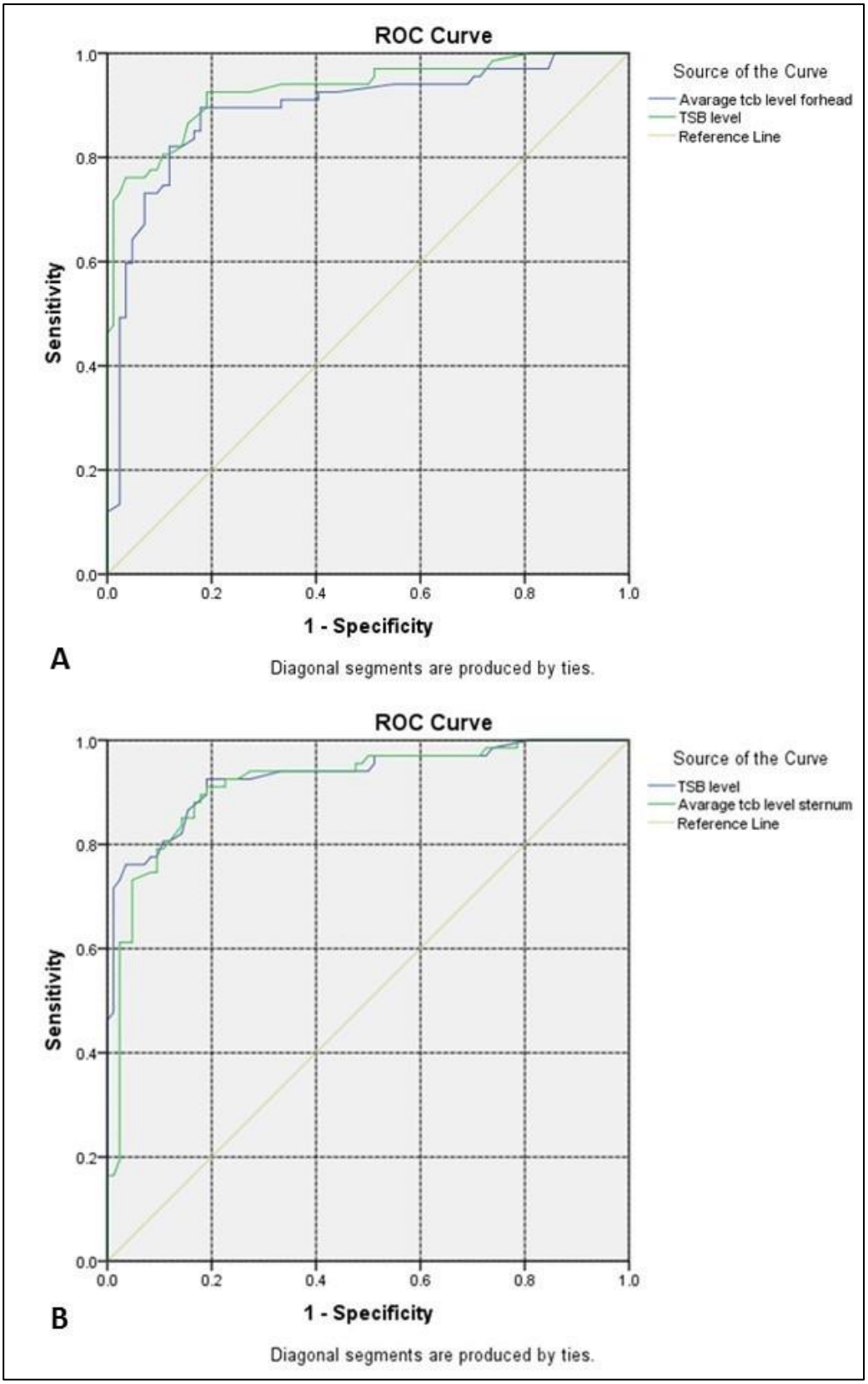

Figure 11. ROC curves for TSB level and average TcB levels at (A) forehead and (B) sternum.

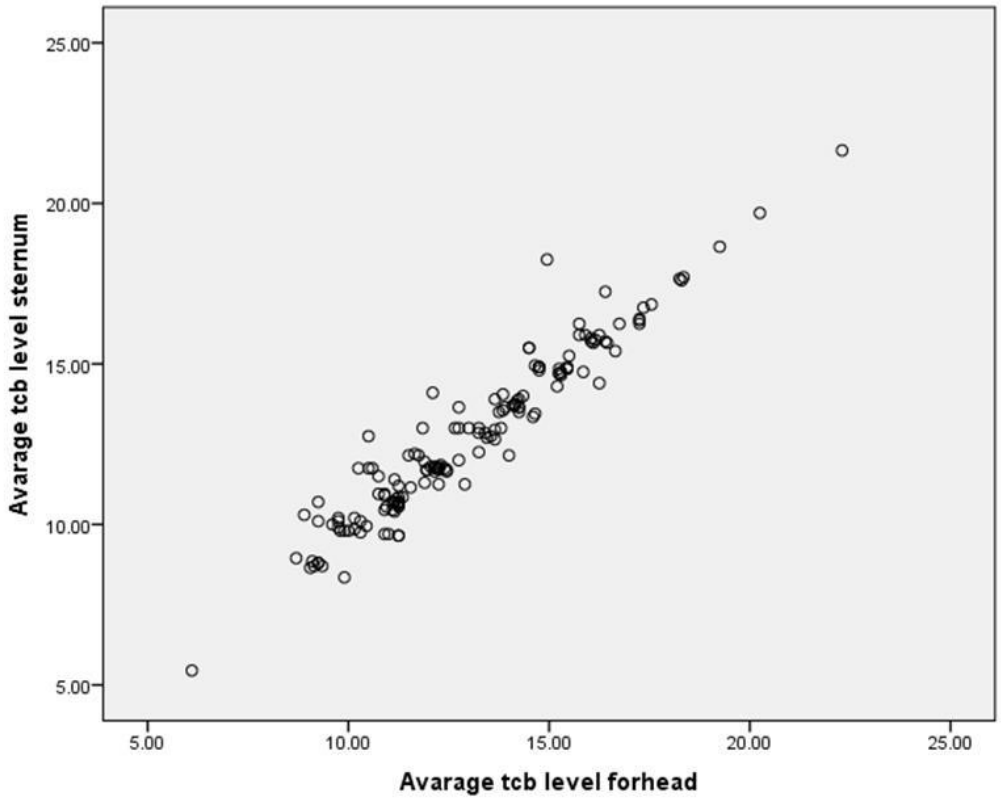

Figure 12. Scatter diagram showing linear correlation between TcB levels at sternum and TcB levels at forehead.

TcB values at the sites of sternum and forehead were compared (Figure 12). There was a strong linear correlation of 0.960 (Pearson correlation at 5% level of significance) between average TcB values at sternum and forehead. This suggested that there was no significant difference between TcB values taken at sternum and forehead.

Table 13. Comparison Between Average TcB levels at Forehead and Sternum with Gestational Age Group.

Average TcB level	Gestational Age Group	N	Mean	SD	Significance
Forehead	34 - <37 Weeks	15	13.2338	2.25011	P = 0.612 (NS)
	≥37 Weeks	136	12.9688	2.78304	
Sternum	34 - <37 Weeks	15	12.9235	2.19891	P = 0.675 (NS)
	≥37 Weeks	136	12.7094	2.71792	

Table 13 shows the comparison between average TcB levels over forehead and sternum and the correlation with gestational age group. It can be seen from the table that there was no statistically significant difference between average TcB levels over forehead in gestational age group of <37 weeks and ≥ 37 weeks ($P = 0.612$). Similarly, there was no statistically significant difference between average TcB levels over sternum in gestational age group of <37 weeks and ≥ 37 weeks ($P = 0.675$). This shows that there was no statistically significant difference in TcB levels at sternum or forehead and there was also no statistically significant difference between TcB levels based on gestational age.

Table 14. Association of Gestational Age and Phototherapy Status

Gestational Group		**Intervention**		**Total**
		No Phototherapy	Phototherapy Given	
34 – <37 Weeks	Count	7	8	15
	% of Total	4.64%	5.30%	9.93%
≥ 37 Weeks	Count	77	59	136
	% of Total	50.99%	39.07%	90.07%
Total	Count	84	67	151
	% of Total	55.60%	44.40%	100.00%

As seen in Table 14 Phototherapy was given to 67 babies (44.4%) in our study. It was observed that 8 babies of total 15 babies with gestational age 34 to 37 weeks received phototherapy (53.33%) and 59 babies of total 136 babies (43.38%) with gestational age ≥ 37 weeks received phototherapy. There was no statistically significant difference in terms of gestational age and phototherapy (P = 0.461).

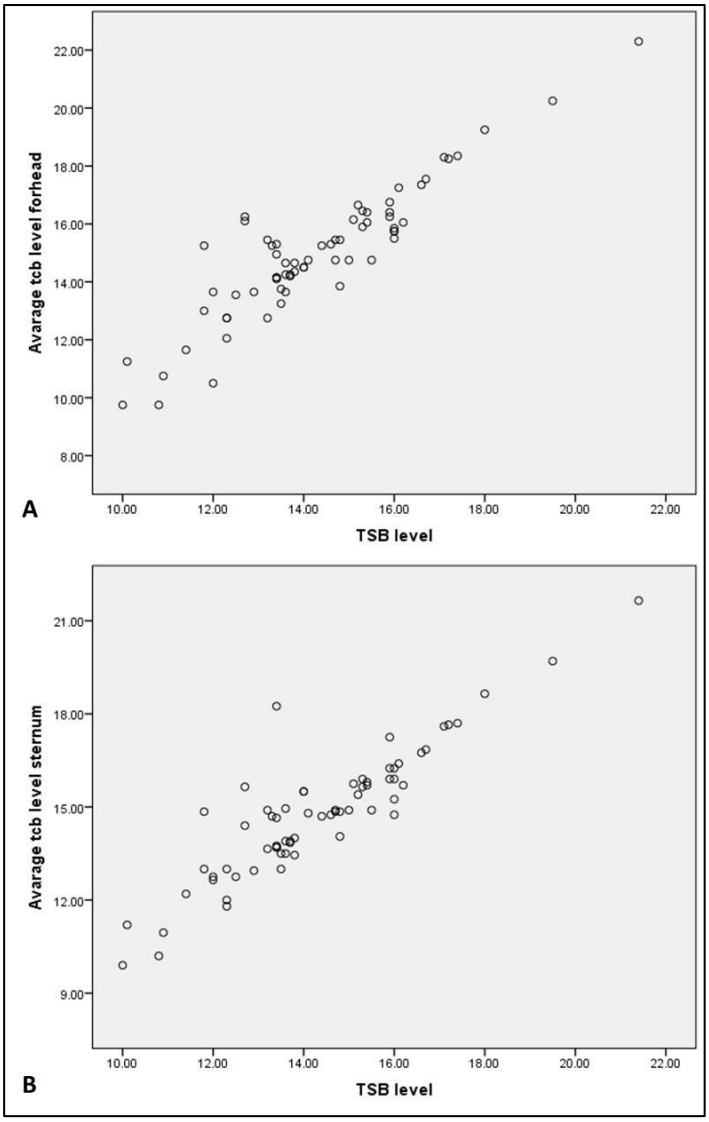

Figure 13. Comparison between average TcB values at (A) forehead and (B) sternum with TSB level in neonates undergoing phototherapy.

Figure 13 shows correlation between average TcB values at the level of forehead and sternum with average TSB levels in neonates who underwent phototherapy. There was a strong linear positive linear correlation between average TSB values with average TcB values over forehead (Karl Pearson's correlation value 0.911) and average TSB value with average TcB values over sternum (Karl Pearson's correlation value 0.901).

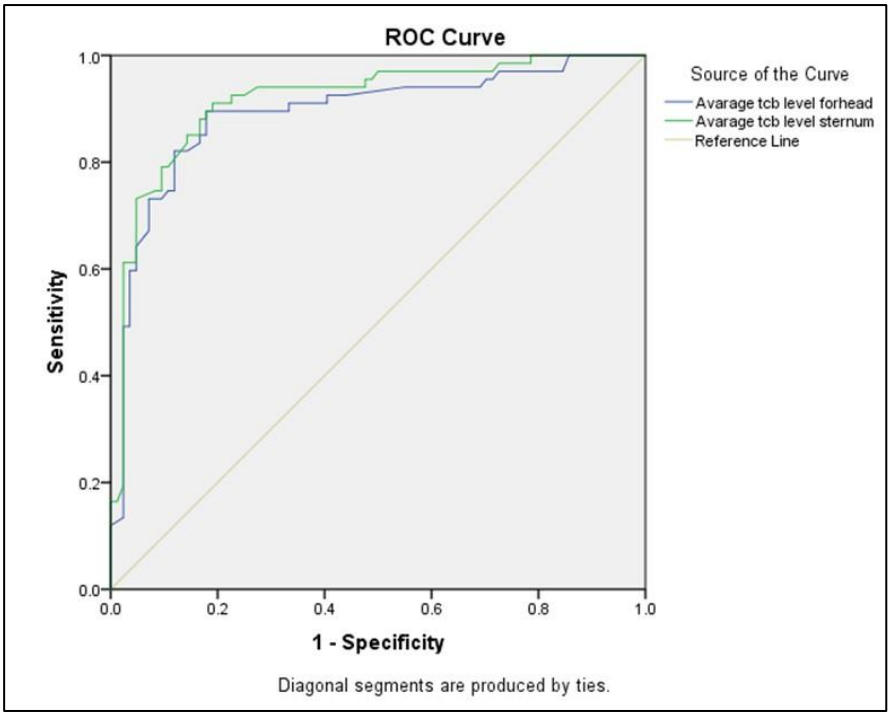

Figure 14. Area under curve statistics comparing average TcB values over forehead and sternum with TSB values in neonates undergoing phototherapy.

Figure 14 shows AUC plot comparing average TcB values over forehead and sternum with TSB values in neonates undergoing phototherapy. The AUC for average TcB values over forehead was 0.891 (95% CI: 0.835 to 0.948) when compared with TSB levels, which showed strong correlation between TcB value over forehead with TSB levels. Similarly, the AUC for average TcB values over sternum was 0.916 (95% CI: 0.869 to 0.963), suggestive of strong correlation between TcB value over sternum with TSB levels.

Table 15. Overall Values of TSB, TcB (Forehead) and TcB (Sternum) to Beyond Which Phototherapy is Indicated

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	Specificity
Average TcB level forehead	12.0000	.910	.667
TSB level	11.3500	.940	.665
Average TcB level sternum	11.9750	.925	.774
TSB level	11.7500	.925	.810

[a]The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Overall, it was observed that average TcB level ≥ 12.00 mg/dl at forehead showed sensitivity of 91% and specificity of 66.7%beyond which phototherapy is indicated, whereas TSB level ≥ 11.35 mg/dl showed sensitivity of 94% and specificity of 66.5% for the same. Similarly, average TcB level ≥ 11.975 mg/dl at sternum showed sensitivity of 92.5% and specificity of 77.4% beyond which phototherapy is indicated and TSB level of ≥ 11.75 mg/dl showed sensitivity of 92.5% and specificity of 81% for the same. It was concluded that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of neonatal jaundice, beyond which phototherapy is indicated and is comparable to TSB levels (Figure 11 and Table 15).

DISCUSSION

Hyperbilirubinemia is the most common condition requiring evaluation and treatment in newborns[13].Neonatal hyperbilirubinemia is a frequent problem as neonatal jaundice affects 60% of full-term infants and 80% of preterm infants in the first three days of life. Although transient, the condition accounts for up to 75% of hospital readmission in the first week after birth[15].TcB measurement as a screening tool for estimation of neonatal hyperbilirubinemia is based on assumption that serum and tissue bilirubin are in constant equilibrium[16].TcB works by determining the intensity of specific wave length bands which are reflected from the skin of neonate[16].

In our study of 151 patients we compared the efficacy of TcB at the level of forehead and sternum with TSB, which is the currently accepted standard technique for determining serum bilirubin.

In our study there were 58 females (38.4%) and 93 males (61.6%) with a male to female ratio 1.6:1. Our results are similar to data reported by Kurnianto et al, who in their study of 150 Asian origin infants also reported similar distribution of male and female infants (54.7% and 45.3% respectively)[26]. A similar observation was also made by Varughese et al[27] and Surana et al[29].

The gestational age ranged from 35 to 42 weeks (mean 38.36 ± 1.3 weeks) with bodyweight ranging from 2100 g to 3920 g (mean 2825 g ± 477 g).

Our results are comparable to findings reported by Olusanya et al, who reported the average gestational age to be 38.18 ± 1.62 weeks[30]. Surana et al also reported mean gestational age of 38.23 ± 2.01 weeks[29]. A similar birthweight was also reported by Varughese et al and Kurnianto et al[26,27]. Surana et al however reported a mean lower birthweight in their study (2.403 ± 0.61 kg)[29].

O positive was the commonest maternal blood group associated with neonatal jaundice in 60 babies (39.7%) followed by B positive (n = 48; 31.8%), A positive (n = 29; 19.2%), AB positive (n = 8; 5.3%) and lastly B negative (n = 6; 4%).

The higher percentage of maternal blood group O and B are not surprising considering O positive is the commonest blood group in general population. A multicentric study by Agrawal et al showed that O is the commonest blood group among south Indians (38.99%) followed by B (33.07%), A (20.68%) and lastly AB (6.25%). The percentage of Rh-negative cases is very less (6.08%) among south Indians[41].

In our study, the TSB levels ranged between 5.20 mg/dl and 21.40 mg/dl (mean 12.35 ± 2.47 mg/dl). The range of TcB values at forehead 1 was 6.2 to 22.40 mg/dl,

forehead 2 was 6 to 22.2 mg/dl, sternum 1 was 5.5 to 21.8 mg/dl and sternum 2 was 5.4 to 21.5 mg/dl.

Our findings are slightly different from study performed by Surana et al, who reported TSB levels ranging from 4.9 to 21 mg/dl and TcB levels ranging from 3.9 to 19.5 mg/dl[29]. However, Chimhini et al reported a wide variability in neonatal bilirubin levels with TSB (range 4.96 to 23.85 mg/dl), TcB forehead (9.93 to 31.8 mg/dl) and TcB sternum (6.95 to 29.81 mg/dl). The wide variation could be attributed to the different patient ethnicity in the Chimhini study, which was conducted in Zimbabwe[31]. Additionally, these studies used JM 103 as opposed to JM 105, used in our study[29,31]. The older version could also be the culprit showing wide variability in TcB values. JM 105 has been reported to eliminate the interfering factors that affect spectral reflectance from skin such as skin pigmentation and dermal maturity. Kurnianto et al, reported TSB range from 4.15 to 21.66 mg/dl, TcB forehead range from 4.03 to 19.5 mg/dl and TcB sternum range from 4.3 to 19.83 mg/dl, which was performed using JM 105. They also reported good correlation with TSB and TcB at forehead and sternum (correlation coefficient, r = 0.897 and 0.891 respectively, $P< 0.01$), which could be attributed to use of JM 105[26].

In our study, jaundice was more common in term/AGA babies (84.11%) followed by late preterm/AGA babies (8.61%), term/SGA babies (5.96%) and lastly late preterm/SGA babies (1.32%).

Surana et al also reported majority of term babies in their studies (n = 129/160; 80.625%) and remaining babies were preterm[29]. Varughese et al also found that incidence of hyperbilirubinemia was more common among AGA babies (n = 396; 88%), followed by SGA (n = 52; 11.6%) and lastly LGA (large for gestational age) in 2 babies (n = 0.2%; negligible)[27]. This is important considering this study was performed in South Indian population.

The serum bilirubin levels as per TSB were 12.3523 ± 2.47302 mg/dl (mean ± SD), per TcB forehead was 13.0285 ± 2.66756 mg/dl (mean ± SD) and per TcB sternum was 12.7576 ± 2.60471 mg/dl (mean ± SD). The difference between TSB and TcB forehead levels was statistically significant ($P = 0.23$), whereas the difference between TSB and TcB sternum was not statistically significant ($P = 0.167$). This shows that TcB sternum correlates closely with TSB. Although the difference between TcB forehead and TSB was significant, numerically, the values were similar.

Our findings are similar to that reported by Ho et al, who reported a higher correlation with TcB at sternum to TSB levels (coefficient 0.814) when compared with TcB at forehead to TSB levels (coefficient 0.718)[42]. Pendse et al in their study also reported excellent correlation with TcB at sternum using JM105 and TSB levels ($P<0.001$)[28].

There was no statistically significant difference between average TcB levels over forehead in gestational age group of <37 weeks and ≥ 37 weeks (P = 0.612). Similarly, there was no statistically significant difference between average TcB levels over sternum in gestational age group of <37 weeks and ≥ 37 weeks (P = 0.675). This shows that there was no statistically significant difference in TcB levels at sternum or forehead and there was also no statistically significant difference between TcB levels based on gestational age. There was also no statistically significant difference between gestational age and phototherapy. There was a strong linear positive linear correlation between average TSB values with average TcB values over forehead (Karl Pearson's correlation value 0.911) and average TSB value with average TcB values over sternum (Karl Pearson's correlation value 0.901).

Overall, it was observed that average TcB level ≥ 12.00 mg/dl at forehead showed sensitivity of 91% and specificity of 66.7% beyond which phototherapy is indicated, while TSB level ≥ 11.35 mg/dl showed sensitivity of 94% and specificity of 66.5% for the same. Similarly, average TcB level ≥ 11.975 mg/dl at sternum showed sensitivity of 92.5% and specificity of 77.4% beyond which phototherapy is indicated and TSB level of ≥ 11.75 mg/dl showed sensitivity of 92.5% and specificity of 81% for the same. It was concluded that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of neonatal jaundice, beyond which phototherapy is indicated and is comparable to TSB levels.

Different studies have reported good correlation coefficient (r) between TcB and TSB from 0.87 to 0.92 in babies with neonatal jaundice[29].

It is also interesting to note that TcB and TSB may evaluate different physiologic changes. While TcB determines the bilirubin that has migrated from serum into tissue, laboratory-based methods such as TSB determine the bilirubin circulating in blood. It is therefore possible that TcB can provide additional information provided by TSB; however, this hypothesis is yet to be proven[26].

Our study had certain limitations. It was performed in a single tertiary care hospital and not population-based study. We also did not include babies undergoing phototherapy, which would have demonstrated the performance of TcB at forehead and sternum with TSB levels in these babies. We also did not evaluate the performance of JM 105 in children with skin disorders as we hypothesized that it could affect the spectral reflectance and alter the results.

CONCLUSION

We conclude that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of hyperbilirubinemia and is comparable to TSB. TcB at the level of sternum and forehead can be considered as an accurate non-invasive tool for diagnosis and estimation of neonatal hyperbilirubinemia. Furthermore, it is easy to perform and presents little clinical challenge in day-to-day practice.

SUMMARY

Hyperbilirubinaemia, presenting as jaundice, is a ubiquitous and frequently benign condition in newborn babies. Mostly about 85% of term newborns and premature infants develop jaundice. Newborn jaundice occurs in up to 85% of all live births. In the absence of haemolysis, sepsis, birth trauma or prematurity, it usually resolves within 3–5 days without significant complications. However, epidemiological evidence suggests that severe neonatal jaundice results in substantial morbidity and mortality. Visual assessment of neonatal jaundice is known to be unreliable and determination of serum bilirubin (SB) is, after the routine screening for inborn errors, the most frequent reason for blood draws in neonates. Although the use of transcutaneous bilirubin (TcB) measurement is a valid method for determination of the severity of jaundice and is used in increasing frequency, its use is still not widespread worldwide yet. Recently, it has been shown that the use of TcB can be applied reliably in preterm infants with gestational age of 28 to 35 weeks as well, emerging the question of what reduction in blood draws can be achieved in this group of neonates.

This study was performed to measure TSB by using lab method, to measure TcB by using JM -105 bilirubinometer, to compare the values of both methods and to establish cut off values using JM-105.

The cross-sectional observational study was conducted in the postnatal wards and NICU of R. L. Jalappa Hospital & Research Centre, Kolar for a period of one year

from Jan 1st 2017 to December 31st 2017. Neonates with clinical jaundice fulfilling the inclusion criteria were enrolled in the study after obtaining informed consent from the parents. A detailed correlation between TSB values and TcB measurements at the two sites in forehead and sternum were evaluated. Study subjects were divided into 4 groups based on weight and gestational age as follows: term appropriate for gestational age (AGA), term small for gestational age (SGA), preterm AGA and preterm SGA. TcB measurements were made with a Tc bilirubinometer "JM-105" by gently pressing against the skin (free of bruises, hair, birth marks and hematoma) over forehead and upper end of sternum. The jaundice meter determines the yellowness of the subcutaneous tissue by measuring the difference in the optical densities for light in the blue (450 nm) and green (550 nm) wavelength regions. Bilirubin concentration was displayed digitally on the device screen in mg/dl. A total of 4 TcB measurements were taken (two over the forehead; two over the sternum) and the mean value of each site was recorded. Within 30 minutes of TcB determination, blood sample was drawn in a plain vial for TSB estimation and sent to laboratory. Precautions were taken to keep the vials away from sunlight to prevent photocoagulation. TSB was estimated in the laboratory by diazotized sulfanilic test. Correlation between TSB values and TcB measurements at the two sites were performed. Cut-off points for "JM-105" with desirable sensitivity and specificity values for detecting need of treatment were determined.

Usefulness of "JM- 105" as a diagnostic tool was evaluated by sensitivity and specificity. The inclusion criteria were all newborns referred to the neonatal unit with history of jaundice and neonates in postnatal wards and NICU with evidence of clinical jaundice. The exclusion criteria were neonates with major congenital anomalies, sick

neonates (sepsis, shock, and birth asphyxia), neonates with evidence of liver disease, neonates receiving phototherapy, neonates who have received blood transfusion/ exchange transfusion and neonates with skin disorders.

The measurable variables were analyzed and interpreted between them by the student's t test and the ordinal and categorical variables between them were interpreted by Chi- square ($\chi 2$) test. The predictive value of TcB values when compared with TSB values was estimated by the ROC curve. *P*-value of less than 0.05 ($P<0.05$) was considered as statistically significant.

The gestational age ranged from 35 to 42 weeks (mean 38.36 ± 1.3 weeks) with bodyweight ranging from 2100 g to 3920 g (mean 2825 g ± 477 g). The TSB levels ranged between 5.20 mg/dl to 21.40 mg/dl (mean 12.35 ± 2.47 mg/dl). The range of TcB values at forehead 1 was 6.2 to 22.40 mg/dl, forehead 2 was 6 to 22.2 mg/dl, sternum 1 was 5.5 to 21.8 mg/dl and sternum 2 was 5.4 to 21.5 mg/dl.

Limbs were the commonest site of appearance associated with hyperbilirubinemia in 102 babies (67.55%) followed by palms/soles (n = 39; 25.8%), abdomen (n = 9; 6%), and lastly chest (n = 1; 0.7 %).

In our study, jaundice was more common in term/AGA babies (84.11%) followed by late preterm/AGA babies (8.61%), term/SGA babies (5.96%) and lastly late preterm/SGA babies (1.32%).

The mean serum bilirubin levels with TSB and TcB (forehead and sternum) were compared. The serum bilirubin levels as per TSB were 12.3523 ± 2.47302 mg/dl (mean ± SD), per TcB forehead was 13.0285 ± 2.66756 mg/dl (mean ± SD) and per TcB sternum was 12.7576 ± 2.60471 mg/dl (mean ± SD). The difference between TSB and TcB forehead levels was statistically significant (P = 0.23), whereas the difference between TSB and TcB sternum was not statistically significant (P = 0.167). This shows that TcB sternum correlates closely with TSB. Although the difference between TcB forehead and TSB was significant, numerically, the values were similar.

The mean TcB levels at forehead 1 and 2 were 13.0172 ± 2.67112 mg/dl (mean ± SD) and 13.0397 ± 2.6849 mg/dl (mean ± SD), which was not statistically different (P = 0.559). Similarly, the mean TcB levels at sternum 1 and 2 were 12.7834 ± 2.635 mg/dl (mean ± SD) and 12.7318 ± 2.596 mg/dl (mean ± SD), again the difference was not statistically significant (P = 0.196).

The Karl Pearson's correlation coefficients between TSB levels with two set of TcB levels of forehead and sternum were compared. It can be seen that there is a strong correlation between TSB levels with that of TcB levels of forehead and TcB levels of sternum. The *P*-value is significantly correlated at 99 percent level of significance. This suggests that TcB levels at individual sites correlate with TSB levels. There was significant correlation between TSB levels and TcB levels at individual sites (forehead 1, forehead 2, sternum 1 and sternum 2).

The optimal cut off values for individual TcB measurements at forehead 1, forehead 2, sternum 1 and sternum 2, which show high sensitivity and specificity. ROC curve suggested the cutoff values of sensitivity and specificity for two TCB level of forehead and two TCB level of sternum, it is found the that sensitivity for TCB level of first forehead is approximately 86.6% and specificity with 82.1% (cut off value 12.9 mg/dl) and for TCB level of second forehead is approximately 83.6% and specificity with 87.9% (cut off value 13.45 mg/dl).The sensitivity and specificity for TCB level of sternum first is 80.6% and 88.1% respectively (cut off value 13.2 mg/dl). The sensitivity and specificity for TCB level of sternum second is 85.1% and 85.7% respectively (cut off value 12.85 mg/dl). This suggests that TcB measurement at sternum and forehead have high sensitivity and specificity comparable with TSB measurements for diagnosis of neonatal jaundice.

Overall, it was observed that average TcB level ≥ 12.00 mg/dl at forehead showed sensitivity of 91% and specificity of 66.7% beyond which phototherapy is indicated, while TSB level ≥ 11.35 mg/dl showed sensitivity of 94% and specificity of 66.5% for the same. Similarly, average TcB level ≥ 11.975 mg/dl at sternum showed sensitivity of 92.5% and specificity of 77.4% beyond which phototherapy is indicated and TSB level of ≥ 11.75 mg/dl showed sensitivity of 92.5% and specificity of 81% for the same. It was concluded that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of neonatal jaundice, beyond which phototherapy is indicated and is comparable to TSB levels.

We concluded that average TcB level ≥ 11.975 mg/dl at the level of sternum and TcB level ≥ 12.00 mg/dl at the level of forehead is highly sensitive and specific for diagnosis of hyperbilirubinemia and is comparable to TSB. TcB at the level of sternum and forehead can be considered as an accurate non-invasive tool for diagnosis and estimation of neonatal hyperbilirubinemia. Furthermore, it is easy to perform and presents little clinical challenge in day-to-day practice.

BIBLIOGRAPHY

1. Ambalavanan N, Carlo WA. Jaundice and hyperbilirubinemia in the newborn. In: Kliegman RM, Behrman RE, Stanton BF, Schor NF, St Geme III JW Eds. Nelson text book of Pediatrics. 20th ed. Philadelphia: Elsiever; 2016: 871-5.
2. Gibbins S. Transcutaneous bilirubin measurements in the assessment and management of neonatal jaundice. 2015. Koninklijke Philips NV: 1-4.
3. el-Beshbishi SN, Shattuck KE, Mohammad AA, Petersen JR. Hyperbilirubinemia and transcutaneous bilirubinometry. Clin Chem 2009; 55:1280–7.
4. Taeusch H, Ballard R, Avery M. Diseases of the Newborn. 6th ed. Philadelphia: W.B. Saunders Company; 1991.
5. Lee KS, Perlman M, Ballantyne M, Elliott I, To T. Association between duration of neonatal hospital stay and readmission rate. J Pediatr 1995;127:758-66.
6. Joint Commission for Accreditation of Hospital Organizations. Kernicterus threatens healthy newborns. Sentinel Event Alert 2001;18:1-4.
7. Bhutani VK, Zipursky A, Blencowe H, et al. Neonatal hyperbilirubinemia and rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels. Pediatr Res 2013;74:86–100
8. Olusanya BO, Teeple S, Kassebaum NJ. The Contribution of Neonatal Jaundice to Global Child Mortality: Findings From the GBD 2016 Study. Pediatrics 2018;141. pii: e20171471.
9. Mussavi M, Niknafs P, Bijari B. Determinig the correlation and accuracy of three methods of measuring neonatal bilirubin concentration. Iran J Pediatr 2013;23:333-9.

10. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297-316.
11. Taylor JA, Burgos AE, Flaherman V, Chung EK, Simpson EA, Goyal NK, et al. Discrepancies between transcutaneous and serum bilirubin measurements. Pediatrics 2015;135:224–231.
12. Bertini G, Rubaltelli FF. Non-invasive bilirubinometry in neonatal jaundice. Semin Neonatol 2002; 7:129-33.
13. Taylor JA, Burgos AE, Flaherman V, Chung EK, Simpson EA, Goyal NK, et al. Discrepancies between transcutaneous and serum bilirubin measurements. Pediatrics. 2015;135:224-31.
14. 13.O'Connor MC, Lease MA, Whalen BL. How to use: transcutaneous bilirubinometry. Arch Dis Child Educ Pract Ed 2013;98:154–159
15. Maisles MJ, Mcdonag AF. Phototheraphy for neonatal jaundice. N Engl J Med 2008;358:920-8
16. Engle WD, Jackson GL, Engle NG. Transcutaneous bilirubinometry. Semin Perinatol 2014;38:438–51.
17. Wickremasinghe AC, Karon BS, Saenger AK, Cook WJ. Effect of universal neonatal transcutaneous bilirubin screening on blood draws for bilirubin analysis and phototherapy usage. J Perinatol 2012;32:851–5
18. Thayyil S, Marriott L. Can transcutaneous bilirubinometry reduce the need for serum bilirubin estimations in term and near term infants? Arch Dis Child 2005;90:1311–2

19. Martin CR, Cloherty JP. Neonatal Hyperbilirubinemia. In Cloherty JP, Eichenwald EC, Stark AR, eds. Manual of neonatal care: 6 ed. New Delhi: Wolters Kluwer, 2008:181-212.
20. Whitington PF, Alonso EM. Disorder of bilirubin metabolism. In Nathan DG, Orkin SH, David Ginsberg, A. Thomas look hematology of infancy and childhood. 6thed, Saunders company, 2003;86-120.
21. IAP-NNF Guidelines 2006 on jaundice in newborn.188-209
22. Ambalavanan N, Carlo WA. Jaundice and Hyperbilirubinemia in the Newborn. In Kliegman RM, Staton BF, St Geme III JW, Schor NF, Behrman RE, eds. Nelson text book of Pediatreics. 20thed. Philadelphia, PA; Saunders Elsevier. 2016;871-5.
23. Bhutani V. Performance evaluation of neonatal phototherapy. Indian Pediatr 2009;46:19-21.
24. Deorari AK, Agarwal R. Phototherapy units. J Neonatol2001;1:61-68.
25. Maisels MJ, Ostrea EM Jr, Touch S, Clune SE, Cepeda E, Kring E, et al. Evaluation of a new transcutaneous bilirubinometer.Pediatrics2004;113:1628-35.
26. Kurnianto A, Bermawi H, Bahar E, Ramadanti A, Indrayadi. The correlation study of transcutaneous bilirubin measurements in neonates. Eur J Biotech Biosci 2016;4:34-7.
27. Varughese PM, Krishnan L, Ravichandran. Does color really matter? Reliability of transcutaneous bilirubinometry in different skin-colored babies. Indian J Paediatr Dermatol 2018;19:315-20.
28. Pendse A, Jasani B, Nanavati R, Kabra N. Comparison of transcutaneous bilirubin measurement with total serum bilirubin levels in preterm neonates receiving phototherapy. Indian Pediatr 2017;54:641-3.

29. Surana AU, Patel S, Prasad R, Tilwani S, Saiyad A, Rathod M. Comparison of transcutaneous bilirubin with serum bilirubin measurements in neonates at tertiary care center in western part of India. Int J Contemp Pediatr 2017;4:1445-9.
30. Olusanya BO, Imosemi DO, Emokpae AA. Differences between transcutaneous and serum bilirubin measurements in black African neonates. Pediatrics 2016;138:e20160907.
31. Chimhini GLT, Chimhuya S, Chikwasha V. Evaluation of transcutaneous bilirubinometer (DRAEGER JM 103) use in Zimbabwean newborn babies. Matern Health Neonatol Perinatol 2018;4:1.
32. Leite MG, Granato VA, Facchini FP, Marba ST. Comparison of transcutaneous and plasma bilirubin measurement. J Pediatr (Rio J) 2007;83:283-6.
33. Mahajan G, Kaushal RK, Sankhyan N, Sharma RL, Nakra M. Transcutaneous bilirubinometer in assessment of neonatal jaundice in Northern India. Indian Pediatr 2005; 42: 41-5.
34. Povaluk P, Shwetz EA, Kliemann R. Comparative study between plasma and transcutaneous bilirubin measurements in newborns. Rev Paul Pediatr 2011; 29(1): 6-12.
35. Kaynak-Turkmen MK, Aydogdu SA, Gokbulut C, Yenisey C, Soz O, Cetinkaya-Cakmak B. Transcutaneous measurement of bilirubin in Turkish newborns: comparison with total serum bilirubin. Turkish J Pediatr 2011; 53: 67-74.
36. Nagar G, Vandermeer B, Campbell S, Kumar M. Reliability of transcutaneous bilirubin devices in preterm infants: A systematic review. Pediatrics 2013; 132(5): 871-81.

37. Kaur V, Chopra B, Kaur A, Verma M, Singh K. Hyperbilirubinemia and transcutaneous bilirubin estimation- An update. IOSR J Dental Medical Sciences 2014; 13(8): 71-6.
38. Miguez C, Salto MF, Maranon R. Measurement of transcutaneous bilirubin with BiliCheck as a jaundice screening method in neonates in Pediatric emergency departments. Open J Pediatr 2015; 5: 240-7.
39. Mansouri M, Mahmoodnejad A, Sarvestani RT, Gharibi F. A comparison between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) measurements in term neonates. Int J Pediatr 2015; 3: 633-41.
40. Sadik IA, Abidiquader M, Osman NS, Mohammed NAE, Alhmeed MA, Eizaki NM. Comparative study serum and cutaneous total bilirubin among newborns with hyperbilirubinemia in Khartoum estate. Int J Med Health Research 2015; 1(5): 14-7.
41. Agrawal A, Tiwari AK, Mehta N, Bhattacharya P, Wankhede R, Tulsiani S, et al. ABO and Rh (D) group distribution and gene frequency; the first multicentric study in India. Asian J Transfus Sci 2014;8:121–5.
42. Ho EY, Lee SY, Chow CB, Chung JW. BiliCheck transcutaneous bilirubinometer: a screening tool for neonatal jaundice in the Chinese population. Hong Kong Med J 2006;12:99-102.

ANNEXURE I

Proforma for Thesis

1. Name: ……. IP No: ……

2. Gender: M / F: ……

3. DOB/ TOB: ……

4. Age of baby at the time of investigation for jaundice (in days of life & hours): …….

5. Mother's blood group and typing: ……..

6. Mode of delivery: NVD/ LSCS/Assisted Delivery: …….

7. Exclusively breast feeding: Yes / No

8. Birth Weight (in g): ……

9. Gestational Age (Ballard scoring): ……..

10. Baby's blood group and typing: …….

11. Age at appearance of clinical jaundice (in days of life and hours): …….

12. Site of appearance of clinical jaundice:

Face / Chest / Abdomen/ Limbs /Palms and Soles.

13. Study Group:

Term AGA/ Term SGA/Preterm AGA /Preterm SGA

14. TSB Level: …… (mg/dl)

15. TcB Measurement:

Forehead: 1st reading (a): ……

2nd reading (b): …….

ANNEXURE I

Mean (y): a+b/2: …….

Sternum:

1st reading (c): ……..

2nd reading (d): ……

Mean (z): c+d/2: ……...

16. Intervention:

Phototheraphy / Exchange Transfusion / No intervention

ANNEXURE II

Informed Consent Form

Name of the Investigator. DR. SAHIL CHAUDHARY SL.NO.....

Name of the organization SRI DEVARAJ URS MEDICAL COLLEGE

Name of the participant.....

Title of the study- **"Comparison between transcutaneous bilirubin measurements and serum total bilirubin levels in neonates with clinical jaundice-An observational study"**

You are invited to take part in the research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask any queries.

You are being ask to participate in this study because you satisfy the eligibility criteria which are

1. All late preterm and term newborns referred to the neonatal unit with history of jaundice.
2. Late preterm and term neonates in post-natal wards and NICU with evidence of clinical jaundice.

My signature below constitutes my acknowledgement that the benefits and risks have been explained to my satisfaction by a qualified health professional. The following has been explained to me:

The blood would be drawn from my child for testing the bilirubin levels. TcB measurements will be made with a Tc bilirubinomter "JM-105" by gently pressing against the skin over forehead and upper end of sternum. Within 30 minutes of TcB determination, blood sample will be drawn in a plain vial for TSB estimination.

Participation is totally voluntary. The results will be treated with medical confidentiality and will not be disclosed to any outsider except if it is required by law.

I give consent for the information to be used for medical research, test validation or education as long as my privacy is maintained.

I understand that I remain free to withdraw from this study at any time and this will not change my future care.

ANNEXURE II

I have read and received a copy of this consent form. I understand the information provided in this document and I have had the opportunity to ask questions I might have about the study, the associated risks and alternatives.

Date: …….

Parent's (or guardian's) Name & Signature:

……
……

Person obtaining consent form and his/her Name & Signature:

……
……

For any clarification you are free to contact the investigator.

Principal Investigator: Dr. Sahil Chaudhary

Contact number: 9481525187

ANNEXURE II

PATIENT INFORMATION SHEET

Study Title**: "Comparison between transcutaneous bilirubin measurements and serum total bilirubin levels in neonates with clinical jaundice-An observational study"**

Neonatal hyperbilirubinemia (jaundice) is a common problem encountered in term infants and of preterm infants during the first week of life. A good correlation between TcB and TSB values in clinically jaundiced newborns would be very helpful to reduce invasive blood sampling and the possible complications, as well as cost and parent's anxiety.

Approximately 150 children will be enrolled in the study. Your child's participation in the study will be for 2 days. History will be noted and physical examination will be done.

TcB measurements will be made with a Tc bilirubinometer "JM-105" by gently pressing against the skin over forehead and upper end of sternum. . Within 30 minutes of TcB determination, blood sample will be drawn in a plain vial for TSB estimation.

This informed consent document is intended to give you a general knowledge of the study. Please read the following information carefully and discuss with your family members. You can ask your queries related to the study at any time during the study. If you are willing to allow your child to participate in the study, you will be asked to sign an informed consent form by which you are acknowledging your child's participation in the study and that the entire study procedure is explained to you by study doctor. You are free to withdraw your child from participating in the study at any time.

Principal Investigator: DR. SAHIL CHAUDHARY

Date:

ANNEXURE III

Key to master chart

AGA = Appropriate for gestational age

BBG = baby blood group

Dob = date of birth

F = female

F1 = first reading by TcB at forehead

F2 = second reading by TcB at forehead

LSCS = lower segment Caesarian section

M = male

MBG = mother’s blood group

NVD = normal vaginal delivery

S1 = first reading by TcB at sternum

S2 = second reading by TcB at sternum

TcB = transcutaneous bilirubin

TSB = total serum bilirubin

Master Chart - Comparison between transcutaneous bilirubin measurements and serum total bilirubin levels in neonates with clinical jaundice: an observational study.

Sl. no.	Study ID	Gender	Dob	Tob	MBG	Mode of delivery	Weight (in kg)	Gestational age (Ballard scoring)	BBG	Time of investigation (days/hours)	Site of apperance	Study group	TSB level (in mg/dl)	TcB level (in mg/dl)				Intervention (Phototherapy)
														Forehead		sternum		
														F1	F2	S1	S2	
1	567561.4	F	16/9/17	12.27 a.m	o+	lscs	2.58	38 week	o+	43 h	limbs	term/aga	11.4	10.2	11	11.5	12	no
2	286112.6	M	20/9/17	4.23 a.m	b+	nvd	2.48	40 week	o+	76 h	soles	term/aga	15.5	15	14.5	14	15.8	Yes
3	924877.4	M	28/7/17	9.53 a.m	b+	lscs	3.56	38 week	o+	70 h	soles	term/aga	16	15.7	16	14	15.5	Yes
4	312037	M	25/7/17	5.03 a.m	o+	lscs	3.1	40 week	o+	38 h	limbs	term/aga	12	11.5	12.1	12.5	13	Yes
5	596058	F	21/7/17	7.04 p.m	a+	nvd	2.89	39 week	a+	87 h	limbs	term/aga	10	9	9.5	10.2	10	no
6	308467.2	F	25/7/17	4.12 a.m	ab+	nvd	2.24	40 week	b+	54 h	limbs	term/aga	16	15.5	16	16.5	16	Yes
7	761730.1	M	17/8/17	8.20 p.m	b+	nvd	3.71	41 week	b+	61 h	limbs	term/aga	14	14	15	16	15	Yes
8	419122.9	F	7/8/2017	6.22 p.m	o+	lscs	2.56	40 week	o+	day 7	abdomen	term/aga	11.5	13.8	14.2	11.8	12.5	no
9	740204.9	F	18/8/17	5.26 a.m	o+	lscs	2.72	38 week	o+	52 h	limbs	term/aga	11	11.6	10.9	9	10.3	no
10	501821.3	M	15/8/17	7.28 p.m	o+	lscs	2.7	36 week	o+	day 5	limbs	term/aga	16	15	16	14.9	15.6	Yes
11	947072.2	F	15/6/17	8.27 p.m	b+	nvd	2.62	38 week	b+	36 h	limbs	term/aga	10	9.2	10	9.5	10.5	no
12	907920.8	M	24/7/17	7.10 a.m	o+	nvd	2.78	38 week	o+	48 h	limbs	term/aga	10	9.8	10.2	10.2	9.4	no
13	39790.92	M	12/9/2017	11.37 p.m	b+	lscs	2.64	39 week	b+	86 h	abdomen	term/aga	11	10.5	11	12	11	no
14	729388.4	M	4/11/2017	10.30 a.m	a+	nvd	2.18	37 week	ab+	120h	limbs	term/sga	13.6	14.8	14.5	15	14.9	Yes
15	301906.3	M	1/11/2017	9.15 a.m	o+	lscs	2.24	36 week	b+	123h	limbs	late preterm/sga	11.4	11.5	11.8	12.4	13	Yes
16	28577.52	M	5/11/2017	11.56 p.m	o+	nvd	2.22	40 week	o+	55 h	limbs	term/sga	10.1	11.5	11	10.4	12	Yes
17	417937.7	M	8/11/2017	2.48 a.m	a+	nvd	2.78	39week	a+	65h	limbs	term/aga	10.4	9.4	10.2	10	9.6	no
18	483258.3	F	11/11/2017	12.20 pm	b+	lscs	2.9	38 week	ab+	106 h	palms/soles	term/aga	11.1	10.8	11	11	10.9	no
19	457752.6	M	15/11/17	5.46pm	o+	lscs	3.42	39week	o-	38h	palms/soles	term/aga	10.8	9.5	10	10.2	9.8	Yes
20	744113.6	M	15/11/17	2.12 a.m	o+	nvd	2.78	38week	o+	54h	palms/soles	term/aga	12.3	11.8	12.2	12	11.6	Yes
21	96053.96	F	15/11/17	8.25 p.m	o+	lscs	3.06	39 week	o+	108 h	limbs	term/aga	10.4	9.8	10	10.2	9.4	no
22	51808.5	F	27/11/17	4.28 a.m	o+	nvd	3.8	39 week	o+	50 h	palms/soles	term/aga	15.3	15.8	16	16.2	15.6	Yes
m	548135.5		22/11/17	1.09 a.m	b+	nvd	2.78	40 week	b+	103 h	limbs	term/aga	12.3	12.5	13	11.8	12.2	Yes

AGA = Appropriate for gestational age; BBG = baby blood group, Dob = date of birth; F = female; F1 =first reading by TcB at forehead; F2 = second reading by TcB at forehead; LSCS = lower segment Caesarian section; M = male; MBG = mother's blood group, NVD = normal vaginal delivery; S1 = first reading by TcB at sternum; S2 = second reading by TcB at sternum; TcB = transcutaneous bilirubin; TSB = total serum bilirubin

Master Chart - Comparison between transcutaneous bilirubin measurements and serum total bilirubin levels in neonates with clinical jaundice: an observational study.

Sl. no.	Study ID	Gender	Dob	Tob	MBG	Mode of delivery	Weight (in kg)	Gestational age (Ballard scoring)	BBG	Time of investigation (days/hours)	Site of apperance	Study group	TSB level (in mg/dl)	TcB level (in mg/dl)				Intervention (Phototherapy)
														Forehead		sternum		
														F1	F2	S1	S2	
24	176239.7	M	22/11/17	12.30 p.m	o+	lscs	2.74	39 week	o+	92 h	limbs	term/aga	12.3	13	12.5	12.8	13.2	Yes
25	918325.6	F	5/10/2017	9.50 p.m	b+	lscs	2.3	36 weeks	b+	120 h	limbs	late preterm/aga	10	10.1	10.5	10.2	10	no
26	193846.9	F	11/10/2017	12.03 p.m	o+	lscs	3.54	39 weeks	o+	92 h	limbs	term/aga	16.2	16	16.1	15.8	15.6	Yes
27	429178.8	M	27/9/17	3.18 a.m	o+	nvd	2.68	37 weeks	o+	64 h	limbs	late preterm/aga	13.5	13	13.5	12.5	13.5	Yes
28	508919.3	M	27/9/17	9 a.m	b-	nvd	2.76	39 weeks	o+	23 h	limbs	term/aga	10	9.5	10	10	9.8	Yes
29	237786.1	F	30/9/17	6.17 a.m	A+	lscs	2.8	41 weeks	a+	38h	limbs	term/aga	16	16	15.5	15.8	16	Yes
30	30487.01	F	30/9/17	9.30 a.m	B+	nvd	3	40 weeks	b+	47 h	limbs	term/aga	15	15	14.5	14.8	15	Yes
31	854739.6	F	22/11/17	8.41 a.m	o+	nvd	2.42	38 week	o+	96 h	palms/soles	term/aga	14.8	13.8	14.2	14	14.1	Yes
32	263047.7	M	25/11/17	10.45 p.m	b+	lscs	2.62	38 week	o+	82 h	abdomen	term/aga	10.7	10.8	11.5	11	11.8	no
33	899085	M	26/11/17	7.58 a.m	o+	lscs	2.28	38 week	o+	72 h	limbs	term/sga	11.8	13.2	12.8	13.4	12.6	Yes
34	578311.1	M	23/4/17	10.47 a.m	b+	lscs	3.1	38 week	o+	155 h	limbs	term/aga	12	11.6	12.6	14.1	14.1	no
35	496275	M	24/4/2017	3.05 a.m	b+	lscs	2.71	38 week	b+	60 h	limbs	term/aga	13.4	15.1	14.8	19	17.5	Yes
36	812600.3	F	27/4/17	6.28 p.m	o+	nvd	3.05	38 week	o+	73 h	palms/soles	term/aga	11	12.4	11.3	13	13	no
37	251915	M	17/8/17	8.20 p.m	b+	nvd	3.71	41 week	b+	61 h	limbs	term/aga	14	14	15	16	15	Yes
38	407867.6	M	7/7/2017	1.58 p.m	o+	nvd	3.59	38 week	o+	55 h	limbs	term/aga	13.2	15.2	15.7	14.4	15.4	Yes
39	56644.65	F	18/8/17	5.26 a.m	o+	lscs	2.72	38 week	o+	52 h	limbs	term/aga	11	11.6	10.9	9	10.3	no
40	458642.9	M	7/7/2017	2.30 p.m	o+	nvd	3.12	39 week	o+	33 h	limbs	term/aga	11.2	13.5	14.1	13.4	12.6	no
41	13913.69	F	5/4/2018	11.38 a.m	o+	lscs	3.3	38 week	o+	80 h	limbs	term/aga	13.6	13.5	13.8	14	13.8	Yes
42	445478.7	M	6/4/2018	5.08 a.m	a+	nvd	2.88	39 week	o+	77 h	limbs	term/aga	10.5	9.5	9	10.6	10.8	no
43	115428.2	M	2/4/2018	12.21 a.m	a+	lscs	2.68	38 week	a+	146 h	limbs	term/aga	9.8	9	8.8	10	10.6	no
44	317100	M	17/4/18	3.46 a.m	b+	lscs	2.96	37 week	b+	61 h	limbs	term/aga	10.4	11	10.8	10.3	10.6	no
45	551235.8	M	16/4/18	11.50 p.m	b+	nvd	3.02	40 week	o+	65 h	limbs	term/aga	12	11	12	12.5	11.8	no
46	152389.3	M	21/4/18	7.36 p.m	b+	nvd	2.6	39 week	a+	72 h	limbs	term/aga	12.3	11.5	12	12.5	11.8	no

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														Forehead		sternum		
														F1	F2	S1	S2	
47	86328.53	M	21/4/18	5.22 p.m	o+	lscs	2.72	38 week	a+	66 h	limbs	term/aga	12.6	12	11.8	11.9	12	no
48	652135.7	M	23/4/18	12.12 p.m	b+	lscs	3.76	39 week	b+	99 h	palms/soles	term/aga	14.7	15	14.5	14.8	15	Yes
49	596631.8	M	25/4/18	6.25 p.m	o+	lscs	3.78	39 week	o+	115 h	palms/soles	term/aga	12.8	12.8	12.5	12.8	13.2	no
50	171231.1	M	6/9/2018	11.35 p.m	o+	lscs	3.21	40 week	o+	46 h	limbs	term/aga	8.8	8.5	8.9	9	8.9	no
51	167398.7	M	3/9/2018	1.oo p.m	b+	lscs	3.3	40 week	b+	139 h	limbs	term/aga	11.4	9.8	11.2	12	11.5	no
52	475320	F	6/9/2018	10.31 a.m	b+	nvd	2.32	35 week	b+	131 h	limbs	late preterm/aga	13.2	12.5	13	13.8	13.5	Yes
53	688286.4	M	9/9/2018	2.59 a.m	ab+	lscs	2.42	38 week	ab+	57 h	limbs	term/aga	10.2	9.8	10.5	10.3	10.1	no
54	694673.8	M	8/9/2018	4.37 p.m	ab+	lscs	2.4	37 week	b+	113 h	limbs	term/aga	11.3	10	10.5	12	11.5	no
55	968838.9	F	11/9/`18	5.36 a.m	b+	nvd	1.83	37 week	b+	88 h	limbs	term/sga	15.9	16	16.8	17	17.5	Yes
56	688735.9	M	12/9/2018	12.26 p.m	b+	lscs	3.92	39 week	b+	75 h	limbs	term/aga	13.6	14	14.5	13.8	13.2	Yes
57	684526.3	M	15/9/18	2.04 p.m	b+	lscs	2.5	39 week	b+	69 h	soles	term/aga	10	9.8	9.7	10	10.2	no
58	631319.5	M	16/9/18	12.01 pm	o+	lscs	2.38	38 week	b+	71 h	soles	term/sga	17.2	18	18.5	17.8	17.5	Yes
59	236715.3	M	15/9/18	7.20 p.m	o-	lscs	2.34	36 week	b+	91 h	limbs	late preterm/aga	11.4	12	11.9	11.9	11.5	no
60	329320.6	F	15/9/18	10.47 a.m	b+	lscs	3.24	38 week	b+	96 h	limbs	term/aga	12.9	13	13.5	12.8	12.9	no
61	248993.6	M	16/9/18	2.29 p.m	a+	lscs	2.75	36 week	a+	123 h	limbs	late preterm/aga	12	13.5	13	12.5	12	no
62	881154.6	M	20/9/18	6.32 a.m	b+	nvd	2.32	36 week	b+	81 h	limbs	late preterm/aga	16.1	17	17.5	16.5	16.3	Yes
63	306667.9	F	20/9/18	12.36 a.m	b+	nvd	2.48	38 week	b+	110 h	limbs	term/aga	10.7	13	12.8	11	11.5	no
64	563697	M	22/9/18	2.12 p.m	b+	lscs	3.7	39 week	o+	69 h	limbs	term/aga	14.6	15	15.6	14.8	14.7	Yes
65	472478.3	F	22/9/18	4.48 p.m	a+	nvd	2.68	38 week	a-	93 h	limbs	term/aga	11.7	17	17.5	16	16.5	no
66	328188.5	F	3/10/2018	2.30 p.m	o+	nvd	3.2	40 week	o+	123 h	palms/soles	term/aga	15.2	16.5	16.8	15.5	15.3	Yes
67	841884.1	M	7/10/2018	3.36 p.m	o+	lscs	2.42	39 week	o+	60 h	limbs	term/aga	11.5	12	12.5	11.8	11.7	no
68	861694.5	F	30/9/18	2.19 a.m	o+	nvd	2.36	36 week	a+	69 h	palms/soles	late preterm/sga	12.7	16	16.5	14	14.8	Yes

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														Forehead		sternum		
														F1	F2	S1	S2	
69	877925.9	M	24/4/17	3.05 a.m	b+	lscs	2.71	38 week	b+	60 h	limbs	term/aga	13.4	15.1	15.5	14.5	14.8	Yes
70	299979.9	F	26/9/18	11.33 p.m	a+	lscs	3.02	37 week	a+	64 h	limbs	term/aga	10.3	11	11.5	10.8	10.5	no
71	919642.2	M	17/10/18	10.52 a.m	a+	nvd	2.81	38 week	a+	96 h	limbs	term/aga	12.5	17	17.5	16.5	16.2	no
72	746670.6	M	17/10/18	11.43 p.m	a+	nvd	3.26	40 week	a+	79 h	palms/soles	term/aga	12.9	13.8	13.5	13	12.9	Yes
73	195576.2	M	28/10/18	2.00 p.m	b+	nvd	2.8	38 week	b+	75 h	limbs	term/aga	14.4	15.5	15	14.8	14.6	Yes
74	749000.2	F	14/10/18	2.15 a.m	b+	nvd	3.07	40 week	o+	58 h	palms/soles	term/aga	12	13.8	13.5	12.5	12.8	Yes
75	342351.6	M	7/10/2018	2.45 a.m	o+	lscs	3.48	38 week	o+	57 h	limbs	term/aga	11.8	15	15.5	14.8	14.9	Yes
76	972456.8	F	13/3/18	1.04 p.m	a+	lscs	2..66	36 week	a+	118 h	limbs	late preterm/aga	13.5	14	13.5	13.8	13.2	Yes
77	670312.8	M	13/3/18	1.05 p.m	a+	lscs	2.9	36 week	a+	118 h	limbs	late preterm/aga	10.9	10.5	11	10.8	11.1	Yes
78	562151.1	F	14/3/18	10.25 p.m	o+	nvd	3.66	39 week	o+	69 h	palms/soles	term/aga	11.5	11	10.8	10.6	11.2	no
79	133813.1	M	12/3/2018	2.39 am	a+	lscs	3.5	39 week	a+	90 h	limbs	term/aga	14.1	15	14.5	14.6	15	Yes
80	311776.1	M	7/10/2018	9.45 a.m	a+	lscs	3.25	37 week	a+	123 h	limbs	term/aga	13.1	14	13.8	13.5	13.8	no
81	895164.1	M	6/10/2018	11.43 p.m	b+	nvd	3.16	40 week	b+	79 h	palms/soles	term/aga	11.3	12.5	12	11.8	11.6	no
82	665369.1	M	6/10/2018	12.02 a.m	o-	lscs	3.46	39 week	o+	76 h	limbs	term/aga	9.6	11.2	10.8	9.8	9.6	no
83	967163.4	M	6/10/2018	10.13 p.m	a+	lscs	2.88	37 week	a+	139 h	limbs	term/aga	13	14.5	14	13.8	13.5	no
84	476868.1	F	9/10/2018	3.32 a.m	a+	nvd	3	40 week	a+	99 h	palms/soles	term/aga	13.2	14.5	14	13.8	13.5	no
85	887470.7	F	26/9/18	7.16 p.m	o+	lscs	2.9	40 week	o+	67 h	abdomen	term/aga	10.2	11.5	11	10.8	10.6	no
86	816127.2	M	26/9/18	4.15 p.m	b+	lscs	3.14	39 week	b+	71 h	limbs	term/aga	13.3	15.5	15	14.8	14.6	Yes
87	4689.922	F	29/9/18	8.26 p.m	o+	lscs	1.82	38 week	o+	64 h	palms/soles	term/sga	15.3	16.5	16.4	15.8	15.5	Yes
88	296351	F	30/9/18	2.19 a.m	o+	nvd	2.36	36 week	a+	69 h	palms/soles	late preterm/aga	12.7	16.2	16	15.8	15.5	Yes
89	621733.5	F	10/11/2018	12.45 p.m	b+	nvd	2.7	40 week	b+	49 h	limbs	term/aga	9.5	10.8	11	9.8	9.6	no
90	471887	F	4/11/2018	7.23 p.m	a+	nvd	2.4	39 week	a+	67 h	limbs	term/aga	10.7	11.5	11	10.9	10.8	no

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														Forehead		sternum		
														F1	F2	S1	S2	
91	116849.3	F	17/10/18	5.05 p.m	o+	lscs	2.6	37 week	o+	72 h	limbs	term/aga	18	19	19.5	18.8	18.5	Yes
92	156915.6	M	17/10/18	9 a.m	b+	lscs	2.7	39 week	b+	84 h	palms/soles	term/aga	13.8	14.5	14.8	13.9	13	Yes
93	585397	M	18/10/18	12.06 a.m	b+	lscs	3.2	39 week	o+	62 h	thighs	term/aga	13.7	14.5	14	14	13.8	Yes
94	194134.4	M	28/10/18	3.23 p.m	b+	lscs	3.2	38 week	b+	73 h	limbs	term/aga	11.5	12.5	12.3	11.8	11.7	no
95	634284.3	M	28/10/18	4.20 p.m	ab+	lscs	2.82	39 week	ab+	72 h	limbs	term/aga	10.6	12	11.8	11.6	11	no
96	316850.6	F	27/10/18	2.20 p.m	b+	lscs	2.7	40 week	b+	118 h	limbs	term/aga	11	12.5	12	11	11.5	no
97	684184.8	M	31/11/18	6.36 p.m	a+	lscs	3	40 week	a+	67 h	limbs	term/aga	12.5	13.6	13.5	12.8	12.7	Yes
98	949855.9	F	31/10/18	6.15 p.m	b+	lscs	2.7	39 week	b+	89 h	limbs	term/aga	8.2	9.4	9.3	8.8	8.6	no
99	515845.7	F	20/10/18	4.35 p.m	o+	lscs	2.86	40 week	a+	84 h	limbs	term/aga	8.1	9	9.1	8.5	8.8	no
100	910886.8	M	25/10/18	3.25 a.m	a+	lscs	2.72	36 week	o+	82 h	limbs	late preterm/aga	11.4	12.5	12.4	11.8	11.6	no
101	237873.6	M	7/11/2018	8.41 a.m	b+	nvd	2.94	39 week	o+	52 h	limbs	term/aga	11.4	12.4	12.5	11.8	11.5	no
102	189306.1	F	4/11/2018	12.23 p/m	ab+	lscs	3.14	38 week	ab+	75 h	limbs	term/aga	8	9.8	10	8.5	8.2	no
103	360322.2	F	6/11/2018	7 a.m	b+	nvd	2.62	38 week	ab+	80 h	palms/soles	term/aga	16.7	17.6	17.5	16.9	16.8	Yes
104	181831	M	11/11/2018	12.03 a.m	ab+	lscs	2.76	39 week	ab+	110 h	palms/soles	term/aga	15.4	16.5	16.3	15.8	15.6	Yes
105	166729.7	F	11/11/2018	6.34 a.m	o+	nvd	2.89	36 week	o+	68 h	palms/soles	late preterm/aga	10.4	11.5	11	10.8	10.6	no
106	53277.2	M	10/11/2018	11.45 a.m	o+	lscs	2.86	37 week	a+	98 h	limbs	term/aga	10.5	11.3	11	10.8	10.6	no
107	74043.64	M	18/11/18	8.27 p.m	o+	lscs	2.76	37 week	o+	63 h	palms/soles	term/aga	15.9	16.2	16.3	15.9	15.9	Yes
108	40201.69	M	18/11/18	7.35 a.m	o+	nvd	2.94	38 week	o+	76 h	limbs	term/aga	11.1	11.5	11.6	11.2	11.1	no
109	191325.7	F	17/11/18	5.50 p.m	a+	lscs	2.64	38 week	a+	46 h	abdomen	term/aga	9.8	10.2	10.1	9.9	9.8	no
110	954264.4	M	15/11/18	5.57 p.m	o+	lscs	2.92	38 week	o+	65 h	abdomen	term/aga	10.4	11	10.9	10.5	10.6	no
111	101645.3	M	17/11/18	4.35 p.m	b+	lscs	3.2	38 week	b+	91 h	limbs	term/aga	13.3	13.9	13.8	13.5	13.6	no
112	129549.5	M	18/11`/18	11.34 a.m	o+	nvd	2.54	39 week	o+	71 h	limbs	term/aga	13.4	14.2	14.1	13.8	13.7	Yes
113	747989	M	14/11/18	12.02 p.m	o+	nvd	2.73	37 week	b-	69 h	palms/soles	term/aga	12.5	13.5	13.4	12.8	12.6	no

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														Forehead		sternum		
														F1	F2	S1	S2	
114	682401.7	F	3/12/2018	10.31 p.m	a+	lscs	2.8	38 week	o+	109 h	palms/soles	term/aga	10.9	11.2	11	10.5	10.4	no
115	222506.8	F	31/12/18	1.17 p.m	a+	lscs	3.74	38 week	o+	74 h	palms/soles	term/aga	13.4	14.2	14	13.8	13.6	Yes
116	733121.8	F	31/12/18	3.40 p.m	b+	lscs	2.8	40 week	b+	66 h	limbs	term/aga	10.6	11.4	11.3	10.9	10.8	no
117	828680.2	F	29/11/18	8.43 p.m	o-	lscs	2.64	40 week	o+	10 h	abdomen	term/aga	5.2	6.2	6	5.5	5.4	no
118	753257.6	M	14/12/18	6.16 a.m	a+	lscs	2.82	37 week	a+	118 h	limbs	term/aga	11.3	12	11.9	11.8	11.6	no
119	726592.2	M	13/12/18	10.55 p.m	a+	lscs	3.64	38 week	a+	60 h	limbs	term/aga	15.1	16.2	16.1	15.9	15.6	Yes
120	886203.1	M	17/12/18	6.24 p.m	b+	lscs	2.82	37 week	o+	67 h	limbs	term/aga	9.9	10.5	10.4	10	9.9	no
121	989823.3	M	14/12/18	12.10 a.m	b+	lscs	2.5	38 week	b+	35 h	limbs	term/aga	10.5	11.3	11.2	10.8	10.6	no
122	511791.6	M	18/12/18	12.01 a.m	o+	lscs	2.52	38 week	o+	86 h	limbs	term/aga	8	9.5	9	8.9	8.7	no
123	100745.7	F	16/12/18	10.05 p.m	a+	lscs	2.6	37 week	a+	97 h	palms/soles	term/aga	13.4	14.2	14.1	13.8	13.6	Yes
124	743893.6	F	18/12/18	6.45 a.m	o+	nvd	3.03	38 week	o+	80 h	abdomen	term/aga	14.7	15.5	15.4	14.9	14.8	Yes
125	117743.2	F	17/1/19	11.22 a.m	o+	lscs	2.92	36 week	o+	118 h	limbs	late preterm/aga	10.3	11.2	11.3	10.7	10.5	no
126	736773.3	F	16/1/19	3.48 p.m	o+	lscs	2.8	39 week	o+	121 h	limbs	term/aga	14.1	15.1	15.3	14.4	14.2	no
127	674420.6	F	15/1/19	1.28 a.m	o+	nvd	3.39	39 week	o+	177 h	limbs	term/aga	21.4	22.4	22.2	21.8	21.5	Yes
128	103567.4	F	17/1/19	11.25 p.m	o+	lscs	2.28	39 week	o+	44 h	limbs	term/aga	8.6	9.3	9.2	8.9	8.7	no
129	292060.6	F	14/1/19	11.54 p.m	a+	lscs	2.66	36 week	b+	83 h	limbs	late preterm/aga	11.3	12.3	12	11.8	11.5	no
130	411145.1	F	21/12/18	12.20 a.m	o+	nvd	2.23	38 week	b+	59 h	limbs	term/aga	15.4	16.1	16	15.9	15.7	Yes
131	532273.1	M	15/1/19	2.46 a.m	a+	nvd	3.09	39 week	a+	81 h	palms/soles	term/aga	17.1	18.4	18.2	17.8	17.4	Yes
132	47832.83	F	14/1/19	8.40 p.m	b+	nvd	2.75	39 week	b+	88 h	palms/soles	term/aga	11.7	12.4	12.2	11.9	11.8	no
133	494934.5	M	14/1/19	12.45 p.m	o+	nvd	3.16	39 week	o+	69 h	limbs	term/aga	8.6	9.2	9	8.9	8.8	no
134	915167.9	M	14/1/19	2.56 p.m	o+	nvd	3.54	38 week	o+	71 h	limbs	term/aga	11.5	12.2	12.1	11.8	11.7	no
135	92870.46	M	14/1/19	10.57 p.m	ab+	lscs	2.72	38 week	ab+	63 h	limbs	term/aga	10.6	11.3	11.1	10.9	10.7	no
136	36875.61	F	14/1/19	8.13 p.m	o+	lscs	2.72	40 week	o+	65 h	limbs	term/aga	9.6	10.4	10.2	9.8	9.7	no

AGA = Appropriate for gestational age; BBG = baby blood group, Dob = date of birth; F = female; F1 =first reading by TcB at forehead; F2 = second reading by TcB at forehead; LSCS = lower segment Caesarian section; M = male; MBG = mother's blood group, NVD = normal vaginal delivery; S1 = first reading by TcB at sternum; S2 = second reading by TcB at sternum; TcB = transcutaneous bilirubin; TSB = total serum bilirubin

Master Chart - Comparison between transcutaneous bilirubin measurements and serum total bilirubin levels in neonates with clinical jaundice: an observational study.

Sl. no.	Study ID	Gender	Dob	Tob	MBG	Mode of delivery	Weight (in kg)	Gestational age (Ballard scoring)	BBG	Time of investigation (days/hours)	Site of apperance	Study group	TSB level (in mg/dl)	TcB level (in mg/dl)				Intervention (Phototherapy)
														Forehead		sternum		
														F1	F2	S1	S2	
137	127537.7	F	14/1/19	3.07 p.m	o+	nvd	2.66	37 week	o+	69 h	limbs	term/aga	13.7	14.3	14.1	13.9	13.8	Yes
138	672245.9	M	10/1/2019	5.19 a.m	b+	nvd	3	39 week	b+	53 h	palms/soles	term/aga	16.6	17.5	17.2	16.8	16.7	Yes
139	126439.5	M	11/1/2019	2 a.m	o+	nvd	2.76	37 week	b+	89 h	limbs	term/aga	11.2	12.3	12	11.9	11.7	no
140	771027	M	9/1/2019	8.04 p.m	a+	lscs	2.9	39 week	a+	64 h	palms/soles	term/aga	12.7	13.5	13.3	12.9	12.8	no
141	372637.7	M	10/1/2019	8.44 p.m	b+	nvd	2.6	39 week	b+	87 h	palms/soles	term/aga	11.3	12.5	12	11.9	11.7	no
142	148351.5	M	22/1/19	2.30 a.m	o+	nvd	2.84	39 week	o+	38 h	limbs	term/aga	15.9	16.8	16.7	16.2	16.3	Yes
143	883016.9	M	21/1/19	2.30 p.m	o+	nvd	2.72	39 week	o+	73 h	limbs	term/aga	9.8	11.3	11.2	10.5	10.6	no
144	231857.4	M	22/1/19	6.35 a.m	b+	nvd	2.58	39 week	b+	56 h	abdomen	term/aga	14.8	15.5	15.4	14.9	14.8	Yes
145	626565.2	M	21/1/19	12.38 p.m	b+	nvd	1.8	38 week	o+	69 h	palms/soles	term/sga	17.4	18.4	18.3	17.8	17.6	Yes
146	889746.7	M	21/1/19	4.35 a.m	o-	nvd	2.68	39 week	b+	66 h	palms/soles	term/aga	19.5	20.3	20.2	19.8	19.6	Yes
147	872693.5	F	20/1/19	2 a.m	o+	lscs	2.91	42 week	b-	106 h	palms/soles	term/aga	13.1	14.9	14.3	13.4	13.3	no
148	388523.9	M	19/1/19	7.20 p.m	ab+	lscs	2.6	37 week	a+	57 h	palms/soles	term/aga	13.8	14.4	14.3	13.9	14.1	Yes
149	341325.1	M	14/1/19	2.36 p.m	o-	nvd	2.3	39 week	O-	70 h	chest	term/sga	10	11.2	11	10.8	10.6	no
150	191500.6	M	16/1/19	2.45 p.m	o+	lscs	3.04	39 week	o+	113 h	limbs	term/aga	8	9.2	9.1	8.8	8.6	no
151	582723.5	M	20/1/19	10.17 p.m	o+	lscs	2	37 week	o+	95 h	limbs	term/sga	10.1	11.1	11.2	10.5	10.3	no

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