



A Prospective Observational Study on the Appraisal of Common Cause and Efficacy of Continuous Phototherapy in Patients with Neonatal Jaundice

V. Premsai¹, G. Ramya¹, Y. Kavya Chowdary¹,
Syeda Zaineb Humaira Hussaini^{2*} and C. Aparna³

¹Department of Pharmacy, Bhaskar Pharmacy College, Hyderabad, Telangana, India.

²Department of Pharmacy Practice, Bhaskar Pharmacy College, Hyderabad, Telangana, India.

³AIIMS, AVIS Ankura Hospital for Women and Children, Hyderabad, Telangana, India.

Authors' contributions

This work was carried out in collaboration among all authors. Authors VP, GR and YKC designed the study, wrote the protocol, managed the analyses of the study, performed the statistical analysis and managed the literature searches. Author SZHH wrote the first draft of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2019/16i130135

Editor(s):

(1) Dr. Maria Manuel Azevedo, Department of Microbiology, Faculty of Medicine, University of Porto, 4200-319 Porto, Portugal.

Reviewers:

(1) Anslem Ajugwo, Madonna University, Nigeria.

(2) Simon Pius, University of Maiduguri, Nigeria.

(3) Karen Cordovil, Brazil.

Complete Peer review History: <http://www.sdiarticle3.com/review-history/50443>

Original Research Article

Received 03 June 2019

Accepted 11 August 2019

Published 24 August 2019

ABSTRACT

Background: Neonatal jaundice is generally harmless, but high concentrations of unconjugated bilirubin may rarely cause kernicterus. Hyperbilirubinemia is the most common cause of neonatal readmission to the hospital, in the majority of cases.

Aims: The study aims to determine incidence rate of neonatal jaundice as well as evaluate the commonest cause and determine the efficacy of continuous phototherapy.

Study Design: A Prospective observational study.

Place and Duration of Study: The study was conducted in Avis Ankura hospital for women and children. It is a well-recognized, authorized hospital where obstetrics and neonatal care is provided. The study was conducted between October 2018 to March 2019.

*Corresponding author: E-mail: humaira_hz@yahoo.com;

Methodology: The study was conducted in Avis Ankura hospital for women and children. It is a well-recognized, authorized hospital where obstetrics and neonatal care is provided. A total of 162 neonates were considered. Informed consent was obtained from all the subject's care takers. Subjects enrolled in the study were admitted in NICUs'. This study appraises the conventional cause of NNJ, evaluates the efficacy of continuous phototherapy and detects the phototherapy induced adverse reactions by using Naranjo's causality assessment scale.

Results: Among 162 patients, 94 patients (58%) were found to be males and 68 patients (42%) were found to be females. Low birth weight neonates (43.20%) were found to be more prone to neonatal jaundices. In this study, it was found that duration of phototherapy was longer in extremely low birth weight neonates (34 hours) in relation to birth weight and average duration of phototherapy. Based on the conventional cause, physiological cause (56.79%) was observed to be highest among other causes of neonatal jaundice. The short term adverse reactions due to phototherapy were identified using Naranjo's Causality Assessment Scale. The TSB levels were increased before phototherapy (pre- treatment) and decreased after phototherapies (post-treatment) which were assessed by using American Academy of Pediatrics guidelines.

Conclusion: From this study, it was concluded that males were more prone to develop neonatal jaundice when compared with females. Physiological jaundice contributes majority of cases among the total cases. The use of phototherapy was inversely related to gestational age and birth weight.

Keywords: Neonatal Jaundice (NNJ); phototherapy; Total Serum Bilirubin (TSB); Naranjo's Causality Assessment Scale (NCAS).

1. INTRODUCTION

Jaundice is one of the most common conditions that require medical attention in new-born babies [1]. The concept of neonatal icterus is a common finding in new-born that is generally benign and self-limited [2]. Neonatal jaundice (NNJ) refers to yellow dis-colouration of the skin and the sclera (whites of the eyes) of new-born babies that result from the accumulation of bilirubin pigment in the skin and mucous membranes. This is associated with a raised level of bilirubin in the circulation, a condition known as hyperbilirubinemia.

Newborn babies' red blood cells (RBCs) have a shorter lifespan than those of adults. The concentration of RBCs in the circulation is also higher in Newborn babies (NBs) than it is in adults, so bilirubin levels are higher than they are later in life. The metabolism, circulation and excretion of bilirubin are also slower than in adults. Thus a degree of HB occurring as a result of this normal physiological mechanism is common in NB babies and usually harmless. It is difficult to tell which babies are at risk of developing high levels of bilirubin that could become dangerous, or who have a serious problem as the explanation for their jaundice [3].

2. TYPES OF JAUNDICE BASED ON CAUSES

2.1 Physiological Jaundice

Physiological jaundice refers to the common, generally harmless, jaundice seen in many newborn babies in the first weeks of life and for which there is no underlying cause [3]. It is the most abundant type of NB HB, having no serious consequences. Jaundice attributable to physiological immaturity of neonates to handle increased bilirubin production is termed as 'physiological jaundice'. TSB level usually rises in term infants to a peak level by 3 days of age and then falls [4]. Physiological jaundice includes:

2.1.1 Breast feeding jaundice

It is known as breastfeeding jaundice (BFJ) or "breast-non feeding jaundice [3]. Infants who are breastfed receive only small volumes of colostrum in the first days of life, which leads to dehydration and increased uptake of conjugated bilirubin from the intestines, both of which worsen HB [5]. This type of BFJ may result from caloric deprivation and/or insufficient frequency of feeding. Insufficient caloric intake resulting from maternal and/or infant breastfeeding difficulties may increase serum UCB concentrations. This is

the infantile equivalent of adult starvation jaundice [6].

2.1.2 Breast Milk Jaundice (BMJ)

This condition is a type of neonatal jaundice associated with breastfeeding that is characterized by indirect hyperbilirubinemia (IHB) in an otherwise healthy breastfed NB that develops after the first 4-7 days of life, and has no other identifiable cause [5]. The biochemical cause of breast milk jaundice remains under investigation. Some research reported that lipoprotein lipase, found in some breast milk, produces non-esterified long-chain fatty acids, which competitively inhibit glucuronyl transferase conjugating activity. Decreased (*UGT1A1*) activity may be associated with prolonged HB in BMJ [7].

2.2 Pathological Jaundice

Pathologic jaundice is the most serious type of jaundice. 'Pathological jaundice' occurs when TSB concentrations are not in 'physiological jaundice' range. It occurs within 24-48 hours after birth [7]. Pathological jaundice includes the following:

2.2.1 ABO incompatibility

A and B are two major erythrocyte membrane antigens. The incidence of the incompatibility of the ABO blood groups of the mother and fetus, when the mother has the blood group O and the NB has the A or B blood group, is 15–20% of all pregnancies. Jaundice owing to ABO incompatibility usually appears 24 h after the birth [8].

2.2.2 Rh factor incompatibility

RHDN results from maternal red-cell alloimmunization. Rh is an antigen carried only on red blood cells. Most women are Rh-positive; however certain populations have a higher prevalence of Rh-negative women [9].

2.2.3 Cephalohematoma

Cephalohematoma generally occurs during labor and delivery. In some instances, there is evidence of birth trauma, but in other cases, there is no indication of any sort of trauma. However, the use of forceps during delivery has been linked with a heightened risk of cephalohematoma [10].

2.2.4 Polycythemia

Neonatal polycythemia, defined as a venous hematocrit $\geq 65\%$ (0.65), is a common problem in NBs. Infants born post-term or small for gestational age (GA), infants of diabetic mothers, recipient twins in twin-to-twin transfusion syndrome, and those who have chromosomal abnormalities are at higher risk [5].

2.2.5 Intestinal obstruction

Intestinal atresia (IA) is a broad term used to describe a complete blockage or obstruction anywhere in the intestine. The frequencies, symptoms and methods of diagnosis differ depending on the site of intestinal involvement. The different types of intestinal atresia are Pyloric Atresia and Duodenal Atresia [11,12].

2.2.6 Sepsis

Jaundice and hepatic dysfunction frequently accompany a variety of bacterial infections. Sepsis is more likely to manifest with jaundice in infants and children than in adults. Jaundice has been associated with infections caused by several organisms including aerobic and anaerobic gram negative and gram positive bacteria [13].

2.2.7 Jaundice associated with G6PD deficiency

It is an inherited X-linked recessive disorder with varied clinical presentations including neonatal jaundice, hemolysis, and acute icterus after exposure to chemicals and drugs, anemia. Decreased bilirubin conjugation resulted from variation in the *UGT1A1* and *OATP2* genes play an important role in the progression of HB in G6PD deficient NBs [14].

2.2.8 Gilbert Syndrome (GS)

GS is a relatively mild condition characterized by periods of elevated levels of a toxic substance called bilirubin in the blood (HB). This substance is removed from the body only after it undergoes a chemical reaction in the liver, which converts the toxic form of bilirubin (UCB) to a nontoxic form called conjugated bilirubin.

2.2.9 Crigler-Najjar Syndrome (CNSy)

CNSy's a rare genetic disorder characterized by an inability to properly convert and clear bilirubin

Table 1.1. Parameters of types of jaundice based on its etiology [15]

Parameter	Physiological jaundice	Pathological jaundice
Definition	Jaundice that occurs due to physiological changes in neonates.	Jaundice that occurs due to pathological changes in neonates.
Frequency	Most common	Less common when compared to physiological jaundice.
Onset	Appears after day3 to day7 of life (approx.).	Appears within 24-48 hours of life.
Persistence rate	Term neonates <8days Pre-term neonates <14days	Term neonates >8days Pre-term neonates >14days
Rate of increase in TSB	Less per 24hrs	More per 24hrs
Predominant type of bilirubin	UCB (α -bilirubin)	Conjugated (β -bilirubin) or unconjugatedbilirubin (α -bilirubin)
Condition of neonate	Healthy	Unhealthy
Treatment	Disappears without treatment.	Requires treatment according to the cause.

from the body. Normally, bilirubin created in this process is converted from an unconjugated form to a form that can be dissolved in water and excreted from the body [16,17,18,19,20].

3. EPIDEMIOLOGY

Babies who are either small or large for gestational age are at an increased risk of developing NNJ. Signs of NNJ are seen with in the first three days of birth in 80% of preterm babies and 60% of full term infants. NNJ is the commonest abnormal physical finding during the first week of life. Neonatal hyperbilirubinemia is a significant cause of neonatal morbidity and prolongation of hospital stay, which in turn increases the chances of sepsis and mortality. HB is recognized as clinical jaundice in approximately 20-50% of full term and 80% of preterm neonates. About 10% of breast-fed babies are still jaundiced at 1 month of age. Identification of the risk factors, timely detection and optimal management of NNH are thus crucial to prevent brain damage and subsequent neuro motor retardation due to bilirubin encephalopathy.

4. PATHOPHYSIOLOGY

4.1 Physiological Hyperbilirubinemia

Short lifespan of erythrocytes in the NB (during the first three months, fetal haemoglobin (HbF) is replaced by adult haemoglobin (HbA) as a result, haemoglobin levels drop and bilirubin levels rise) + Impaired bilirubin metabolism (due to immature

hepatic conjugation and elimination pathways) + Enterohepatic circulation of bilirubin (UCB is reabsorbed and recycled into the circulation). All these factors lead to jaundice or hyperbilirubinemia in neonates.

4.2 Pathological Hyperbilirubinemia

It can be caused by multiple mechanisms:

- Increased production of bilirubin (E.g. conditions with increased haemolysis), Decreased hepatic uptake (E.g. Crigler-Najjar syndrome),
- Decreased conjugation,
- Impaired excretion (E.g. cholestasis),
- Increased enterohepatic circulation (E.g. decreased intestinal motility, breast milk jaundice) [21].

5. CLINICAL MANIFESTATIONS

The most pervasive sign of infant jaundice is yellow skin and sclera (the whites of the eyes). This typically starts at the head, and spreads to the chest, stomach, arms, and legs. Yellowing of the skin and the whites of the eyes - the main sign of infant jaundice usually appears between the second and fourth day after birth. Drowsiness, pale stools - breast-fed babies should have greenish-yellow stools, while those of bottle fed babies should be a greenish-mustardcolour, poor sucking orfeeding, dark urine - a NB's urine should becolourless, yellow abdomen orlimbs, inability to gainweight, poorfeeding, irritability [22].

6. DIAGNOSIS

6.1 Visual Inspection

Visual inspection of neonatal jaundice is thought to be unreliable, but if is performed properly, then it is almost as good as transcutaneous bilirubinometry (TcB) especially if the TSB levels are less than 12-14 md/dl [23,24].

6.2 Measurement of Serum Bilirubin

6.2.1 Bio-chemical

The gold standard for the estimation of TSB is high performance liquid chromatography (HPLC). But this can be used for research purpose only. Estimation of TSB is usually performed by Van den Bergh reaction in the laboratory.

6.2.2 Micro-methods

It uses 10 microliter of blood sample and is based on spectrophotometry [25,26].

7. MANAGEMENT

7.1 Phototherapy (PT)

Phototherapy remains the mainstay of treating HB in neonates. It acts by converting insoluble bilirubin (unconjugated) into soluble isomers that can be excreted in urine and feces [27,28]. The

decrease of TSB during PT is a result of formation of photo-isomers. Light absorption in the skin transforms the toxic nonpolar Z,Z-bilirubin molecule into more extractable polar photo-isomers: the configurational isomers Z,E-bilirubin and E,Z-bilirubin and the structural isomers Z-lumirubin and E-lumirubin. In addition, a small amount of photo-oxidation products is formed [29,30,31]. Generally photo-isomers are induced shortly after phototherapy is initiated. Presumably they are less toxic than bilirubin and less able to cross the blood-brain barrier. The most commonly used PT units include blue compact florescent lamps (CFL), high intensity light emitting diodes (LED) and fibr1optic units [32,33].

7.2 Exchange Transfusion

Double volume exchange transfusion (DVET) should be performed if the TSB levels reach to age specific cut-off for exchange transfusion or the infant shows signs of bilirubin encephalopathy irrespective of TSB levels [34].

7.3 Intravenous Immunoglobulins (IVIG)

IVIG was used quite commonly for reducing hemolysis and consequent HB in Rh.I and ABO incompatibility. However, subsequent studies did not prove the efficacy and its use. We do not use Intravenous immunoglobulins (IVIG) for treating iso-immune HJ [35].



Grade	Extent of jaundice
0	None
1	Face and neck only
2	Chest and back
3	Abdomen below umbilicus to knees
4	Arms and legs below knees
5	Hands and feet

Fig. 1. Visual assessment scale of neonatal jaundice [36,37]

7.4 Hydration

Infants with severe HB and evidence of dehydration (e.g. excessive weight loss) should be given IV hydration. An extra fluid of 50 mL/kg of N/3 saline over 8 hr 11 decreases the need for exchange transfusion [38].

8. METHODOLOGY

The study was conducted in Avis Ankura hospital for women and children. It is a well-recognized, referral hospital where Obstetrics and neonatal care is provided. A total of 162 neonates were considered. Subjects enrolled in the study were admitted in NICUs'. This study appraises the conventional cause of NNJ, evaluates the efficacy of continuous phototherapy and detects the phototherapy induced adverse reactions by using Naranjo's causality assessment scale.

8.1 Research Participants

A total of 162 neonates comprising of 94 males and 68 females were considered and the disease condition was evaluated after obtaining the informed consent from each of their care takers. Patient details including demographics, maternal details, chief complaints, history of present

illness, past medical history, family history, other co-morbidities, physical examination, laboratory investigations, phototherapy, contact details and other relevant information has been collected from case reports. The obtained clinical data and the test results were re-examined and entered in the data collection forms and further results obtained were tabulated. The subject's caretakers were counselled which helped them to improve and prevent their disease condition, improve quality of life and to a certain extent helped in prevention of adverse reactions.

9. RESULTS

9.1 Distribution of Patients based on the Gestational Age

Out of 162 neonates majority of neonates belonged to the gestational age of Late pre-term 60 (37.03%).

9.2 Distribution of Patients Based on the Blood Group

Neonates with blood groups 'A' and 'B' have shown equal and highest incidence of ABO incompatibility, when compared to neonates with 'AB' blood group.



Fig. 2. Jaundiced neonate on phototherapy

Table 1.2. Distribution of patients based on the gestational age

Gestational age	No. of neonates	Percentage
Extremely Pre-term(< 28 weeks)	8	4.93%
Very Pre-term(28-32 weeks)	42	25.9%
Late Pre-term(32-37 weeks)	60	37.03%
Early Term(37-39 weeks)	22	13.5%
Full Term(39-41 weeks)	28	17.2%
Late Term(41-42 weeks)	2	1.2%

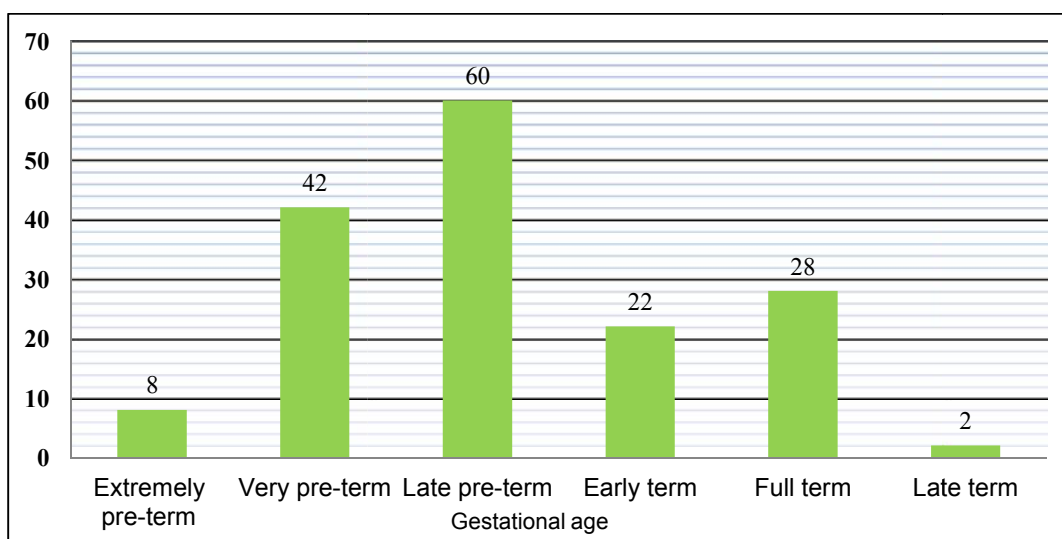


Fig. 3. Distribution of patients based on the gestational age

Table 1.3. Distribution of patients based on the blood groups

Blood group	A	B	AB	O
A	14	2	-	6
B	8	38	4	14
AB	4	6	2	-
O	14	14	2	34

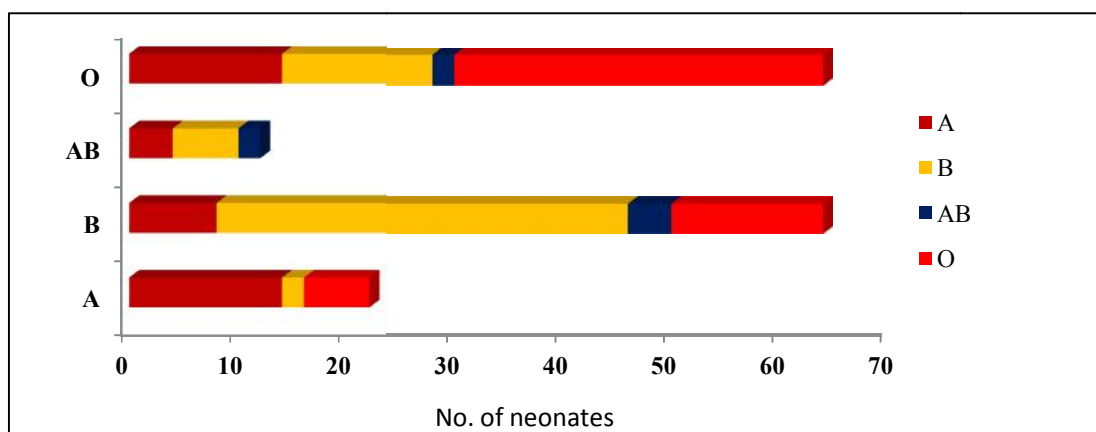


Fig. 4. Distribution of patients based on the blood groups

Table 1.4. Distribution of patients based on the birth weight

Birth weight	No. of patients	Percentage
NBW(2500-4000g)	52	32.09%
LBW(1500-2499g)	70	43.20%
VLBW(1000-1499g)	24	14.81%
ELBW(< 1000g)	16	9.87%

9.3 Distribution of Patients Based on the Birth Weight

On the basis of birth weights, neonates with low birth weight (LBW) were found to be more in number to develop jaundice, whereas those with extremely low birth weight (ELBW) were least to develop those signs and symptoms.

9.4 Relation between Birth Weight and Average Duration of Phototherapy

It was observed that the duration of phototherapy was significantly longer in the lowest birth weight group i.e. extremely low birth weight group & it decreased with increasing birth weight.

9.5 Relation between Gestation Period and Average Duration of Phototherapy

It was observed that the duration of continuous phototherapy was relatively more in Pre-term infants when compared to Term infants.

9.6 Distribution of Patients Based on the Cause

Physiological jaundice accounted for bulk of cases of neonatal jaundice i.e. 92 (56.79%).

9.7 Distribution of Patients Based on Adverse Reactions by Using Naranjo's Scale

It was observed that electrolyte disturbances accounted for the majority of adverse

reactions followed by diarrhea and hypocalcaemia.

9.8 Based on the Variance of TSB Values in Relation to Duration of Phototherapy

The above data justifies our study regarding the efficacy of phototherapy by explaining it graphically where, the pre-treatment serum bilirubin levels are high which are decreased after the phototherapy is done in neonates.

9.9 Risk Assessment Based on TSB Values in Relation to Age and Gestational Age of the Patient.

The best documented method for assessing the risk of subsequent hyperbilirubinemia is to measure the TSB and plot the results on a nomogram (Fig. 10).

Table 1.5. Relation between birth weight and average duration of phototherapy

Birth weight	Avg. duration of phototherapy
NBW	29 hours
LBW	30 hours
VLBW	31 hours
ELBW	34 hours

Table 1.6. Relation between gestation period and average duration of phototherapy

Gestation period	Avg. duration of phototherapy
Pre-Term	31 hrs
Term	27 hrs

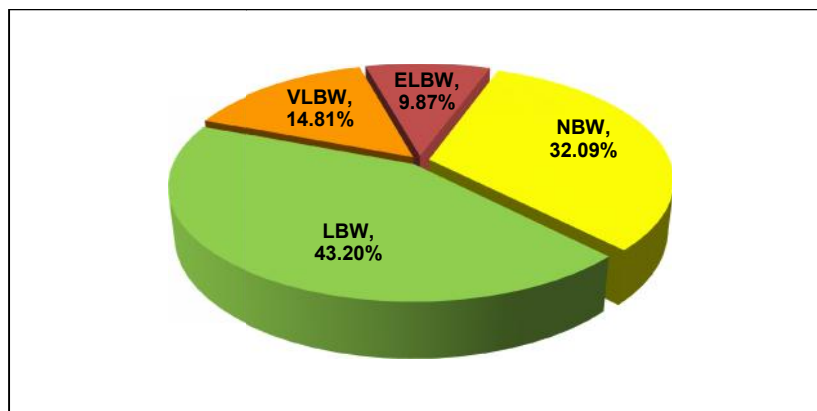


Fig. 5. Distribution of patients based on the birth weight

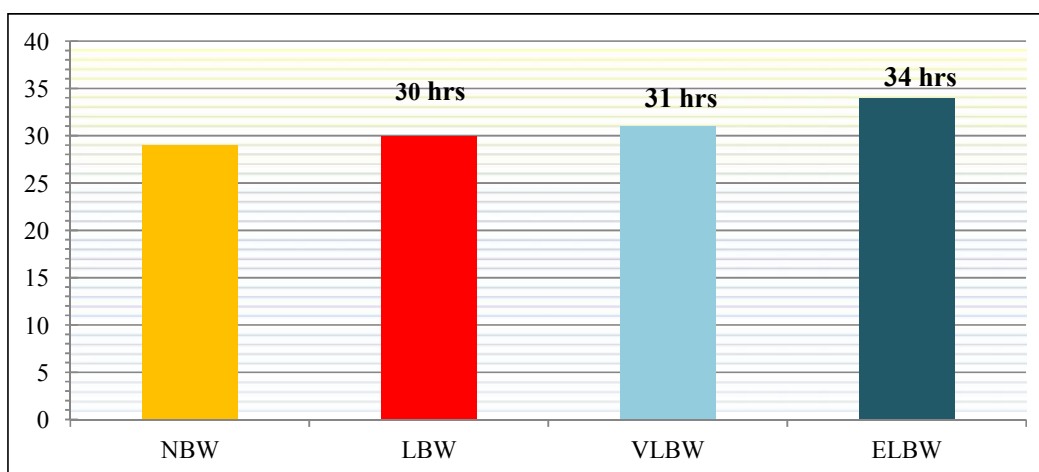


Fig. 6. Relation between birth weight and average duration of phototherapy

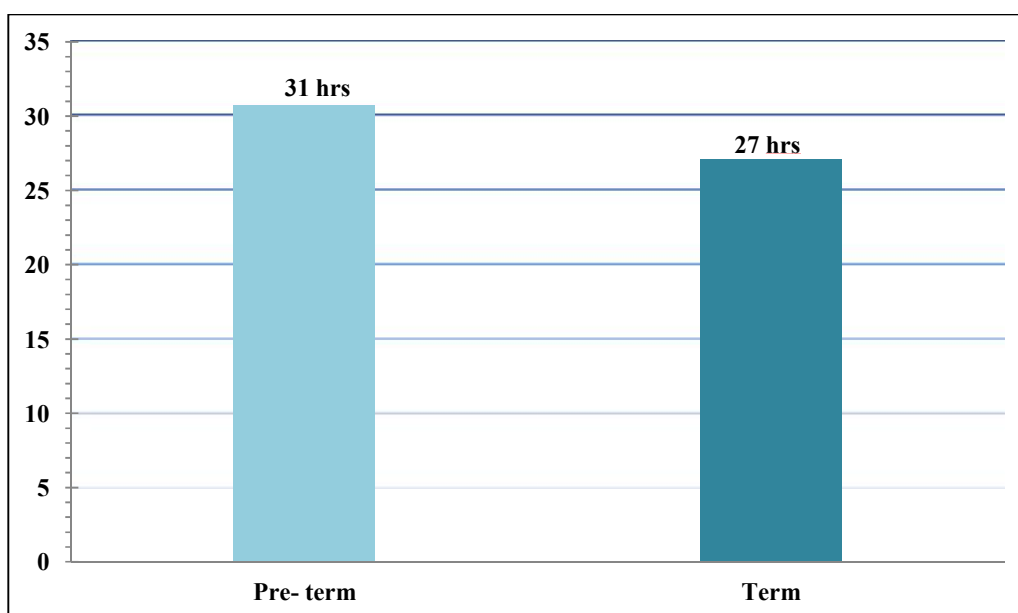


Fig. 7. Relation between gestation period and average duration of phototherapy

Table 1.7. Distribution of patients based on the cause

Cause	No. of patients	Percentage
Physiological	92	56.79%
ABO incompatibility	18	11.11%
Rh incompatibility	12	7.40%
Sepsis	10	6.17%
Breast feeding jaundice	10	6.17%
Intestinal obstruction	6	3.70%
Polycythemia	4	2.46%
Idiopathic neonatal hepatitis	4	2.46%
Cephalohematoma	2	1.23%
Haemolysis	2	1.23%
Tyrosinemia	2	1.23%

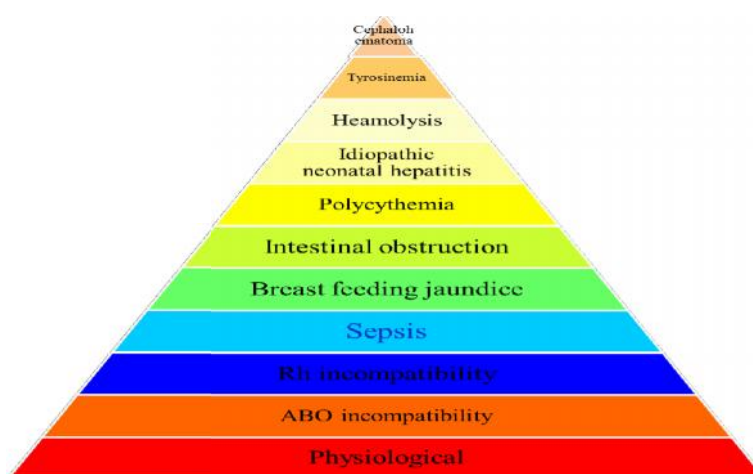


Fig. 8. Distribution of patients based on the cause

Table 1.8. Distribution of patients based on adverse reactions by using Naranjo's scale

Type of adverse reaction	No. of patients	Causality
Electrolyte disturbances	20	Possible
Diarrhoea	8	Possible
Hypocalcaemia	6	Possible

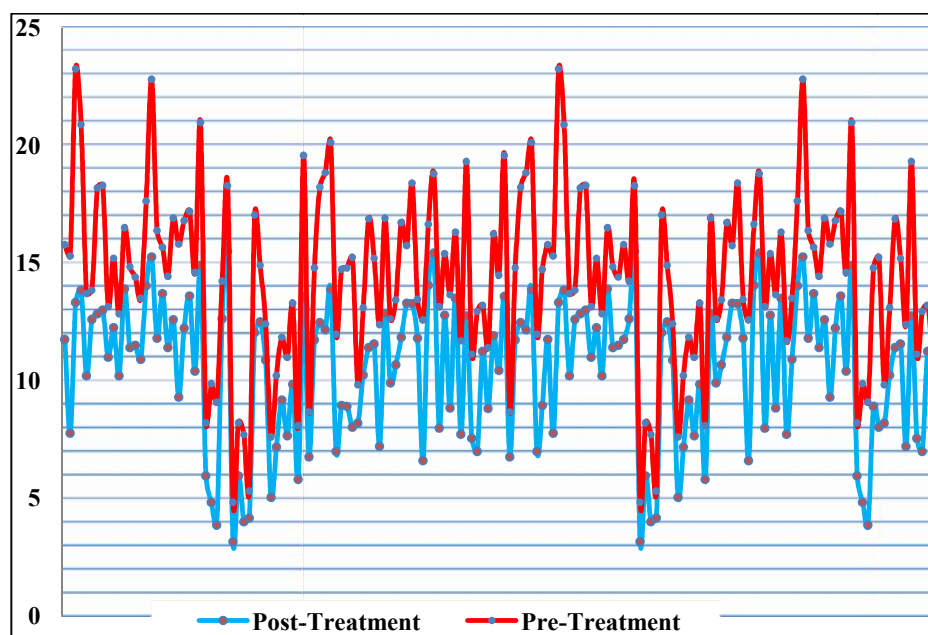


Fig. 9. Variance of TSB values in relation to duration of phototherapy

10. DISCUSSION

We have conducted our study to assess the conventional cause and efficacy of continuous phototherapy in patients with neonatal jaundice. In this prospective observational study, a total of

162 patients were considered based on inclusion and exclusion criteria. The patients were treated with continuous phototherapy for a period of 1-3 days. Of 162 patients, 94 patients (58%) were found to be males and 68 patients (42%) were found to be females. Our results were in

Table 1.9. Risk assessment based on the TSB values in relation to their age and gestational age of the patient

Age	Risk classification based on TSB values		
	High risk (<28-32 weeks)	Intermediate risk (32-39 weeks)	Low risk (39-42 weeks)
24 hours	8	9.9	11.7
48 hours	11.4	13.1	15.3
72 hours	13.6	15.5	17.7
96 hours	14.5	17.5	19.9
> 120 hours	15	18	21

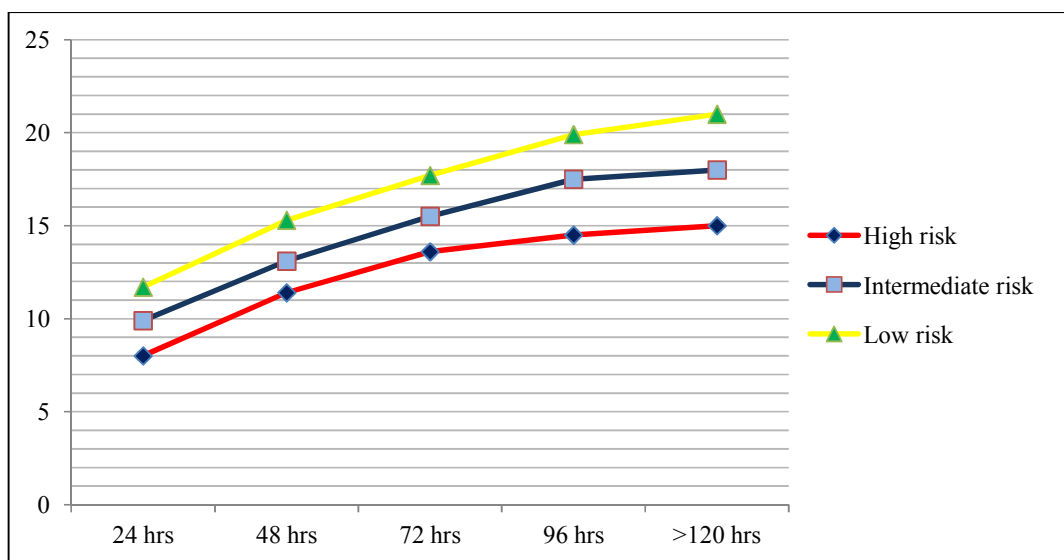


Fig. 10. Risk assessment based on the TSB values in relation to their age and gestational age of the patient

concurrency with prospective observational study conducted by Anil Narang. The author evaluated 551 cases which were divided into two groups. There was a male predominance with 56.2% of cases in group-1 and 64.2% of cases in group-2 being males.

On the basis of gestational period, the mostly effected groups were preterm neonates i.e, 110 patients (67.9%) with neonatal jaundice. Based on gestational age, majority are found to be late preterm (37.3%). Based on the birth weight, low birth weight neonates (43.20%) were found to be more prone to neonatal jaundice. Our results were in concurrence with a literature review study conducted by J F Watchko. It was observed that Hyperbilirubinemia in preterm infants is more prevalent, more severe, and its course more protracted than in term neonates.

Based on the age, 2 days aged neonates (54.32%) were most effected with jaundice. Our

results were in concurrence with a case control study with cross-sectional design conducted by Price adoba evaluated 150 neonates out of which majority (54%) of neonates developed jaundice within 1-3 days after birth with 10% having it at birth.

Based on blood group, the patients with A and B blood groups have shown highest incidence of ABO incompatibility when compared to AB blood groups. Our results were in concurrence with a prospective observational study conducted by Apexa S. Patel. 200 new-born with ABO incompatibility causing clinically significant hyperbilirubinemia were enrolled for the study. In ABO incompatibility group, 90% new born developed clinical jaundice. In treated group, out of 88 new born, 82 were from O-A and O-B incompatibility group.

In this study, it was found that duration of phototherapy was longer in extremely low birth

weight neonates (34 hours) in relation to birth weight and average duration of phototherapy. Based on relationship between gestation period and average duration of phototherapy it was found that duration of continuous phototherapy was increased in preterm infants (31 hours) when compared to term (27 hours). Our results were in concurrence with prospective observational study conducted by Khalaf. The study population was 5382 infants admitted to the 21 NICUs in Norway. Data recorded daily included patient characteristics, diagnosis, duration, the ages at the start and discontinuation of phototherapy. The use of phototherapy was inversely related to birth weight and gestational age. The duration was significantly longer in the lowest birth weight and gestational age groups and decreased with increased birth weight and gestational age groups.

Based on the conventional cause, physiological cause (56.79%) was observed to be highest among other causes of neonatal jaundice. Our results were in agreement with an observational study conducted by Shemeena Valiyat. The author evaluated a total of 110 jaundiced neonates. Physiological jaundice was seen in 44 (42%) of neonates followed by other etiologies such as ABO incompatibility 24 (21.8%), sepsis 11 (10%), Rh incompatibility 9 (8%), idiopathic 9 (8%), prematurity 8 (7.3%), cephalohematoma 7 (6.4%), breast feeding jaundice 7 (6.4%) and hemolytic anaemia 1 (0.9%). Physiological jaundice accounted for bulk of cases of neonatal jaundice.

Based on adverse reactions due to phototherapy, electrolyte disturbances (58.8%) were found to be more. Our results were in agreement with a cross-sectional study conducted by Khan M. A total of 123 term neonates with jaundice of either gender managed by phototherapy were enrolled in the study. The frequency of hypocalcemia is significant (28/123) in the jaundiced neonates treated with phototherapy.

Based on co-morbidities, respiratory distress syndrome (65.5%) was found to be highest. Our results were in concurrence with retrospective study conducted by Jyotsna Verma. 1424 newborns admitted within 24 hours of birth were included in the study. Among various causes of NICU admission Respiratory distress was present in 555 (39%) neonates followed by perinatal asphyxia and sepsis. We categorised the neonates into high, intermediate and low risk

categories based on the hour-specific nomogram for risk stratification published in 'Management of hyperbilirubinemia in the newborn infant' (2004) by the AAP journal. Based on the TSB values recorded before and after undergoing phototherapy, we observed a fall in TSB values of all neonates after the treatment.

11. CONCLUSION

The incidence of neonatal hyperbilirubinaemia was assessed in a tertiary care hospital. Through this study, we systematically estimated the number of infants with severe hyperbilirubinaemia and the underlying causes. From this study, it was concluded that males were more prone to develop neonatal jaundice when compared with females. 1-3 days aged preterm neonates were found to be more prone to neonatal jaundice.

Physiological jaundice constitutes the majority of cases among the total cases. Physiological cause occurs mostly due to immaturity of bilirubin-conjugating system, increased entero-hepatic circulation, decreased calorie intake (breast feed), higher rate of hemolysis. Neonates with 'A' and 'B' blood groups contributed maximum to ABO incompatibility. The impact of birth weight on the duration of continuous phototherapy required to treat NNJ was significant. The use of phototherapy was inversely related to gestational age and birth weight. The duration was significantly longer in the lowest birth weight and gestational age groups and decreased with increasing birth weight and gestational age.

The causality assessment was done using Naranjo's scale which showed higher number of possible adverse reactions. As a result, regular adverse reaction monitoring is required to evaluate and prevent short term and long term side effects respectively in patients with NNJ. Neonates received phototherapy through devices with LEDs'. So, primary outcomes included the rate of fall of total bilirubin (mg/dl) which was indicated by the pre and post treatment serum bilirubin values. We categorized the neonates into high, intermediate and low risk categories based on the hour-specific nomogram for risk stratification published in 'Management of hyperbilirubinemia in the new-born infant' (2004) by the AAP journal.

Every effort should be made to identify at-risk new-born during admission and even before their discharge. This assessment should include

measurement of serum bilirubin levels in infants who appear jaundiced or who have risk factors before they are discharged, preferably in the first few days of life. We recommend screening of infants born to mothers with type 'O' blood, for blood type and Coomb's testing. Appropriate follow-up needs to be arranged before the infants are discharged, including repeat serum bilirubin testing (if necessary) based on predictive hour specific serum bilirubin nomograms used when the infants are discharged.

CONSENT

Informed consent was obtained from all the subject's care takers.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Mitra S, Rennie J. Neonatal jaundice: Aetiology, diagnosis and treatment. *Br J Hosp Med (Lond)*. 2017;78(12):699-704.
- Maisels MJ, Bhutani VK, et al. A brief history of neonatal jaundice, hyperbilirubinemia in the newborn-infant >35 weeks gestation. *Pediatrics*. 2009;124:1193-8.
- NICE Clinical Guidelines, No. 98. National Collaborating Centre for Women's and Children's Health (UK). London: RCOG Press.
- Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. *N Engl J Med*. 2001;344(8):581-90.
- Amanda Yaworski, Ania Van Meer, Eric Wong. Neonatal hyperbilirubinemia. Faculty Reviewer: Dr. Moyez Ladhani, MD, FRCP, FAAP, MSc (Associate Professor, Department of Pediatrics, McMaster University).
- Maisels MJ, McDonagh AF. Phototherapy for neonatal jaundice. *New England Journal of Medicine*. 2008;358(9):920-928.
- Fujiwara R, Maruo Y, Chen S, Tukey RH. Role of extrahepatic UDP-glucuronosyltransferase 1A1: Advances in understanding breast milk-induced neonatal hyperbilirubinemia. *Toxicol Appl Pharmacol*. 2015;289(1):124-32.
- Sana Ullah, Khaista Rahman, Mehdi Hedayati, Murray NA, Roberts IA. Hyperbilirubinemia in neonates: Types, causes, clinical examinations, preventive measures and treatments: A narrative review article. *Hemolytic disease of the newborn*. *ADC Fetal Neonatal Ed*. 2007;92:83-8.
- Sana Ullah, Khaista Rahman, Mehdi Hedayati, Al-Swaf FB, Jumaa RS, Saeed IS. Hyperbilirubinemia in neonates: Types, causes, clinical examinations, preventive measures and treatments: A narrative review article. *Hemolytic disease of newborn due to ABO incompatibility*. *Tikrit Medical Journal*. 2009;15(2):70-78.
- Panuel M, Bourliere-Najean B, Delarue A, Viard L, Faure F, Devred P. Duodenal atresia with bifid termination of the common bile duct. *Arch Fr Pediatr*. 1992;49(4):365-7.
- Haber BA, Erlichman J, Loomes KM. Recent advances in biliary atresia: prospects for novel therapies. *Expert Opin Investig Drugs*. 2008;17(12):1911-24.
- Dòmini M. Gastrointestinal malformations of newborns. In: Buonocore G, Bracci R, Weindling M, (Eds) *Neonatology*. Springer, Cham; 2016.
- Nisha Chand, Arun J. Sanyal. Sepsis induced cholestasis[†] combined effects of the UGT1A1 and OATP2 gene polymorphisms as major risk factor for unconjugated hyperbilirubinemia in Indian neonates. *D'Silva S, Colah RB, Ghosh K, Mukherjee MB. Gene*. 2014;547(1):18-22.
- Rossi F, Francese M, Iodice RM, et al. Inherited disorders of bilirubin metabolism. *Minerva Pediatr*. 2005;57:53-63.
- Available: https://www.amboss.com/us/knowledge/Neonatal_jaundice
- Monaghan G, McLellan A, McGeehan A, et al. Gilbert's syndrome is a contributory factor in prolonged unconjugated hyperbilirubinemia of the newborn. *J Pediatr*. 1999;134:441-446.
- Bosma PJ, Roy-Chowdhury J, Bakker C, et al. The genetic basis of the reduced expression of bilirubin UDP-glucuronosyltransferase 1 in Gilbert's syndrome. *N Engl J Med*. 1995;333:1171-1175.
- Aono S, Adachi Y, Uyama E, et al. Analysis of genes for bilirubin UDP-glucuronosyltransferase in Gilbert's syndrome. *Lancet*. 1995;345:958-959.

19. Koiwai O, Nishizawa M, Hasada K, et al. Gilbert's syndrome is caused by a heterozygous missense mutation in the gene for bilirubin UDP-glucuronosyltransferase. *Hum Mole Genet.* 1995;4:1183-1186.
20. Available: https://www.researchgate.net/figure/Types-of-neonatal-jaundice_tbl1_272472093
21. *Journal Archives of Disease in Childhood - Fetal and Neonatal Edition.*
22. *AIIMS Protocol in Neonatology*, Available on WHO Collaborating Center for Training and Research in Newborn Care, Department of Pediatrics, All Indian Institute of Medical Sciences, New Delhi, India.
23. Askari FK. Crigler-Najjar syndrome. In: *NORD Guide to Rare Disorders*. Lippincott Williams & Wilkins. Philadelphia, PA. 2003;337.
24. Behrman RE, Kliegman RM, Jenson HB, Eds. *Nelson textbook of pediatrics*. 17th Ed. Elsevier Saunders. Philadelphia, PA. 2005;1320-1321.
25. Maisels MJ. Phototherapy—traditional and nontraditional. *J Perinatol.* 2001; 21(Suppl 1):93–7. Crossref PubMed GoogleScholar
26. 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. Crossref PubMedWeb of Science@Google Scholar
27. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in Canada. *CMAJ.* 2006;175:587–90.
28. Newman TB, Kuzniewicz MW, Liljestrand P, Wi S, McCulloch C, Escobar GJ. Numbers needed to treat with phototherapy according to American Academy of Pediatrics Guidelines. *Pediatrics.* 2009;123:1352–9.
29. Xiong T, Qu Y, Cambier S, Mu D. The side effects of phototherapy for neonatal jaundice: What do we know? What should we do? *Eur J Pediatr.* 2011;170:1247–55.
30. Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea TM, et al. Aggressive vs. conservative phototherapy for infants with extremely low birth weight. *N Engl J Med.* 2008;359:1885–96.
31. Tyson JE, Pedroza C, Langer J, Green C, Morris B, Stevenson D, et al. Does aggressive phototherapy increase mortality while decreasing profound impairment among the smallest and sickest newborns? *J Perinatol.* 2012;32:677–84.
32. Hansen TW. Therapeutic approaches to neonatal jaundice: An international survey. *Clin Pediatr.* 1996;35:309–16.
33. Gartner LM, Snyder RN, Chabon RS, et al. Kernicterus: High incidence in premature infants with low serum bilirubin concentration. *Pediatrics.* 1970;45:906.
34. Watchko JF, Oski FA. Kernicterus in preterm newborns: Past, present and future. *Pediatrics.* 1992;90:707–15.
35. Sachdeva M, Murki S, Oleti TP, Kandraj H. Intermittent versus continuous phototherapy for the treatment of neonatal non hemolytic moderate hyperbilirubinemia in infants more than 34 weeks of gestational age: A randomized controlled trial. *Eur J Pediatr.* 2015;174:177–81.
36. Jaundice in newborn babies under 28 days: NICE Clinical Guideline (Released 2010, Updated October 2016).
37. Bratlid D, Nakstad B, Hansen TW. National guidelines for treatment of jaundice in the newborn. *Acta Paediatr.* 2011;100:499–505.
38. Downs E, Gourley GR. Neonatal jaundice and disorders of bilirubin metabolism. In: *Nathan and Oski's Hematology of Infancy and Childhood*, 7th Ed. Orkin SH, Nathan DG, Ginsburg D, Look AL, Fisher DE, Lux SE, Editors. Elsevier Saunders, Philadelphia, PA. 2015;101-127.e12.

© 2019 Hussaini et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sdiarticle3.com/review-history/50443>