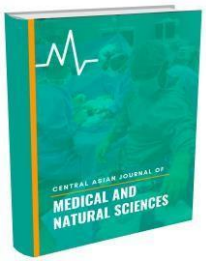

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 05 Issue: 04 | October 2024 ISSN: 2660-4159

Article

Relation of some Physiological and Biochemical Parameters with Jaundice in Newborns

Bahaa al-Din Thayer Hassan al-Khazraji[1]

1. Department of Pathological analyzes, Faculty of Applied Science, University of Samarra

* Correspondence: Bahaa1999thh@gmail.com

Abstract: The current study aimed to know the effect of jaundice in newborns on some physiological and biochemical parameters and compare them with healthy children. The study showed that the incidence rate in male children is greater than female children. As for liver enzymes (ALT) and (ALP), Comparing the results to healthy individuals, it was shown that there was a notable rise in enzyme activity as well as a notable drop in enzyme activity. The study also showed changes in some levels of Glucuronosyl Transferase (GUT1 (oxidative stress MDA) malondialdehyde) and some antioxidants such as (GSH) in the body, where we noticed a decrease in the level of (GSH) compared to healthy people. Thus, we conclude from this current study that jaundice is associated with several factors, including liver metabolism and levels of oxidative stress and the mechanism of bile secretion from the gallbladder.

Keywords: Physiological, Biochemical, Newborn

1. Introduction

Four million children born after or before pregnancy are at risk for life-threatening illnesses and issues, such as pathological jaundice, which can cause permanent disability, according to a 2014 World Health Organization (WHO) study. So, within the first week of life, over 50% of babies suffer from neonatal jaundice, which is the most prevalent condition (Hussein, 2016) and sometimes requires medical care.

Jaundice is divided into two groups, pathological jaundice and physiological jaundice and affects newborns, which is caused by increased decomposition of red blood cells, and begins on the second day after birth and peaks on the fourth or fifth day approximately, and this type of jaundice is very common in newborns and is usually harmless and not associated with other diseases. (Stoll and Kiegman Mojtahedi; 2004 ،2018)

The occurrence of jaundice in a newborn is a common postnatal phenomenon that shows how bilirubin formation and elimination are balanced physiologically and metabolically. If bilirubin production is increased and the mechanisms of its elimination are disturbed, the infant is at risk of developing hyperbilirubinemia and experiencing jaundice (Stevenson et al., 2002 Cortey et al., 2017).

Oxidative stress is due to the increased production and accumulation of intermediate reactive oxygen species (ROS) such as hydrogen peroxide (H202) and hydroxyl radicals. (OH). which affect all biochemical compounds including lipids, proteins and DNA (Ahn et al., 2019), and is closely related to aging and a number of other

Citation: Al-Khazraji, B, A, T, H. Relation of some Physiological and Biochemical Parameters with Jaudice in Newborns.. Central Asian Journal of Medical and Natural Science 2024, 5(4), 681-694.

Received: 10th July 2024
Revised: 11th Aug 2024
Accepted: 24th Aug 2024
Published: 27th Oct 2024

diseases such as arteriosclerosis, hypertension, nephropathy, diabetic and jaundice Jaundice. Free radicals derived from molecular oxygen and nitrogen are highly reactive molecules called active oxygen types (ROS) and active nitrogen types Roychoudhury. Das) (RNS.2014; Hayyan et al. (2016)

Oxidative stress arises as a result of overproduction of ROS and weak antioxidant defense mechanisms(2018,Li) Reactive oxygen species are usually produced and are part of the defense system and by-products of cellular metabolic processes that use oxygen Reactive oxygen types include certain molecules that may be oxidizing agents or convertible to free radicals (Wang et al., 2020).

The aim of the study:

1- Identify jaundice and the reasons for its rise and stability at a certain level in newborns
2- identify the symptoms and causes of jaudince
3- identify ways to prevent jaudince
4- the relationship between the ABO and RH blood group system for the child and the parents
5- knowing the ways the liver gets rid of bilirubin

2. Materials and Methods

The article uses several methods to investigate the relationship between physiological and biochemical parameters and jaundice in newborns. Although the document does not explicitly provide a "Materials and Methods" section, the following methods can be inferred based on the content:

1. Comparative Analysis: The study compares liver enzyme activity (ALT and ALP) between jaundiced and healthy newborns. This is likely done using biochemical assays that measure enzyme levels in blood samples.
2. Measurement of Oxidative Stress Markers: The study measures levels of oxidative stress markers, such as malondialdehyde (MDA) and glutathione (GSH), which suggests the use of spectrophotometric or chromatographic techniques.
3. Liver Function Tests: Tests to assess liver function, possibly through blood tests that evaluate the concentration of bilirubin and liver enzymes.
4. Statistical Analysis: Though not explicitly mentioned, the study likely involves statistical analysis to determine the significance of differences observed between jaundiced and healthy newborns.

3. Results and Discussions

2-1 Jaundice

It is a disease in which bile accumulates in the gallbladder sac higher than the normal limit and thus rises in concentration and secretion in the body, which often affects newborns before reaching the 36th week of gestational age, and is the result of the process of catabolizing hemoglobin molecules and the exit of iron from it and produces the bile called bilirubin, with a molecular weight of (65.584) Dalton

It usually occurs between the second and fifth days after birth and is a natural phenomenon that occurs in more than 50% of newborns during the first week after birth so that parents and doctor can distinguish it from when examining the child (Kaplan et.al 2002) results in yellowing of the skin and whites of the eyes towards yellow and mucous membranes as a result of its rise in body fluids Sadeq (et al. 2019,) and the color usually results from the accumulation of unconjugated and non-polar bilirubin in the skin and is fat-soluble and indirect in Interaction and this type of bilirubin is not easy to remove from the child's body, as the liver converts it from the unpaired type to the action of the liver enzyme Uridin diphospho glucuronic acid, and thus easy to remove from the child's body,

but may cause dysfunction in the liver function of newborns, which leads to the inability of the liver to accomplish its functions effectively, which leads to a high level of bilirubin blood (Kliegman et al., 2016) According to Johnson and Bhutani (2011), early detection of bilirubin-induced neurologic dysfunction in vulnerable newborns can prevent irreversible and long-term brain damage. The condition is characterized by a set of symptoms and signs that describe a specific disease after exposure to high levels of bilirubin. Numerous variables, including physical ones like birth weight and gestational age as well as maternal infectious illnesses during pregnancy, may be significant contributors to newborn hyperbilirubinemia. (Mojtahedi et al. 2018)

About 80% of bilirubin is produced by the reticuloendothelial system's breakdown of hemoglobin, with the other 20% coming from the breakdown of other proteins and inactive red blood cells produced in the bone marrow (Cheifetz, et al., 2011; Kuntz and Kuntz, 2009). The enzyme haemoxygenase converts heme into biliverdin, which is the first significant step in this process. Next, and then the second step, Whereas bilirubin becomes unconjugated bilirubin in the liver through the action of the enzyme clocuronyltransferase, which also makes bilirubin soluble in water; the conjugate form of bilirubin is the predominant form present as a portion of direct bilirubin, most of which travels to the bile sac and then exits to the upper part of the small intestine despite reabsorption. Conjugated bilirubin is sent to the colon rather than being absorbed, while the majority of bile acids are at the end of the ileum to participate in the hepatic intestinal circulation. The coliform bacteria there break down and metabolize bilirubin to produce colorless urobilinogen, which can then undergo oxidation to produce urobilin and stercobilin. When a person has urinated, they are excreting urobilin, which has a yellow tint, while a person who has stercobilin will have brown excrement. Only a very little amount of urobilinogen (1%), as seen in Figure (1-1), is reabsorbed in the hepatic enterocirculation and reexpelled in bile, according to Jasprova et al. (2016), Steensma and Hoffbrand (2019), Steckova and Jirsa (2013), and others.

When bilirubin levels are low or normal, it functions as a non-enzymatic antioxidant. However, when levels rise, it becomes effective and can cause toxic and neurological effects. If levels rise above normal, bilirubin may cause permanent brain damage due to its toxic effect on brain cells. If treatment is delayed, bilirubin can cause neurotoxicity, also known as kernicterus, which can cause neurological weakness and lead to permanent encephalopathy

(Mitra and Wisnowski; 2017 Rennie et al. 2016).

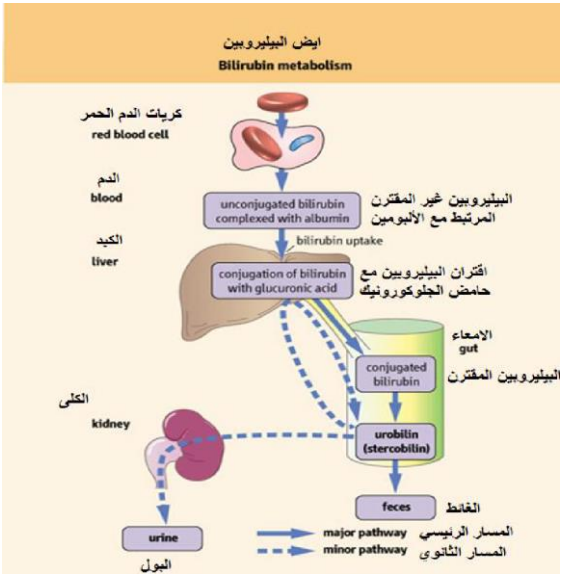

Figure (1-1) Bilirubin metabolism pathway (2017,Gap; 2010,Alajeely)

Hyperbilirubinemia-causing disorders can be classified as either hemolytic (excessive bilirubin production) or enteroplasmic (reduced bilirubin clearance). Newborns are particularly susceptible to hyperbilirubinemia because they have an increase in bilirubin synthesis (high hemoglobin concentrations and a short erythrocyte lifespan), decreased liver absorption, conjugation and secretion of bilirubin (Memon et al., 2016), so the liver resorts to getting rid of bilirubin through four main steps:

1. The process by which liver cells absorb and store unconjugated bilirubin
2. Bilirubin is converted to bilirubin glucuronides.
3. Conjugated bilirubin elimination in the bile
4. Liver cells reabsorbing conjugated bilirubin

2-2- Types of hyperbilirubinemia

ABO incompatibility, Rh incompatibility, glucose phosphate dehydrogenase (G6PD, et al. 2008: Sgro et al., 2016), and pathological jaundice are among the several forms of hyperbilirubinemia that can affect newborns. Hemolytic jaundice is one of the subtypes of hemolytic jaundice.

2-2-1-Physiological jaundice

Jaundice in healthy and fully gesturated newborns is called physiological jaundice, because hyperbilirubinemia occurs globally in newborns TSB usually peaks at 5 to 15 mg / dl on the second or third day after birth (Immenschuh et al. 2007). Physiological jaundice is produced in two ways:

First: Red blood cell lysis proceeds more quickly, which causes secondary elevated bilirubin generation. (high hemoglobin concentration, shorter erythrocyte lifespan, inefficient absorption in the liver, reduced ability to excrete and eliminate bilirubin. Erythrocytes mainly transport gases to and from cells and tissues. This is facilitated by hemoglobin, which has the ability to bind to gases. Two types of hemoglobin are present in humans depending on the individual's adulthood where fetal hemoglobin (HbF) is produced before birth and during fetal life and adult hemoglobin HbA after birth. Fetal hemoglobin production is stopped shortly after birth. Hemoglobin is structurally composed of two alpha chains and two non-alpha chains; where fetal hemoglobin HbF contains the molecular structure of two alpha chains and two Kama U22 heterogeneous chains with two types of Y chains that differ in amino acid composition, either glycin chains (γG) or alanine chains (γA), while adult hemoglobin HbA1 dominant in adults contains about 96-98 HbAA, with the molecular structure alpha chains and two beta 22 chains and 3.5 HbA2 with molecular structure 202, less than 1 2005, Cheesbrough (HbF). Replacing the glutamic acid in the beta chain with valine in the sixth position leads to a

sickle cell disorder called hemoglobin (HbS), which is an abnormal hemoglobin caused by a genetic disease and causes disturbances in oxygen supply.

When people are exposed to low oxygen concentrations, HbS is deposited in elongated crystals that appear in sickle shape instead of disc structure. Sickle cell anemia is characterized by vascular occlusive events leading to pain, organ failure, and sometimes death (Steinberg, 2014). Studies have revealed that HbF usually disappears from infant blood after about 6 months however, the exact time of disappearance of HbF and the signal determining the transition from fetal hemoglobin to adult hemoglobin may vary precisely unknown. Very small amounts of 2% HbF were detected in some adults (Edoh et al., 2006). HbF may be elevated in some cases including B-thalasemia anemia or sickle cell crisis and it is possible that children with high HbF may suffer from one of these diseases (Charache, 1990).

Second: low level of ligandin in liver cells, low activity of the enzyme bilirubin conjugated (Memon) (UDP-glucouronyl transferase2016) This type is the most common and present type in newborns, and its complications are few (Boyd, 2004). Neurodevelopmental disorders, including muscle spasms and hearing loss, and in rare cases mental deficits may occur, all of which are associated with a highly toxic level of bilirubin. Jaundice caused by physiological immaturity peaks between 24-72 hours and between the fourth and fifth days after birth, while in premature babies it is on the seventh day and disappears from day 10-14 after Childbirth (Alkhotani et al. 2014) This is due to the fact that the fetus inside the womb of its mother is very rapid growth, especially during the last trimester of pregnancy, and that this speed of growth and cell division requires an increase in the amount of oxygen that reaches the cells due to the speed in the metabolic rate, which requires an increase in the number of red blood cells at this stage of fetal life and may reach (12 - 15) million cells in mm of blood, while in the normal state it is at its rate in Males and females 5.5, 4.5 million pellets in a ladder respectively (National Collaborating Centre, 2010). At birth, because of the low speed of growth to a large degree, this number of red blood cells drops to the normal level, so it works to break down the excess of them, and that this excess and shattered number is the one that causes the state of congenital jaundice (Claassen, Watchko 1994)

There are many factors that contribute to the development of physiological jaundice in newborns including indirect and inactive hepatic metabolism, shorter lifespan of erythrocytes that are easily dissolved and poorly developed intestinal flora involved in bilirubin breakdown leading to increased indirect bilirubin absorption (Tepan, 2018). The hydrolysis of conjugated bilirubin by beta-ghucuronidase activity increases in newborns due to increased level of Indirect bilirubin leads to more reabsorption while promoting

hepatic intestinal circulation. (Creeden et al., 2021) Physiological jaundice may require regular follow-up if the serum is not conjugated leads to an increase in bilirubin level more than normal, but regular measurement of the total bilirubin level of neonatal jaundice for those who have developed excessive jaundice, and some need to be hospitalized where treatment is prescribed for these patients. (Dantas et al., 2018) There are many factors that lead to the development and elevation of the level of indirect bilirubin that increase the risk of excessive physiological jaundice including premature babies, low birth weight, reduced oral milk intake, which reduces calorie intake and dehydration (McGillivray et al. 2016).

One of the most important features of indirect bilirubin is encephalopathy, sensorineural hearing loss resulting from cochlear damage and neurotoxicity due to exceeding the ability of its binding to albumin in the blood and the displacement of bilirubin from albumin by acidosis or due to some drugs such as sulfonamides Sulfonamide and Ceftriaxone or neonatal infections such as sepsis. It is more common for premature babies to have a higher level of unconjugated bilirubin in the blood due to a low concentration of albumin in the blood and a higher risk of acidosis and sepsis Wisnowski (Septicemia et al., 2016) Children with acute jaundice are treated either by subjecting them to blood exchange operations, which aim to prevent the generation of bilirubin, thus removing all excess bilirubin or subjecting children to ultraviolet rays (UV), which changes the structural properties of unbound bilirubin, and converts them into decomposed derivatives in water by encouraging the binding of bilirubin with glucoronic acid and thus helps in the process of excretion outside the body (Maisels and Hansen: McDonagh et al., 2008).

2-2-2-Pathological Jaundice

Deviation levels of bilirubin from normal and sometimes requiring medical intervention can be described as pathological jaundice (Dantas, et al. 2018, Boyd 2004) Or it is all that is different from physiological jaundice, mother's milk burgan and degradative jaundice, it is a pathological jaundice, this type of jaundice appears within the first 24 hours due to an increase in bilirubin in the blood more than 5 mg/dl per day. The presence of clinical lightning for prolonged periods of more than two weeks and conjugated bilirubin will be classified under this type of jaundice (Sgro, et al., 2016), the causes of this type include pathological disorders such as: toxoplasmosis, rubella rubella and bacterial septicemia (sepsis) (Septicemia et al., 2018).

2-2-3-Breast Milk Jaundice

Breastfed infants have a different physiological pattern of jaundice compared to formula-fed babies Plung in breast milk usually appears for babies who adopt this mode

of feeding after the first week of birth and peaks during the second or third week، Then the cause of this type of jaundice may be due to the presence of the enzyme glucoronidase enzyme in breast milk. Evidence from studies indicates that a mix of environmental and genetic factors (including components of breast milk) results in jaundice from breast milk. (Memon et al., 2016). High bilirubin levels in these infants (Liley Alcock, 2002) were diagnosed in the case of breastfeeding, mild jaundice may take 100-14 days after birth or may recur during breastfeeding due to low milk intake and some cases of dehydration (Mishra, et al. 2008) with the accumulation of very large amounts of bilirubin in the blood and cause brain damage, a condition known as nuclear jaundice (2019. Hamza) KemicterusThis may be followed by injuries, hearing impairment, mental retardation and behavioral disorders. Mild clinical jaundice has also been observed in one-third breastfed babies in the third week of life, which may persist for two to three months after birth in a small number of babies (Victora et al., 2016) .The low frequency of breastfeeding is significantly associated with physiological jaundice. An important measure to control jaundice in a healthy baby is to encourage mothers to breastfeed their babies at least 100 times a day (Kramer, 1969).

Hyperbilirubinemia is also associated with breast milk in babies (Shapiro-Mendoza, 2006). About 2–4% of exclusively breastfed babies suffer from jaundice above 10 mg/serving in the third week of life These babies should be considered in the third week after birth with serum bilirubin levels above 10 mg/dl due to prolonged jaundice (2002, Dennery) The diagnosis of breast milk jaundice should be verified if the bilirubin in the serum is mostly not conjugated, and the other causes of jaundice have been eliminated for long periods and the infant is healthy, strong, well-fed and gaining sufficient weight (Maruo, et al., 2000) male (Maisels, 1998) should advise mothers after stopping breastfeeding unless levels exceed 20 mg/dL. Gartner and Herschel (2001) stated that breast milk should be replaced with artificial feeding. As it reappears again when the infant returns to breastfeeding and the cause of this jaundice is the presence of the enzyme glucuronidases in breast milk and non-sterile fatty acids that inhibit normal bilirubin metabolism.

2-2-4-Hemolytic Jaundice

The most common causes of hemolytic jaundice include (a) hemolytic rhesic factor disease (B), incompatibility of blood groups ABO (C) g6PD dehydrogenase dehydrogenase deficiency and mild blood group incompatibility.

2-2-4-1-Rh incompatility

Neonatal rhodolysis (RHDN) is caused by maternal erythrocyte immunization (maternal red-cell all immunization et al., 2019) .Maternal antibodies are produced against

the erythrocytes of the fetus. When fetal erythrocytes are antigen-positive and usually at any time a baby is born from a Rh negative mother and a Rh positive father (Bhutani et al., 2013) maternal immunoglobulin (IgG) antibodies may cross the placenta into the fetal circulation and cause a variety of symptoms in the fetus ranging from mild to severe hemolytic anemia and fetal hydrocephalus (Fung) fetal hydrops; 2018 Bhutani, Eason et al., 2013).

To facilitate early treatment of newborns who have a suspicion of having RIS should be performed blood type and packed cell volume (PCV) DCT, Rh (stacked cell size) and serum bilirubin from umbilical cord blood. The number of reticulocytes should be sent before the first blood transfusion (ET). Strong photodynamic therapy is required immediately after birth and should continue to a level 5 mg/dL lower than the estimated level of blood exchange (Van Kamp et al., 2005). In premature infants, lower values have been demonstrated for intervention for the treatment of rhesus factor-lysis disease. Eight intravenous immunoglobulin (IVIG) can be used at a dose of 500 mg/kg12 hours × 2 doses after the first intravenous dose. After the first ET may be recommended to start using phenobarbitone5 mg/kg/day ×5 (Mishra et al., 2008).

2-2-4-2-ABO incompatibility

The incidence of maternal-fetal ABO blood group incompatibility is when the mother has blood type O and the newborn has blood type A or B, which accounts for about 15-20% of all pregnancies (Murry Roberts, 2007). Children with blood type O mothers should be closely examined and separated after 72 hours and routine umbilical cord blood testing is not recommended for newborns with mothers of group Yigit et al., 2005). Jaundice caused by ABO incompatibility usually appears 24 hours after birth, if jaundice appears significantly within 24 hours work should be done on pathological jaundice (Yu et al., 2020) .Intensive light therapy is recommended at 17-12 SB mg / dl depending on the age of the child after birth. Birth weight can be used as a standard for phototherapy and ET for newborn infants (Kaplan et al., 2009).

2-2-4-3-Jaundice Associated with G6PD

It is a genetic disease caused by a defect in the proteins that make up the membrane of red blood cells that become spherical and brittle, which results in the destruction and damage of red blood cells in the spleen, leading to hemolytic anemia (Eissa et al., 2019).G6PD is the most vital enzyme for the monophosphate pathway monophosphate_pathway (Hexose Marzban, 2009). Investigations of G6PD deficiency in infants with severe jaundice in a family with a history of significant jaundice or geographical ancestry associated with Bhutani deficiency should be considered (G-6-PD et al., 1999). Reduced bilirubin conjugation led to variation in the UGT1A1 and OATP2

genes that play an important role in the development of hyperbilirubinemia in newborns with D'Silva deficiency (G6PD et al., 2014).

2-3-Causes of jaundice

Zikra Hussain (2016) and Mohammed (2012). There are several causes that lead to jaundice, namely:

1- Premature babie
2- ABO blood group incompatibility between mother and child
3- Bleeding in the skin or head during childbirth
4- The rate of lysis of red blood cell breakdown in newborns is higher compared to Adults, this may due to the short lifespan of red blood cells in newborns, which is 70 day, which leads to an increase in the amont of bilirubin in the blood
5- Immaturity of the liver, where the amount of ligandin protein responsible for bilirubin coupling is low in the body, as well as low activity of the enzyme Glucuronyl transferase responsible for stimulating the process of bilirubin coupling with glucuronic acid, so that it cannot get rid of the excess amount of bilirubin in the blood
6- High bilirubin levels can affect the brain and become dangerous, the accumulation of this substance in the child brain leads to a serious condition called kernicterus,which may lead to mental retardation and motor paralysis
7- Dehydration in newborns and not receiving enough calories
8- Giving the newborn baby water, glucose or water substitute fluids before Breastfeeding based on false ideas to reduce the level of jaundice and thus leads to an increase in jaundice
9- Family medical history if the newborn has a brother or sister had jaundice in the past Gestational diabetes
10- Pregnant mother use some medications such as :Diazepam and Oxytocin

2-4-Symptoms Of Jaundice

The incidence of jaundice has a set of symptoms :

1- Yellow discoloration of the child body
2- Constant drowsiness and lethargy
3- Crying in a high pitched tone
4- The child urine is dark in color
5- Yellow discoloration of the whites of the eyes
6- The babys stool is light in color
7- Swelling in the legs and abdominal distension due to fluid accumulation

2-5-Complications of jaundice

High levels of bilirubin can lead to jaundice, and if left untreated, it leads to the following complications: (Turkistani, 2010)

First: Brain injury: Bilirubin is a substance that has toxicity to brain cells, and in the case of high percentage in the blood, some of them reach brain cells, which leads to the appearance of some symptoms, including

A- Difficulty walking

B- Loud crying

C- High Temperature

D- Poor Ability to swallow food

E- The Chid Looks Emaciated

Second : Nuclear jaundice (Kernicterus)

A- Hearing loss

B- Corneal stability upward

It is brain damage caused by high bilirubin in the blood and the risk of this disorder is higher for preterm infants, severely ill or those using certain medications. The occurrence of this type of jaundice is rare so far but can be prevented almost permanently through early diagnosis and treatment of maternal hyperbilirubinism, but once a brain injury occurs there is no treatment to reverse it.

This type can be diagnosed by the following symptoms :

A- Involuntary and uncontrolled movements

B- Hearing loss

C- Corneal stability upward

D- Mental Impairmant

E- Abnormal growth of tooth enamel

(Deshpande Thyagarajan, 2014;Hamza2019)

2-6-Disease prevention

The American Academy of Pediatrics recommends that all newborns in the near term do the following: Doctors should advise mothers to breastfeed their babies at least 8 to 12 times a day for the first several days, and poor calorie intake or dehydration associated with insufficient breastfeeding may contribute to the development of hyperbilirubinemia. Increasing the frequency of feedings reduces the likelihood of subsequent hyperbilirubinemia in breastfed infants. Providing appropriate support and counseling to breastfeeding mothers increases the likelihood of successful breastfeeding. Doctors should also conduct ongoing systematic evaluations during the neonatal period of an infant's risk of severe hyperbilirubinemia. (Jorgensen et al., 2010) . Turkistani (2010)

showed that the best way to prevent jaundice is to feed the child in sufficient quantity so that breastfeeding is 8 to 12 feedings per day in the first day of his life, andthe amount of milk in artificial feeding is 30-60 milliliters every 2-3 hours a day throughout the first week of his life.

2-7-Ways to get rid of bilirubin from the liver

There are four main steps to rid the liver of bilirubin Uptake and retention of unconjugated bilirubin by hepatocytes using bilirubin glucuronides to conjugate bilirubin Gallea's conjugated bilirubin excretion Hepatocyte reabsorptive capacity of conjugated bilirubin.

1. **Absorption and storage in the liver**

Before entering liver cells, bilirubin separates from albumin. Whether transporters or passive diffusion mediate the first absorption of free bilirubin is unclear (Sorrentino and Berk, 1988). Recent research has categorized the function of membrane-bound OATPs (organic anion transport proteins) in the liver cells' bilirubin absorption process. The OATP superfamily, often referred to as the Anion Transporter Family Member 1B1 (Hagenbuch and Briz) OATP1B1, SLCO1B1, OATP1B3, and SLCO1B3, is comprised of OATPs (2004, Meier et al., 2003),

Research has primarily demonstrated that the primary substrate for these transporters is conjugated bilirubin rather than unconjugated (Briz et al., 2003; Cui et al., 2001). Conjugated bilirubin reabsorption is thus significantly aided by OATPs. Yet, genome-wide analyses have revealed a correlation between increased serum levels of conjugated and unconjugated bilirubin and polymorphisms that resulted in decreased SLCO1B1/OATP1B1 or SLCO1B3/OATP1B3 activity (Zhang et al., 2007; Sanna et al., 2009), providing evidence for the function of OATPs in liver cells in the early absorption of unconjugated bilirubin The cytoplasmic transport protein ligandin, which is a member of the glutathione transport family S (GST), binds to bilirubin much more strongly than albumin does once it enters the liver cells. This interaction facilitates the accumulation and storage of bilirubin in the liver (Erlinger et al., 2014).

2. **Conjugted**

After binding to ligandin, bilirubin is carried to the Smooth Endoplasmic Reticulum, where it binds to the transmembrane protein uridine diphosphate chloronozyl transferrase (Uridine Glucuronosyl Transferase1A1(UGT1A1)), which has two binding sites: one for bilirubin and another for chloronic acid diphosphateuride. The first step in the pairing process consists of two steps. To create bilirubin monoglucuronide, UGT1A1 catalyzes the transfer of a clucuronic acid molecule to one of the carboxyl groups on bilirubin. Bilirubin diglucuronide is created when another

molecule of clocuronic acid is added to the second carboxylic group. Dichloronide and monobilirubin are both readily excreted in bile and soluble in water. Erlinger and associates, 2014).

3. Conjugated bilirubin excretion in bile

After exiting the endoplasmic reticulum and entering the cytoplasm, bilirubin chloronide diffuses toward the lateral (sinusoidal) or apical (ductal) surface of the hepatocelle and is effectively secreted into bile by Cassette (ABC) transporters. Multidrug resistance carrier associated protein 2 (MRP2) is the predominant ABC transporter in charge of bilirubin secretion.

associated with multidrug resistance (Jemnitz, 2010).

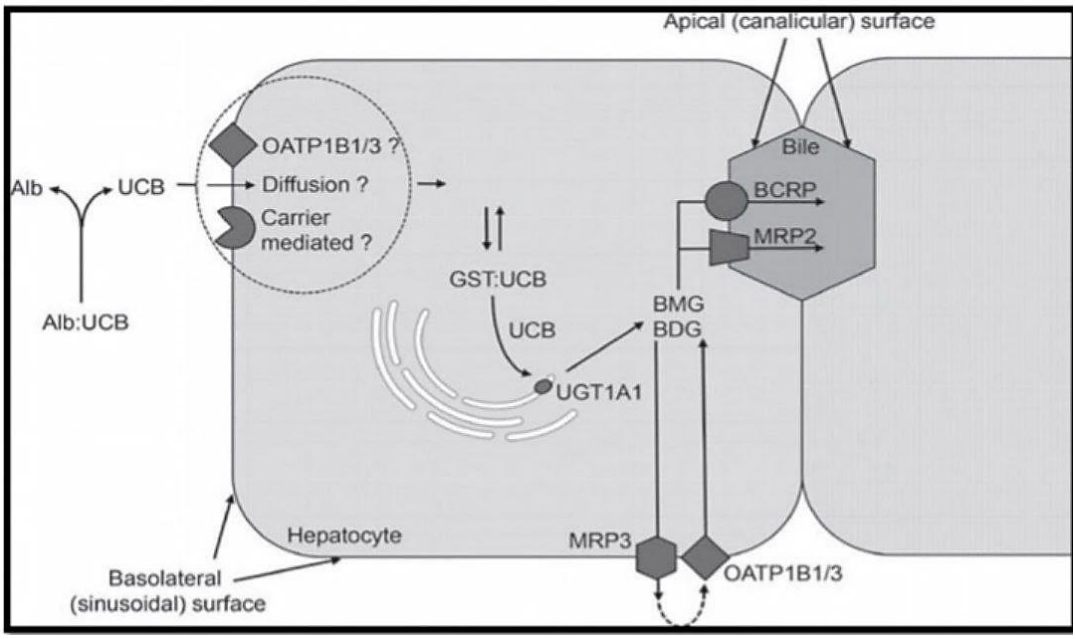

Figure (2-2) Schematic presentation of carriers and enzymes involved in hepatic bilirubin clearance (Memon et al., 2016)

4. Reabsorption of conjugated bilirubin by liver cells

Curiously, a sizable amount of bilirubin chloronide is eliminated into sinus blood and subsequently reabsorbed by hepatic cells for the purpose of secreting bile channels. According to SLCO1B3/OATP1B3 et al. (2012), the transporter ABCC3/MRP3 is responsible for the conjugated bilirubin secretion on the lateral surface, which is then reabsorbed by transporters/SLCO1B1; OATP1B1 and van. As hepatocytes near the central vein express more OATP1B1 and OATP1B3, it is thought that this recovery keeps upstream hepatocytes, or those close to the portal routes, from reaching their maximum capacity for biliary secretion (Jirsa Sticova, 2013).

4. Conclusion

1-Hyperbilirubinemia is one of the most common problems faced by newborns.

2-Males showed a greater effect than females in the incidence of hyperbilirubinemia in terms of number and severity of infection

3-Multiple risk factors for newborns, including (natural birth route, breastfeeding, carriers of blood type A, and males) are more susceptible to hyperbilirubinemia, as their percentage was higher than the groups of sick and control children

4-There is a direct relationship between the intensity of bilirubin concentration and the duration of treatment with ultraviolet rays

5-Jaundice has an effect on liver enzymes, activity and effectiveness through its effect on ALT, ALP, GUT1A1 enzymes compared to control, while a significant decrease was recorded in the effectiveness of the AST enzyme compared to control.

5. Recommendation

1-Conduct a genetic and molecular study to investigate whether there is a defect in the genes responsible for the production of bilirubin in the body and responsible for jaundice.

2-Conduct a study that includes the effect of neonatal jaundice on the nervous system and brain and measure some vital indicators of the nervous system in newborns.

3-The current study recommends conducting a study on the effect of ultraviolet rays within the wavelength and treatment period but within different periods on the cells and tissues of young laboratory animals.

4-Measure the activity of some antioxidants such as GSH and the oxidative stress indicator MDA for children with hyperbilirubinemia.

5. Examine the activity of the enzyme Glucoronidase in breast milk, especially in the first days after birth.

REFERENCES

1. Turkistani, Suhail Abdullah. (2010). Neonatal Jaundice. Saudi Society for Family and Community Medicine.
2. Hussein, Talib Abdullah. (2016). Study of Hematological and Biochemical Changes in Neonatal Jaundice. Anbar
3. University Journal of Pure Sciences, Vol. 10, No. 2.
4. Ahn, B., Ranjit, R., Premkumar, P., Pharaoh, G., Piekarz, K. M., Matsuzaki, S., ... & Van Remmen, H. (2019). Mitochondrial oxidative stress impairs contractile function but paradoxically increases muscle mass via fibre branching. Journal of cachexia, sarcopenia and muscle, 10(2), 411-428.
5. Alajeely, Sinan Samir.(2010). PREVALENCE AND RISK FACTORS FOR NEONATAL HYPERBILIRUBINEMIA IN MOSUL CITY. Master of Sciences in Nursing. University of Mosul .
6. Cortey, A., Renesme, L., Raignoux, J., Bedu, A., Casper, C., Tourneux, P., & Truffert, P. (2017). Ictère à bilirubine non conjuguée du nouveau-né de 35 semaines et plus: du dépistage au suivi après sortie de la maternité. Recommandations pour la pratique clinique. Archives de Pédiatrie, 24(2), 192-203.
7. Creeden, J. F., Gordon, D. M., Stec, D. E., & Hinds Jr, T. D. (2021). Bilirubin as a metabolic hormone: the physiological relevance of low
8. Das, K., & Roychoudhury, A. (2014). Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. Frontiers in environmental science, 2, 53.
9. Edoh, D., Antwi-Bosaiko, C., & Amuzu, D. (2006). Fetal hemoglobin during infancy and in sickle cell adults. African health sciences, 6(1), 51-54.
10. Hayyan, M., Hashim, M. A., & AlNashef, I. M. (2016). Superoxide ion: generation and chemical implications. Chemical reviews, 116(5), 3029-3085.
11. Hoffbrand, A. V., & Steensma, D. P. (2019). Hoffbrand's essential haematology. John Wiley & Sons.
12. Immenschuh, S., Shan, Y., Kroll, H., Santoso, S., Wössmann, W., Bein, G., & Bonkovsky, H. L. (2007). Marked hyperbilirubinemia associated with the heme oxygenase-1 gene promoter microsatellite polymorphism in a boy with autoimmune hemolytic anemia. *Pediatrics*, *119*(3), e764-e767.
13. Jasprova, J., Dal Ben, M., Vianello, E., Goncharova, I., Urbanova, M., Vyroubalova, K., ... & Vitek, L. (2016). The biological effects of bilirubin photoisomers. PLoS One, 11(2), e0148126
14. Kaplan, M., Na'amad, M., Kenan, A., Rudensky, B., Hammerman, C., Vreman, H. J., ... & Stevenson, D. K. (2009). Failure to predict hemolysis and hyperbilirubinemia by IgG subclass in blood group A or B infants born to group O mothers. *Pediatrics*, *123*(1), e132-e137.

15. Kuntz, E., & Kuntz, H. D. (2009). Hepatology: Textbook and atlas. Springer Science & Business Media
16. Li, S., Zou, Q., Li, Y., Yuan, C., Xing, R., & Yan, X. (2018). Smart peptide-based supramolecular photodynamic metallo-nanodrugs designed by multicomponent coordination self-assembly. Journal of the American Chemical Society, 140(34), 10794-10802.
17. Menon, S., & Amanullah, N. (2017). Maternal and neonatal determinants of neonatal jaundice-a case control study journal of medical science and clinical research,5(03)19659-19665.
18. Mishra, S., Agarwal, R., Deorari, A. K., & Paul, V. K. (2008). Jaundice in the newborns. The Indian Journal of Pediatrics, 75(2), 157-163.
19. Mitra, S., & Rennie, J. (2017). Neonatal jaundice: aetiology, diagnosis and treatment. British Journal of Hospital Medicine, 78(12), 699-704.
20. Mojtahedi, S. Y., Izadi, A., Seirafi, G., Khedmat, L., & Tavakolizadeh, R. (2018). Risk factors associated with neonatal jaundice: a cross-sectional study from Iran. Open access Macedonian journal of medical sciences, 6(8), 1387.
21. Sadeq, T. N., Feyad, H. F., & Hameed, G. R. A. (2019). Risk Factors of Neonatal Jaundice at Al Kadhimiya Pediatrics Hospital in Baghdad, Iraq. Al-Rafidain University College For Sciences, (44).
22. Sgro , M., Kandasamy, S., Shah, V., Ofner, M., & Campbell, D. (2016). Severe neonatal hyperbilirubinemia decreased after the 2007 Canadian guidelines. The Journal of pediatrics, 171, 43-47.
23. Tepán Lema, M. E. (2018). Hiperbilirrubinemia, características y factores asociados en neonatos. Hospital José Carrasco Arteaga. 2015-2017 (Master's thesis, Universidad del Azuay).
24. Wang, X. Q., Wang, W., Peng, M., & Zhang, X. Z. (2020). Free radicals for cancer theranostics. Biomaterials, 120474.
25. Wisnowski, J. L., Panigrahy, A., Painter, M. J., & Watchko, J. F. (2016). Magnetic resonance imaging abnormalities in advanced acute bilirubin encephalopathy highlight dentato-thalamo-cortical pathways. The Journal of pediatrics, 174, 260-263