A PROSPECTIVE OBSERVATIONAL EXPLORATION OF MATERNAL AWARENESS OF NEONATAL JAUNDICE AND RISK ASSESSMENT

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Abstract. Jaundice is the condition which is characterised by yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. This condition is most commonly found in new-born and infants; however, it affects adults as well. Neonatal hyper bilirubinemia is the most common clinical condition in the newborn evaluation during the first week of postnatal life. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age. Jaundice is caused due to the accumulation of bilirubin (a yellow pigment) in the skin. When blood cells complete their life cycle, they are broken down in the body. Phototherapy and exchange transfusion are the mainstay of treatment for patients with unconjugated hyper bilirubinemia. Newborns with severe hyper bilirubinemia are at risk for bilirubin-induced neurologic dysfunction (BIND). The best prevention of infant jaundice is adequate feeding. Breast-fed infants should have eight to 12 feedings a day for the first several days of life. The primary goals of the current study are to evaluate the risk factors and maternal knowledge of neonatal jaundice and objective includes to educate mothers regarding neonatal jaundice and to increase the awareness about the neonatal jaundice. This survey highlights the mother's level of awareness of newborn jaundice. While mothers were aware of neonatal jaundice, their understanding of potential complications and treatment options was limited. Promoting awareness of neonatal jaundice among mothers is crucial for early detection and treatment, and during our study, the present study endeavoured to enhance mothers understanding of this condition.
Keywords: *neonatal jaundice, maternal awareness, risk assessment, observational study, prospective study, bilirubin*

Introduction

Jaundice is the condition which is characterised by yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. The term "Jaundice" comes from the French language and means "yellow". This condition is most commonly found in new-born and infants; however, it affects adults as well (Salih, 2001). Neonatal hyper bilirubinemia is the most common clinical condition in the newborn requiring evaluation and management and remains a frequent reason for hospital readmission during the first week of postnatal life (*Figure 1*). Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age. In most babies with jaundice there is no underlying disease, and this early jaundice (termed 'physiological jaundice') is generally harmless. However, there are pathological causes of jaundice in the newborn, which, although rare, need to be detected. The high prevalence of neonatal hyper bilirubinemia reflects developmental red blood cell, hepatic, and gastrointestinal immaturities that result in an imbalance favouring bilirubin production over hepatic–enteric bilirubin clearance. For most neonates, hyperbilirubinemia is a benign postnatal

transitional phenomenon of no overt clinical effect. A subset of infants, however, will develop more significant hyperbilirubinemia. The estimated occurrence of hyperbilirubinemia based on peak total serum bilirubin (TSB) severity has been reported as: more than 17 mg/dL (291 µmol/L), defined as significant, at ~1 in 10; more than 20 mg/dL (342 µmol/L), defined as severe, at ~1:70; more than 25 mg/dL (428 µmol/L), defined as extreme, at ~1:700; and more than 30 mg/dL (513 µmol/L), defined as hazardous, at ~1:10,000 live births (Bhutani et al., 2004).

Figure 1. *Neonatal jaundice in new born baby.*

Jaundice is caused due to the accumulation of bilirubin (a yellow pigment) in the skin. When blood cells complete their life cycle, they are broken down in the body. Bilirubin from these cells is released, which further gets filtered in the liver and then excreted. Since the liver of the baby is not fully developed, it cannot filter the entire bilirubin formed, which thus accumulates in the skin, resulting in neonatal jaundice. Neonatal jaundice is usually not harmful and a self-limiting condition; however, very high levels of bilirubin may cause permanent brain damage, a condition called kernicterus. Therefore, it is important to diagnose neonatal jaundice and manage it appropriately (Abbey et al., 2019).

Physiology of bilirubin

Bilirubin (formerly referred to as haematoidin and discovered by Rudolf Virchow in 1847) is a yellow compound that occurs in the normal catabolic pathway involving breakdown of heme in vertebrates (*Figure 2*). This catabolism is a necessary process in the body's clearance of waste products that arise from the destruction of aged red blood cells. First, the haemoglobin gets stripped of the heme molecule which thereafter passes through various processes of porphyrin catabolism, depending on the part of the body in which the breakdown occurs. The production of biliverdin from heme is the first major step in the catabolic pathway, after which the enzyme biliverdin reductase performs the second step, producing bilirubin from biliverdin. Bilirubin is excreted in bile and urine, and elevated levels may indicate certain diseases. It is responsible for the yellow colour of bruises and the yellow discoloration in jaundice. Its subsequent breakdown products, such as stercobilin, cause the brown colour of faeces. A different breakdown product,

urobilin, is the main component of the straw-yellow colour in urine. There is unconjugated bilirubin and conjugated bilirubin. In the liver, bilirubin is conjugated with glucuronic acid by the enzyme glucuronyl transferase, making it soluble in water: the conjugated version is the main form of bilirubin present in the "direct" bilirubin fraction. The measurement of unconjugated bilirubin depends on its reaction with diazosulfanilic acid to create azobilirubin (Sedlak and Snyder, 2004).

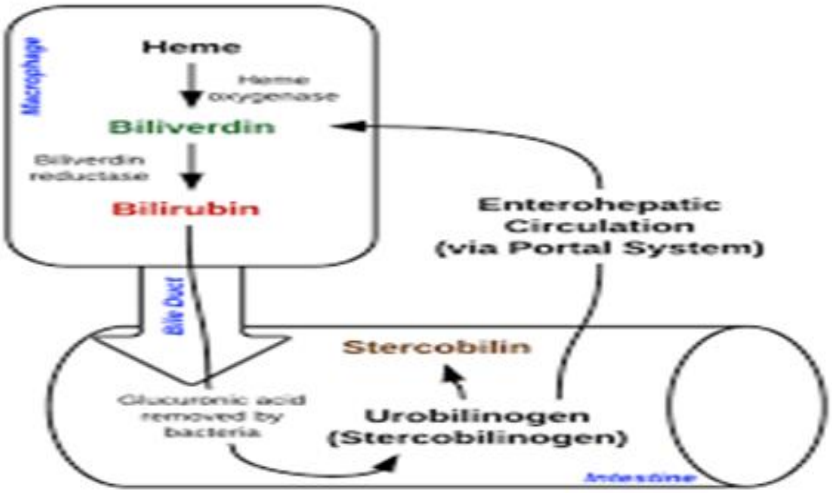

Figure 2. *Pathway of bilirubin.*

Type of jaundice

Physiological jaundice

Most cases of hyperbilirubinemia in neonates are physiologic and lead to no serious complications. In rare cases of physiologic hyperbilirubinemia, where bilirubin levels reach toxic high levels, neurodevelopmental abnormalities could occur including intellectual deficits, athetosis, and loss of hearing. Physiological jaundice usually appears after at least 24 hours of birth, and peak after four or five days. It later disappears after about 2 weeks of life.

Pathological jaundice

Bilirubin levels that deviate from the normal range and requiring intervention would be defined as pathological jaundice. Appearance of jaundice within 24 hours, increase in serum bilirubin beyond 5 mg/dl/day, peak levels above the expected normal range, presence of clinical jaundice beyond 2 weeks and conjugated bilirubin (dark urine staining the clothes) would be categorized under pathological jaundice (*Figure 3*) (Provisional Committee on Quality Improvement & Subcommittee on Hyperbilirubinemia, 1994).

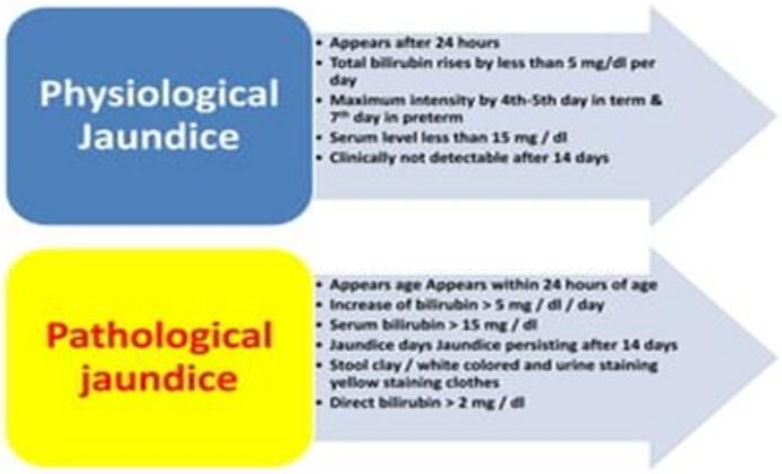

Figure 3. *Difference between physiological and pathological jaundice.*

Breast milk jaunduce

Neonates and infants who are exclusively breastfed can develop other types of jaundice related to breastfeeding. Similar to physiological jaundice, breast feeding jaundice appears after a day or two days of birth, and peaks at the first week of age. However, it can last longer than physiological jaundice, and usually will not completely disappear until the third of fourth week of life. Moreover, infants with breast feeding jaundice have been found to have higher levels of bilirubin than physiological jaundice. Moreover, in some infants, breast feeding jaundice can be recurrent as long as the breastfeeding period continues. It is estimated that up to 30% of breastfed infants will develop a mild jaundice within the first three weeks of their life. This jaundice could sometimes persist for up to three months. On the other hand, the reduction of breastfeeding frequency will increase the risk and severity of physiological jaundice. Therefore, the best management of this jaundice in an otherwise healthy full-term baby is to encourage mothers to continue breastfeeding for at least ten times daily. The breast milk of the mother can also affect the occurrence of hyperbilirubinemia in a neonate. In fact, up to 4% of infants who are exclusively breastfed can develop jaundice within the first three weeks of life, where bilirubin levels can become higher than 10 mg/dl (Schneider, 1986).

Haemolytic jaunduce

PRH factor haemolytic disease

In cases where alloimmunization of maternal RBCs, Rhesus haemolytic disease of the newborns (RHDN) occurs ,in these cases, the mother's body produces antibodies that attack specific antigens on the RBCs of the foetus, most likely, the Rh antigens. This is most likely to occur when an Rh negative mother has a Rh-positive foetus. In these cases, the mother produces antibodies against the Rh antigen, and these antibodies can cross the placenta and enter the circulation of the foetus. This will cause the foetus to develop a clinical picture that ranges from mild haemolytic anaemia, to severe haemolytic anaemia followed by foetal hydrops. Infants who have a risk of developing Rhesus haemolytic disease of the newborns should be early investigated and treated. Investigations for these infants include packed cell volume, blood group, Rh typing,

serum bilirubin, and reticulocytes count. Immediately following birth, these patients should be initiated on phototherapy, which should continue until the level of bilirubin decreases significantly (Stockman and de Alarcon, 2001).

ABO incompatibility

It is estimated that ABO incompatibility between the foetus and the mother can occur in up to 20% of pregnancies, and results from an O mother and who has an A or B foetus. Therefore, it is important to closely monitor mothers who have an O blood group for at least three days after birth (Myle and Al-Khattabi, 2021).

G6PD deficiency

The management of spherocytosis, G6PD deficiency, and similar diseases is similar to the management of ABO incompatibility. Of these, the most common one is G6PD deficiency. It causes significant dysfunction of the hexose monophosphate pathway within the RBCs leading to haemolysis. It should be suspected in any neonate who has a family history with haemolytic jaundice, or who originates from are where G6PD is prevalent (Kaplan and Hammerman, 1998).

Etiology

There are two distinct types of Neonatal hyperbilirubinemia: (a) Unconjugated Hyper Bilirubinemia (UHB) or Indirect Hyper bilirubinemia; and (b) Conjugated Hyperbilirubinemia (CHB) or Direct Hyperbilirubinemia.

Unconjugated Hyper Bilirubinemia (UHB) or Indirect Hyper bilirubinemia

Unconjugated hyper bilirubinemia is the more common type and is either physiological or pathological. Physiological jaundice accounts for 75% of neonatal hyper bilirubinemia and results from a physiological alteration in neonatal bilirubin metabolism. Healthy adults have a normal TSB level of less than 1mg/dl in contrast to neonates, where TSB levels are physiologically higher. Even in healthy full-term newborns, there is an increased bilirubin load owing to increased red blood cells (RBC) mass and a decreased RBC lifespan. Clearance of bilirubin is also compromised due to impaired activity of uridine diphosphate glucuronosyl transferase (UGT), the enzyme needed for bilirubin conjugation. The UGT enzyme in a newborn has an activity of about 1% of the adult level (Gartner and Auerbach, 1987). Based on the mechanism of bilirubin elevation, the etiology of unconjugated hyper bilirubinemia can be subdivided into the following three categories:

Increase bilirubin production

Immune-mediated haemolysis-Includes blood group incompatibilities such as ABO and Rhesus incompatibility. Non-immune mediated haemolysis-includes RBC membrane defects like hereditary spherocytosis and elliptocytosis; RBC enzyme defects like glucose-6-phosphate dehydrogenase (G6PD) deficiency; pyruvate kinase deficiency; sequestration like cephalohematoma, subgaleal haemorrhage, Intracranial haemorrhage; polycythaemia, and sepsis.

Decreased bilirubin clearance

Crigler-Najjar type I & II, and Gilbert syndrome.

Miscellaneous causes

Other miscellaneous etiologies include the infant of a mother with diabetes, congenital hypothyroidism, drugs like sulpha drugs, ceftriaxone, and penicillin's, Intestinal obstruction, pyloric stenosis, breast milk jaundice, breastfeeding jaundice. Exaggerated haemolysis, either immune or non-immune mediated, is the most common cause of pathological hyperbilirubinemia in newborns. Immune-mediated haemolysis is seen with blood group incompatibility such as ABO/RH incompatibility and leads to haemolytic disease of newborns (HDN). In HDN, due to ABO incompatibility, preformed maternal anti-A and anti-B antibodies of immunoglobulin (Ig) G subclass cross the placenta and cause haemolysis and UHB in newborns with blood type A, B, or AB. Although the direct Coombs test is used to aid diagnosis, the sensitivity and positive predictive value for predicting severe UHB are low. ABO incompatibility between mother and foetus exists in about 15% of pregnancies, but HDN due to ABO incompatibility is seen only in 4% of newborns with ABO incompatibility. Breast milk jaundice and breastfeeding jaundice are two other common etiologies of UHB in newborns. Breastfeeding jaundice, also known as breastfeeding failure jaundice, occurs in the first week of life and is due to inadequate intake of breast milk leading to dehydration and sometimes hypernatremia (Shahid and Graba, 2012).

Conjugated Hyperbilirubinemia (CHB) or Direct Hyperbilirubinemia

Conjugated hyperbilirubinemia, also referred to as neonatal cholestasis, is characterized by elevation of serum conjugated/direct) bilirubin (> 1.0 mg/dL) and is due to impaired hepatobiliary function. Distinguishing CHB from UHB is critical because cholestatic jaundice/CHB is almost always pathologic and warrants prompt evaluation and treatment. The causes of neonatal cholestasis/CHB are extensive and can be classified into the following categories: (a) obstruction of biliary flow: biliary atresia, choledochal cysts, neonatal sclerosing cholangitis, neonatal cholelithiasis; (b) infections: CMV, HIV, rubella, herpes virus, syphilis, toxoplasmosis, urinary tract infection (UTI), septicaemia; (c) genetic causes: alagille syndrome, alpha-1 anti-trypsin deficiency, galactosemia, fructosemia, Tyrosinemia type 1, cystic fibrosis, progressive familial intrahepatic cholestasis (PFIC), Aagenaes syndrome, Dubin-Johnson syndrome, Bile acid synthesis disorders (BSAD); and (d) miscellaneous: idiopathic neonatal hepatitis, parenteral nutrition induced cholestasis, gestational alloimmune liver disease/neonatal hemochromatosis, hypotension (Fawaz et al., 2017).

Biliary atresia (BA) is the most common cause of conjugated hyperbilirubinemia in infants. The incidence of BA varies from region to region. It is reported at a frequency of 1 in 6000 live births in Taiwan, the region with the highest incidence. In the United States, it has an incidence of around 1 in 12,000 live births. The etiology of BA is not well understood, but genetic factors along with viral infection, toxins, chronic inflammatory and autoimmune injury to bile ducts seem to play a role in its pathogenesis (The et al., 2007). Cytomegalovirus (CMV) is the most common congenital infection that manifests in various ways. Most infected newborns are asymptomatic, but hepatomegaly and CHB are the most prominent feature of hepatic involvement. Syphilis, toxoplasmosis, herpes, and rubella should be included in the differential diagnosis of neonatal cholestasis, especially when other stigmata of

congenital infection like growth restriction, coagulopathy, skin rash, and thrombocytopenia is present (Plosa et al., 2012).

Alpha-1-antitrypsin deficiency is the most common genetic cause of cholestatic and may mimic biliary atresia in early infancy. Accumulation of anti-trypsin polymers in the endoplasmic reticulum of hepatocytes of a patient with the PiZZ genotype leads to apoptosis of hepatocytes, ultimately resulting in cholestasis and cirrhosis later in childhood. As with ALGS, cholestasis may also improve with age as with ALGS. Galactosemia, fructosemia, and tyrosinemia type 1 are a few of the inborn errors of metabolism known to cause cholestasis in neonates. Newborns with galactosemia present with cholestatic jaundice, cataracts, hepatomegaly, failure to thrive, renal tubular acidosis, and Escherichia coli sepsis after the ingestion of galactose from milk. Galactose-1-phosphate uridyl transferase (GALT) deficiency leads to the accumulation of toxic galactose metabolites in multiple organs. The presence of reducing substances in urine suggests galactosemia, and GALT activity in the liver or erythrocytes confirms the diagnosis (Karadag et al., 2013).

Signs and symptoms

Jaundice usually appears first on the face and then moves to the chest, belly, arms, and legs as bilirubin levels get higher. The whites of the eyes can also look yellow. Jaundice can be harder to see in babies with darker skin colour: (1) drowsiness; (2) pale stools breast-fed babies should have greenish-yellow stools, while those of bottle-fed babies should be a greenish-mustard colour; (3) poor sucking or feeding; (4) dark urine a new born's urine should be colourless (Brown urine); (5) yellow colour of the skin; and (6) high pitch cry vomiting (Maisels and McDonagh, 2008) (*Figure 4*).

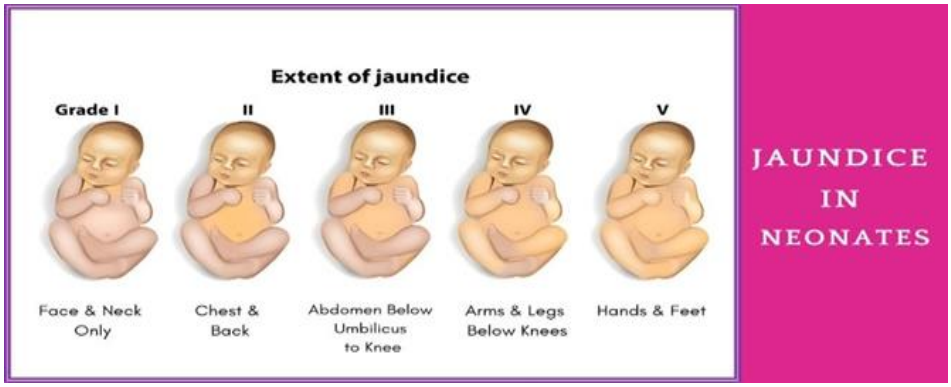

Figure 4. *Grades of jaundice.*

Diagnosis

Diagnosis of unconjugated hyperbilirubinemia

Bilirubin levels can be assessed using a transcutaneous measurement device or blood samples for total serum bilirubin. Transcutaneous estimation of bilirubin reduces the frequency of blood tests, but its utility is limited in infants with dark skin and following phototherapy use. The serum level should be measured when the transcutaneous bilirubin (TcB) level exceeds the 95th percentile on the transcutaneous nomogram or 75% of the TSB nomogram for phototherapy. Another limitation of relying on TcB is the inability to detect the direct fraction of bilirubin required for diagnosing neonatal cholestasis. Recommended workup for identifying a haemolytic disease as the cause of

unconjugated hyperbilirubinemia include maternal/neonatal blood type, Coombs test, complete blood cell (CBC), reticulocyte count, blood smear, and G6PD. Serum albumin should always be checked, especially if TSB level approaches near the exchange transfusion levels, as it is considered a surrogate marker for free bilirubin. Free bilirubin is the fraction responsible for bilirubin-induced toxicity. Bilirubin-albumin ratio(B/A) ratio is, therefore, an additional tool that may predict the risk of kernicterus and may serve as an alternative guide to exchange transfusion (Hulzebos et al., 2014).

Radiographic imaging is usually not required for most cases of UCH. Magnetic resonance imaging (MRI) findings have high sensitivity for bilirubin encephalopathy, with posteromedial borders of the globus pallidus being the most sensitive brain region for detecting signal changes. Infants with bilirubin encephalopathy demonstrate hyperintense signals on T1-weighted sequences in the acute stage that eventually becomes hyperintense on T2-weighted sequences as the disease evolves. Magnetic resonance spectroscopy (MRS) shows increased levels of glutamate and decreased levels of N-acetyl-aspartate and choline. However, the absence of these findings does not exclude the risk of chronic bilirubin encephalopathy (Steinborn et al., 1999).

Diagnosis of conjugated hyperbilirubinemia

In patients with conjugated hyperbilirubinemia, the serum aminotransferases should be ordered for evidence of hepatocellular injury, alkaline phosphatase, and GGT levels for evidence of obstruction in biliary channels, prothrombin time/INR, and serum albumin to evaluate for hepatic synthetic function. Additional tests like TORCH titers, urine cultures, viral cultures, serologic titers, Newborn screening results, specific tests for inborn errors of metabolism, alpha-1 antitrypsin phenotype, and specific genetics tests may be needed depending on the scenario. Radiology is often necessary as part of the workup of neonatal cholestasis. Hepatic ultrasonography may help identify sludging in the biliary tree, gallstones, inspissated bile, and choledochal cysts. Triangular cord sign seen on hepatic ultrasound has high sensitivity and almost 100% specificity for biliary atresia. Hepatobiliary scintigraphy is another tool increasingly used in evaluating neonatal cholestasis. Decreased excretion of tracer 24 hours after introduction suggests obstruction and further helps in excluding nonobstructive causes of cholestasis. Prior treatment with phenobarbitone has been shown to improve the sensitivity for this imaging. Finally, liver biopsy is usually considered the gold standard for diagnosing neonatal cholestasis. Histopathological interpretation by an experienced pathologist will help to identify the correct diagnosis in 90% to 95% of cases and may prevent unnecessary interventions in patients with intrahepatic cholestasis (Benchimol et al., 2009).

Treatment

Treatment of unconjugated hyperbilirubinemia

Phototherapy and exchange transfusion are the mainstay of treatment for patients with unconjugated hyperbilirubinemia.

Phototherapy

Phototherapy (PT) remains the first-line treatment for managing pathological unconjugated hyperbilirubinemia. PT is very effective in reducing TSB to safe levels

and reduces the risk of bilirubin toxicity and the need for exchange transfusion. Phototherapy is started based on risk factors and the TSB levels on the bilirubin nomogram. However, guidelines on the indications for PT in preterm infants are lacking, especially in the United States, because of a lack of evidence. As such most hospitals in the U.S. have instituted their own guidelines for the use of phototherapy and exchange transfusion in preterm infants based on birth weight or gestational age. The efficacy of phototherapy depends on the dose and wavelength of light used as well as the surface area of the infant's body exposed to it. Increasing the dose of PT can be achieved by placing phototherapy units at the minimum safe distance from the infant and increasing the number of units used (*Figure 5*).

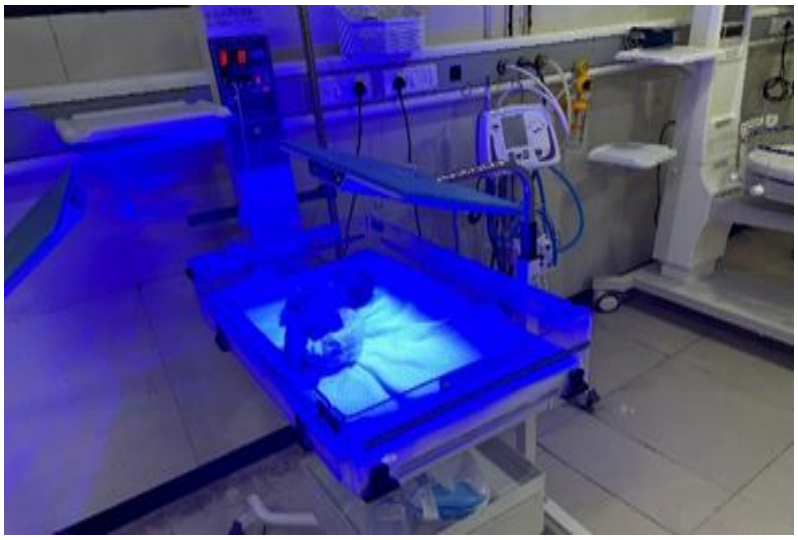

Figure 5. *Photo Therapy for Neonatal Jaundice.*

Bilirubin absorbs light optimally in the blue-green range (460 to 490 nm). PT works by inducing bilirubin photoisomerization and converting bilirubin into lumirubin, which is the rate-limiting step for bilirubin excretion. During phototherapy, the eyes of the newborn must be covered to avoid retinal injury. Measures are necessary to expose maximum body surface area to the light and avoid interruptions in PT. It is important to maintain adequate hydration and ensure normal urine output as most bilirubin is excreted in the urine as lumirubin. After phototherapy is discontinued, there is an increase in the total serum bilirubin level known as the" rebound bilirubin." The "rebound bilirubin" level is usually lower than the level at the initiation of phototherapy and usually does not require reinitiation of phototherapy. PT has been considered relatively safe, but recent evidence points towards possible long-term side effects. Reported side-effects with PT use include rash, dehydration, hypocalcaemia, retinal damage, haemolysis due to oxidative damage, delay in PDA closure in preterm infants, and allergic reactions (Morotti and Jain, 2013).

Few studies have also reported an increased incidence of solid organ tumours and non-lymphocytic leukaemia in children treated with phototherapy.The bronze baby syndrome is another commonly described phenomenon associated with PT and results in irregular pigmentation of the skin, mucous membranes, and urine. It is usually seen in neonates with elevated serum conjugated bilirubin levels. The mechanism is not clear but appears to be related to the accumulation of photo isomers of bilirubin and biliverdin deposition (Itoh et al., 2017).

Exchange transfusion

Exchange transfusion (ET), the first successful treatment ever used for jaundice, is currently the second-line treatment for severe unconjugated hyperbilirubinemia. It is indicated when there is a failure of response to PT, or the initial TSB levels are in the exchange range based on the nomogram. ET rapidly removes bilirubin as well as haemolysis, causing antibodies from circulation. A double volume exchange blood transfusion (160 to 180 ml/kg) is performed, replacing the neonate's blood in aliquots with crossed-matched blood. Since most of the total body bilirubin lies in the extravascular compartment complications, TSB levels immediately following ET is about 60% of the pre-exchange level that later increase to 70 to 80% of pre-exchange levels as a result of equilibrium with an extravascular moiety of bilirubin. During ET, vitals should be monitored closely, and TSB, CBC, serum calcium, glucose, and electrolytes need to be checked following procedure. Complications of ET include electrolyte abnormalities like hypocalcaemia and hypercalcemia, cardiac arrhythmias, thrombocytopenia, blood-borne infections, portal vein thrombosis, graft versus host disease, and necrotizing enterocolitis (NEC). Phototherapy should resume after exchange transfusion until the bilirubin reaches a level where it can be safely discontinued (Jackson, 1997).

Intravenous immunoglobulin (IVIG)

IVIG is used when immune-mediated haemolysis is the cause of UHB jaundice and prevents RBC haemolysis by coating Fc receptors on RBCs. The AAP recommends IVIG infusion in immune-mediated haemolysis if TSB remains within 2 to 3 mg/dl of exchange level despite intensive phototherapy. However, the evidence that the use of IVIG reduces the need for ET is not very clear. Nonetheless, IVIG is often used in clinical practice to manage unconjugated hyperbilirubinemia (Gottstein and Cooke, 2003).

Treatment of conjugated hyperbilirubinemia

Treatment of conjugated hyperbilirubinemia is tailored to the specific etiology. Patients diagnosed with biliary atresia require a Kasai operation (hepatic portoenterostomy) preferably within two months of life for best outcomes. The Kasai operation involves removing the atretic biliary ducts and fibrous plate and Roux-en-Y anastomosis of jejunum with the remaining ducts to provide an alternative pathway for biliary drainage. Infectious causes of cholestasis would be treated with specific anti-microbial, whereas treatment with cholic acid and chenodeoxycholic acid is often curative for many BASDs. Metabolic causes of cholestasis would typically respond to the improvement of the primary disorder and liver functions. Patients with GALD appear to respond well to IVIG and double volume exchange transfusion. Liver transplant, when available, is curative but is technically challenging in this age group. Parenteral nutrition-induced cholestasis is managed with cyclic PN, reducing the duration of exposure and initiating enteral feeds as early as possible. Manganese and copper content of PN should be reduced to minimize liver injury (Feldman et al., 2017).

Complications

Newborns with severe hyperbilirubinemia are at risk for bilirubin-induced neurologic dysfunction (BIND). Bilirubin binds to globus pallidus, hippocampus, cerebellum, and subthalamic nuclear bodies, causing neurotoxicity. Acutely, this manifests as acute bilirubin encephalopathy (ABE), characterized by lethargy, hypotonia, and decreased suck. At this stage, the disease is reversible. However, if ABE were to progress, patients can develop chronic bilirubin encephalopathy/kernicterus, which is then irreversible. It manifests as choreo-athetoid cerebral palsy, seizures, arching, posturing, gaze abnormality, and sensorineural hearing loss. Patients with neonatal cholestasis are at risk of developing liver failure, cirrhosis, and even hepatocellular carcinoma in a few cases. Long-standing cholestasis may also lead to failure to thrive and fat-soluble vitamin deficiencies. The main complication is bilirubin encephalopathy (kernicterus), which can occur with high levels of unconjugated bilirubin.

Bilirubin encephalopathy

Unconjugated bilirubin is lipid-soluble and can cross the blood-brain barrier. It accumulates in the brainstem nuclei, basal ganglia, hippocampus and cerebellum and is neurotoxic. Bilirubin encephalopathy initially presents with lethargy, hypotonia and poor suck reflex. This progresses to hypertonia, opisthotonos, fever, seizures and a high-pitched cry. Early damage to the brain can be reversible but if hyperbilirubinemia is pronounced or prolonged then it can lead to cerebral palsy, sensorineural hearing loss or cognitive impairment (Hankø et al., 2005).

Prevention

Physiological jaundice can't be prevented. But you can reduce the chance of development by frequently feeding your newborn, which their bilirubin pass through the body more quickly. The best prevention of infant jaundice is adequate feeding. Breast-fed infants should have eight to 12 feedings a day for the first several days of life. Formula-fed infants usually should have 1 to 2 ounces (about 30 to 60 millilitres) of formula every two to three hours for the first week (Rennie, 2005).

Aim and objective

The main aim of this article is to assess the risk factors and maternal awareness on neonatal jaundice. And also, it follows the below objectives for assessment of maternal awareness.It is as follows: (1) to assess the risk of jaundice in neonates; (2) to assess the maternal awareness on neonatal jaundice; (3) to comparison between full term neonates with pre-term neonates, both having neonatal jaundice; and (4) to educate mothers regarding neonatal jaundice and to increase the awareness about the neonatal jaundice. Meanwhile, the plan of work can be explain detailed in *Figure 6*.

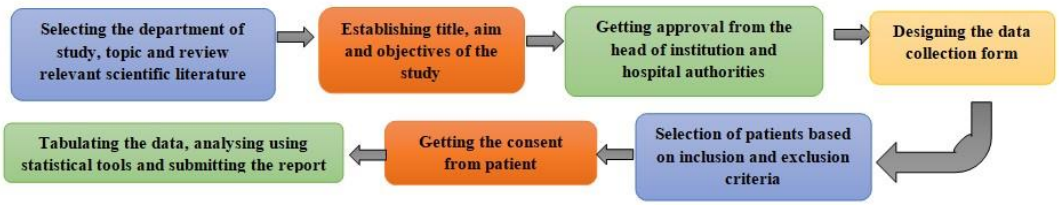

Figure 6. *The plan of work.*

Materials and Methods

The This study design is prospective observational study. The study is conducted IN PATIENT and OUT PATIENT facilities of Department of paediatrics, Arundathi hospital, a 300 bedded tertiary care hospital located in Gandimaisamma, Hyderabad, Telangana. The study period is of 11 months i.e., from February 2023 to December 2023. 70 patients visiting inpatient and outpatient facilities of Department of paediatrics, Arundathi hospital at Gandimaisamma diagnosed with neonatal jaundice along with their mother were included. Out of 70 subjects recruited in the study 9 subjects were excluded due to their lack of interest and improper data. Therefore, we have completed the study with 61 subjects. The subjects were selected from the paediatric Department, which is based on the following inclusion and exclusion criteria. The inclusion are: (1) all the babies along with their mothers were brought during the study; (2) babied of <15 days; and (3) mothers who are interested and can answer the questions. Meanwhile, the exclusion are: (1) babies of age >15 days; (2) babies who are sick and ventilated; (3) mothers who are not interested; as well as (4) mothers who can't give the complete information.

Out of 70 subjects included in the study, 9 were excluded due to lack of information. Hence, we completed this study with the help of 61 subjects. A patient data collection form was prepared with the help of the guide and physician, this form includes the patients details of the following ones; i.e., Demographic data [Name, age, sex, weight, blood group, medical history] and mother's demographic data [Name, age, weight, blood group, lactation, personal history, medical history]and also included with knowledge about jaundice. We used Microsoft excel to perform chi-square test and t test. We calculated mean standard deviation and p value using excel. In patients counselling, all the mothers who are recruited in this study were given clear information about the neonatal jaundice; the counselling section was about 10minutes.The mothers were counselled with their respective mother tongue [Telugu, Hindi, English]; and patient's information leaflet was given to mothers at the end of the counselling section.

Results and Discussion

Out of 70 subjects [mother and neonate pair] recruited in the study, 9 subjects we excluded due to incomplete data. Therefore, we completed the study with 61 subjects. The most numbers of study subjects were in 25-29 age group with 44.26% of the total study population. The least number of study subjects were in 35-39 age group with 8.19% of the total study population, 24.59% of study population were of 20-24 age group and 22.95% were 30-34 age group (*Table 1*). In the total number of study subjects, 32 (52.45%) were male neonates and 29 (47.54%) were female neonates (*Table 1*). Next, the majority of full-term neonates had birth weight of 3.0-3.2kgs and least number of study subjects were 2.2-2.4kgs. In pre term neonates, majority of study subjects had birth weight of 2.8-3.0kgs and least number of them had birthweight of 2-2.2kgs (*Table 2*). In the total population of subjects based residency, majority of subjects were from urban area with 81.96% and 18.03%of subjects from rural (*Table 1*). In the studies subjects on marital life, the marital life of 52 (85.24%) subjects were of non-consanguineous and 9 (14.75%) subjects of consanguineous (*Table 1*).

Table 1. *Demographic profile of study.*

Category	Frequency (N)	Percentage (%)

Mother age		
20-24	15	24.59
25-29	27	44.26
30-34	14	22.95
35-39	5	8.19
Sex		
Male baby	32	52.46
Female baby	29	47.54
Residency		
Rural	11	18.03
Urban	50	81.97
Marital life		
Non-consanguineous	52	85.25
Consanguineous	9	14.75
Education Qualification		
Post graduation	6	9.91
Graduation	30	49.16
Diploma	1	1.6
Intermediate	8	13.11
School	16	26.22
Type of delivery		
Normal	4	6.55
Lower segment cesarean	57	93.45
Interpregnancy		
0-1	22	36.06
1-2	10	16.3
2-3	9	14.7
3-4	7	11.47
4-5	5	8.19
5-6	4	6.55
6-7	2	3.27
7-8	1	1.6
8-9	1	1.6
Duration of jaundice (days)		
1	13	21.31
2	25	40.98
3	15	24.61
4	6	9.83
5	2	3.27
Risk factors		
No feeding duting 1st hour after delivery	39	63.93
No proper lactation	11	18.03
Breast problems	3	4.91
Pre-mature rupture of membrane	7	11.47
Vaginal bleeding	4	6.55
Hypertension	5	8.19
Diabetis mellitus	2	3.27
Gestational diabetis	2	3.27
Preclampsia	1	1.63
Sugn & symptoms		
Yellow eyes	23	37.70
Yellow skin	12	19.67
Yellow skin & eyes	6	9.83
Yellow faeces	1	1.61
Yellow urine	3	4.91
Feeding difficulty	1	1.63
Vomitting & diarrhoea	1	1.63
No faeces & urine	1	1.63
Treatment		
Sunlight	27	44.26
Phototherapy	11	18.03
Warm care	1	1.63
Breast milk	1	1.63

***Table 2**. Distribution of study population based on birth weight.*

Birth weight	Full-term neonate	Pre-term neonate	Total
2.0-2.2	-	1	1
2.2-2.4	4	1	5
2.4-2.6	5	2	7
2.6-2.8	6	3	9
2.8-3.0	5	5	10

3.0-3.2	11	4	15
3.2-3.4	3	2	5
3.4-3.6	3	2	5
3.6-3.8	2	1	3
3.8-4.0	1	-	1
Grand total	40	21	61

During the study period for education qualification, it was found that 30 study subjects have completed their education till graduation, 6 subjects till post-graduation, 8 completed till intermediate, 1 of them completed their diploma and 16 subjects completed their schooling (*Table 1*). The greatest number of study subjects had undergone caesarean type of delivery with 93.44% and the rest of subjects had undergone normal delivery with 6.55% (*Table 1*), based on the type of delivery. During the study based on interpregnancy gap, majority of study subjects had an interpregnancy gap of 0-1 yr with 36.06%, 16.3%of them with 1-2 yr,14.7% with 2-3yrs,11.47% with 3-4yrs,8.19% with 4-5 yrs,6.55%with 5-6 yrs,3.27% with 6-7 yrs and lowest number of subjects had with 7-8 yr and 8-9 yrs with 1.6% (*Table 1*). In the study on duration of jaundice, majority of the subjects had highest duration of jaundice for 2 Days with percentage of 40.98%, 3.27% of the subjects had jaundice for 5 days, 9.83% of them had a duration of jaundice for 4 days and 24.59% of subjects had duration for 3 days (*Table 1*). Considering the risk factors related to the mother, 63.93% of the mothers did not feed their babies for the 1st one hour after delivery, 18.03% had a problem of proper lactation, 4.91% of mothers have breast problem, of mothers had pre-mature rupture of membrane, 6.55% of them had vaginal bleeding, 8.19% of mothers have hypertension, 3.27% of them with diabetes mellitus and the same percentage of mothers with gestational diabetes and 1.63% of the subjects with preeclampsia (*Table 1*).

Considering the risk factors related to neonates, 31.14% of the neonates have a history of previous sibling of jaundice, 4.91% of neonates with pepsis, 18.03% of them had difficulty in feeding, 59.01% of neonates are of male sex, 13.11% of them have ABO incompatibility and 8.19% of neonates have RH incompatibility (*Table 3*). During the study on bilirubin levels on day of admission, majority of full-term neonates had bilirubin levels of 12-14 mg/dl and pre term neonates had bilirubin levels of 12-13 mg/dl on day of admission. Least number of full-term neonates had bilirubin levels of 10-11 mg/dl and 16-17mg/dl and pre term neonates had bilirubin levels of 16-27 mg/dl on day of admission (*Table 4*). During the study, majority of full-term neonates had bilirubin levels of 7-8 mg/dl and pre-term neonates had bilirubin levels of 9-10 mg/dl on day of discharge. Least number full-term neonates had bilirubin levels of 3-4 mg/dl and pre-term neonates had bilirubin levels of 3-4 mg/dl and 11-12 mg/dl on day of discharge (*Table 5*).

***Table 3**. Distribution of study population based on risk factors [related to neonates].*

Risk factors	Full-term neonate N [%]	Pre-term neonate N [%]	Total
Previous Sibling With Jaundice	13[21.3%]	6[9.83%]	19[31.14%]
Sepsis	3[4.91%]	0	3[4.91%]
Difficulty In Feeding	7[11.47%]	4[6.55%]	11[18.03%]
Male Sex	22[36.03%]	14[22.95%]	36[59.01%]
Abo Incompatibility	5[8.19%]	3[4.91%]	8[13.11%]
Rh Incompatibility	3[4.91%]	2[3.27%]	5[8.19%]

***Table 4**. Distribution of study population [neonates] based on bilirubin levels on day of admission.*

Total serum bilirubin [Mg/Dl]	Full-term neonate N [%]	Pre-term neonate N [%]	Total
10-11	2[5%]	2[5%]	4[6.55%]

11-12	3[7.5%]	2[5%]	5[8.19%]
12-13	11[27.5%]	7[33.33%]	18[29.50%]
13-14	11[27.5%]	5[23.8%]	16[26.22%]
14-15	6[[15%]	3[14.2%]	9[14.75%]
15-16	5[12.5%]	1[4.76%]	6[9.83%]
16-17	2[5%]	1[4.76%]	3[4.91%]
Total	40	21	61

***Table 5**. Distribution of study population based on bilirubin levels on the day of discharge.*

Total serum bilirubin [Mg/Dl]	Full-term neonate N [%]	Pre-term neonate N [%]	Total
3-4	1[2.5%]	-	1[1.63%]
4-5	1[2.5%]	-	1[1.63%]
5-6	4[10%]	3[14.29%]	7[11.47%]
6-7	7[17.5%]	4[19.09%]	11[18.03%]
7-8	9[22.5%]	2[9.52%]	11[18.03%]
8-9	8[20%]	1[4.76%]	9[14.75%]
9-10	5[12.5%]	6[28.57%]	11[18.03%]
10-11	2[5%]	3[14.29%]	5[8.19%]
11-12	2[5%]	2[9.52%]	4[6.55%]
12-13	1[2.5%]	-	1[1.63%]
Total	40	21	61

In the total study population 70.49%of mothers have the knowledge of jaundice, 57.37% have the knowledge of treatment for neonatal jaundice and only 19.67% know the seriousness of jaundice (*Table 6*). During the study the highest number of mothers answered yellow eyes (37.70%) as signs and symptoms, 19.67% answered yellow skin and 9.83% answered both yellow skin and eyes, 4.91% of the mothers knew yellow urine as symptom, 1.63% of the mothers answered as yellow faeces, Difficulty in feeding, vomiting and diarrhoea, no faeces and urine as signs and symptoms of jaundice (*Table 1*). In the study population of knowledge of mother on treatment of neonatal jaundice, majority of mothers knew the treatment for jaundice is sunlight (44.26%), 18.03% of mothers have knowledge of phototherapy as the treatment for neonatal jaundice and 1.63% of mothers answered as warm care and breast milk (*Table 1*).

***Table 6**. Knowledge of mothers on neonatal jaundice.*

Question	Frequency (N)	Percentage (%)
Does Mother Know Anything About Neonatal Jaundice?	43	70.49
Does Mother Know Any Sign Or Symptom Of Jaundice?	43	70.49
Do Mothers Think Whether Neonatal Jaundice Is Normal?	38	62.29
Does Mother Know Seriousness Of Neonatal Jaundice?	12	19.67
Does Mother Know Any Treatment Option For Neonatal Jaundice?	35	57.37

Based on the distribution of study population (mothers and neonates) based on demographic, the most numbers of study subjects were in 25-29 age group with 44.26% of the total study population. The least number of study subjects were in 35-39age group with 8.19% of the total study population. In the total number of study subjects, 32 (52.45%) are male neonates and 29 (47.54%) are female neonates. In the total study population, majority of subjects are from urban area (81.96%) and subjects belonging to rural area (18.03%). In the total study population, the marital life of 52 subjects is non-consanguineous with 85.28% and 9 subjects is consanguineous with 14.75%. While in the birth weight and pre-term neonate or full-term neonate, in the total study population, the majority of full-term neonates had birth weight of 3-3.2 kgs and least number of study subjects was 3.8-4 kgs. In pre-term neonates, majority of study subjects had birth weight of 2.8-3 kgs and least number of them had birthweight of 2-2.2 kgs. In a systemic review performed by Hassan Boskabadi,el al. have found that prematurity was associated with neonatal jaundice (Boskabadi et al., 2020). The study based on type of

delivery, the greatest number of study subjects had undergone caesarean type of delivery with 93.44% and the rest of the subjects had undergone normal delivery with 6.55%. In retrospective cross-sectional design, Murekatete et al. (2020) have found that caesarean type of delivery was one of the risk factors for neonatal jaundice. During the study based on duration of jaundice, majority of the study subjects had an interpregnancy gap of 0-1 year with 36.06% and lowest number of subjects had 7-9 years gap with 1.6 %. In the study period, majority of the subjects had highest duration of jaundice for 2 days with a percentage of 40.98%. In risk factors (related to mother), the most common risk factor related to mothers was found to be no feeding during 1st hour after delivery (63.93%) and the least common risk factor was found to be preeclampsia (1.63%). Refering to the risk factor related to neonates, the most common risk factor in both full term and pre term neonates was male sex with percentages of 36.06% and 22.95% respectively. The least common risk factor in full term neonates was sepsis and Rh incompatibility (4.91%) and in pre-term neonates was Rh incompatibility (3.27%). According to the articles based on neonatal jaundice, they have found that Gestational age, Birth weight, neonatal gender, prematurity and C-section was associated with neonatal jaundice. In another study performed by Bizuneh et al. (2020) found out prolonged labour low birth weight, sepsis, birth asphyxia, hypothermia, sex were risk factors of neonatal jaundice, study performed by Wagemann and Nannig (2019) found out male, sex, prematurity, excessive weight loss and blood group incompatibility were the risk factors for severe hyperbilirubinemia.

In study population (neonates) based on bilirubin levels on day of admission, majority of full-term neonates had bilirubin levels of 12-14 mg/dl and pre-term neonates had bilirubin levels of 12-13 mg/dl on day of admission. Least number of full-term neonates had bilirubin levels of 10-11mg/dl and 16-17 mg/dl and pre-term neonates had bilirubin levels of 15-16 mg/dl and 16-17 mg/dl on day of admission. While based on bilirubin levels on day of discharge, majority of full-term neonates had bilirubin levels of 7-8mg/dl and preterm neonates had bilirubin levels of 9-10mg/dl on day of discharge. Least number of full-term neonates had bilirubin levels of 3-4 mg/dl and 4-5 md/dl and 12-13 mg/dl and pre-term neonates had bilirubin levels of 3-4 mg/dl and 8-9 mg/dl on day of discharge. Continuously, knowledge of mothers on neonatal jaundice shows 70.49% of mothers have the knowledge of neonatal jaundice, 57.37% have the knowledge of treatment for neonatal jaundice and only 19.67% know the seriousness of jaundice. Similar studies were performed by Goodman et al. (2015), and the studies found that the awareness of neonatal jaundice among mothers 75.58%. Knowledge of mothers about signs and symptoms of neonatal jaundice, the highest number of mothers answered yellow eyes (37.70%) as signs and symptoms of neonatal jaundice. And also, knowledge of mothers on treatment of neonatal jaundice, majority of mothers knew the treatment for jaundice is sunlight (44.26%). And followed by this only (17.89%) know about the phototherapy, the least percent of mothers i.e. (1.05%) knows about the treatment through warm care and breast milk. In a study performed by Amegan-Aho et al. (2019), 52% of mothers know at least any one sign or symptom.

Conclusion

Neonatal jaundice or neonatal hyper bilirubinemia results from elevated total serum bilirubin (TSB) and clinically manifests as yellowish discoloration of the skin, sclera, and mucous membrane. The term jaundice derives from the French word "jaune," which

means yellow. In this study, the most common risk factor among mothers is no feeding during 1st hour after delivery and moreover it is seen in male sex due to Bili in LBW (low body weight) infants is significantly higher in males when compared to females, and also Bili levels in infants <1500g are influenced more significantly by factors other than the gender: such as sepsis and IVH. While mothers were aware of neonatal jaundice, their understanding of potential complications and treatment options was limited. Promoting awareness of neonatal jaundice among mothers is crucial for early detection and treatment, and during our study, we endeavoured to enhance mothers understanding of this condition. In limitation, a more extensive sample size would have been essential for drawing more conclusions, and this could have been achieved by extending the study period. As we got less sample size, we have concluded this case study with less number, due to lack of interest in mothers.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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