

Vitamin D status in neonates with hyperbilirubinemia

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Abstract

Background: Physiological Jaundice is more common in neonates. While causes such as incompatibility of blood groups or polycythemia can be easily identified, most are still undiagnosed. Phototherapy is an effective way to reduce the accumulation of bilirubin. Vitamin D is a fat-soluble vitamin that plays an important role in bone remodeling. It is also considered a steroid hormone, plays an important role in the main function of various organ systems, and can be a risk factor for changing the risk of many chronic diseases. There is a link between vitamin D and jaundice. Newborns with hyperbilirubinemia have low serum vitamin D levels.

Conclusion: There is an association between indirect hyperbilirubinaemia and vitamin D levels in neonates with jaundice at the level necessary for phototherapy.

Keywords: Vitamin D , Jaundice , Phototherapy .

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Introduction

1. Physiological Jaundice

1.1-Definition

Neonatal hyperbilirubinemia is a common problem in neonates, about 60% occurring in full term neonates and 80% in preterm ones. It is the most common cause of hospitalization during postnatal period (**Mostafa et al.,2019**).

1.2-Etiology

Physiological jaundice is caused by increasing bilirubin production due to accelerated erythrocyte degeneration, decreased excretory capacity due to immature liver cells, and decreased activity of bilirubin uridine-conjugated bilirubin (UG).(**Mitra and Rennie,2017**).

Pathological hyperbilirubinemia occurs when additional factors accompany the basic mechanisms described above. Examples include immunosuppressive or non-immune hemolytic anemia, polycythemia. Decreased bilirubin excretion may play a role in breast milk jaundice (**Alkhotani et al., 2014**).

Yellowish skin and sclera in newborns with jaundice is due to untreated bilirubin accumulation. In most neonates, indirect hyperbilirubinemia reflects a normalization phenomenon. However, serum bilirubin levels may increase too much in some neonates, which is a

cause for concern because the increasing bilirubin is a neurotoxic disorder and can lead to neonatal death and lifelong neurological consequences in surviving babies (kernicterus) (**Mitra and Rennie 2017**).

Clinically, the neurotoxicity of bilirubin leads to bilirubin encephalopathy in the form of hypotension and poor suction, an intermediate phase characterized by stupor, irritability and hypertension, and an advanced phase described by coma or occasional seizures. Although the early phase is reversible with treatment, the middle and late phases are believed to be irreversible, resulting in a kernicterus (**Kitai et al., 2020**).

1.3-Pathophysiology:

Neonates are predisposed to develop hyperbilirubinemia as a result of increased bilirubin production and decreased excretion. Increased production is due to the greater number of red blood cells combined with their shortened survival, which leads to an increased turnover of erythrocytes compared to red blood cells in adults(**Waqar and Razzaq 2013**).

Newborns have limited ability to conjugate bilirubin, unconjugated bilirubin accumulates and is not easily excreted(**Waqar and Razzaq 2013**).

These limitations lead to physiological jaundice that begins around 3 to 5 days of life and reaches a maximum of 5 to 6 mg / dL by the end of the first week and returns to normal levels in infants by 10 to 12 days dropping can take 3 weeks in premature babies.(**Waqar and Razzaq, 2013**).

1.4-Risk factors include the following:

- Geography: Rate of jaundice throughout the world are high. Greeks seem more ordinary than those living in another country.(**Mitra and Rennie 2017**).
- Genetics and familial causes: Occurrence in neonates with siblings, mutations, polymorphisms in molecular genes for enzymes and proteins involved in bilirubin metabolism, homozygous or heterozygous (G6PD) deficiency, and other hereditary hemolytic anemia(**Memon et al., 2016**).
- Nutrition: Rates are higher in breastfed babies. When there is insufficient feeding amount, increased hepatic circulation of bilirubin may participate in prolonged jaundice(**Kumral et al., 2009**).
- Maternal factors: Babies of diabetic mothers have a higher birth rate. Some medications can cause an increase while others decrease the incidence. Treatment with certain herbs taken by nursing mothers may

cause worsen hyperbilirubinemia in babies.(**T Rahman 2018**).

- Race: Birth rates are higher in East Asian countries and Native Americans and lower African / Afro-American(**Brits et al., 2018**).
- Birth weight and gestational age: Birth rates are higher in preterm babies and others with low birth weights.(**Wang., 2019**).
- Congenital infection.

1.5-Physical Examination

- Newborn jaundice is first seen on the face and forehead. Determination is obtained by compressing the skin. Jaundice then gradually appears on trunk and extremities. The reason for this phenomenon is not well understood, but changes in bilirubin-albumin binding to pH as well as differences in temperature and blood flow have been suggested(**Purcell and Beeby, 2009**).

1.6-Differential Diagnoses (Ebbesen et al., 2017) :

- Jaundice of breast milk
- Cholestasis
- Dubin-Johnson Syndrome
- Galactosemia
- Haemolytic disease of neonates
- Hepatitis B.
- Neonatal biliary atresia
- Neonatal cytomegalovirus infection
- Neonatal duodenal atresia

1.7-Laboratory investigations

Measurement of hyperbilirubinemia may include the following:

- Transcutaneous bilirubinometry can be used with a hand-held devices that contains light algorithms. The use of such devices has been shown to reduce the need for blood tests in neonates with jaundice. However, it can not be used to track the progress of the phototherapy. **(Mishra et al., 2009).**
- Transcutaneous bilirubinometry is better than visual evaluation. The last one is not a reliable technique for assessing bilirubin levels. **(Keren et al., 2009).**
- Neonates with mild jaundice, transcutaneous bilirubinometry is satisfied to ensure that all bilirubin levels are below the safety level in which no need for intervention. **(Rylance et al., 2014).**
- In neonates with moderate jaundice, transcutaneous bilirubinometry may be helpful in selecting patients who require phlebotomy or blood tests for serum bilirubin measurement. **(El-Kabbany et al., 2017).**

1.8-Imaging techniques

- Ultrasound for liver and biliary tract is required for neonates with laboratory or cholestatic symptoms. **(Singh et al., 2014).**
- If extrahepatic biliary atresia is suspected, (HIDA) is required. **(Khan et al., 2014).**

1.9-Management

Principle:

Phototherapy: The discovery of light as a therapy for neonatal hyperbilirubinemia was made in 1958 by a UK nurse who observed a remarkable disappearance of jaundice when the baby was exposed to sunlight. Since its discovery, phototherapy has been a widely used and accepted form of treatment for jaundice in newborns **(Cremer et al., 1958).**

In the absence of hemolysis, phototherapy reduces serum bilirubin by 25 to 50% during the first 24 to 48 hours after application. The higher the total serum bilirubin, the faster the phototherapy decreases. There is evidence that phototherapy can be discontinued as soon as total serum bilirubin falls by 50 μmol / liter (3 mg / dL) **(National Collaborating Centre for Women's and Children's Health 2010).**

2-Vitamin D

2.1-Definition

Vitamin D is a fat-soluble vitamin that plays an important role in bone remodeling. It is also considered a steroid hormone, plays an important role in the main function of various organ systems, and can be a risk factor for changing the risk of many chronic diseases **(Kawao and Kaji 2015).**

2.2-Vitamin D metabolism

Synthesis and Stimulation
Endogenous Vitamin D synthesis begins in the skin .Both epidermis and dermis contain 7-dehydrocholesterol (DHC). When UVB radiation (280-315 nm) passes through this embedded layer, the 7-dehydrocholesterol (DHC)in the body absorb the UVB photons and stimulate its conversion to previtamin D3.(**Battault et al., 2013**).

This imaging is followed by a thermal isomerization of previtamin D3, which leads to the formation of a molecule of vitamin D3, also known as collect calciferol. During prolonged exposure to the sun, previtamin D3 is preferred over lumisterol and tachysterol, both of them are biologically ineffective (**Battault et al., 2013**).

Once formed, vitamin D3 is binded specifically to the vitamin D-binding protein (DBP), which facilitates its migration into the general circulation.(**Chun et al., 2017**).

2.3-Function

The two main points of rotation of 1alpha, 25 (OH) 2D are:

- (1) Increases the absorption of calcium and phosphorus in the intestine.

- (2) Maturation of pre-osteoclasts to osteoclasts.(**Holick ., 2007**)

2.4-Vitamin D status

A recent report by the Institute of Medicine (IOM) identified "vitamin D insufficiency" when serum concentrations of 1,25 (OH) D were <20 ng / ml. The Endocrine Society determined that a vitamin deficiency of 25 (OH) D should be less than 20 ng / ml, a "insufficiency" of 25 (OH) D between 20 and 30 ng / ml, and that the recommended target for treatment should be to achieve 25 (OH) D above 30 ng / ml.(**Ross et al., 2011**).

2.4-vitamin D supplementation

A study by the National Institute for Child Health and Human Development reported these doses 400 IU / day, 2000 IU / day, and 4000 IU / day. While doses of 2000 IU / day and 4000 IU / day have been used in Thrasher studies(**Wagner et al., 2013**).

3- Vitamin D levels And Jaundice

Serum bilirubin was significantly reduced in newborns treated with vitamin D and phototherapy compared to newborns treated with combined melatonin with phototherapy.(**Elfaragy et al., 2019**).

The association between serum vitamin D levels and the prevalence of hyperbilirubinemia (indirect) in

neonates indicates strong correlation between vitamin D levels and NIH.(Mehrpisheh et al., 2018).

Conclusion

In summary, there is a relation between indirect hyperbilirubinemia and vitamin D levels in neonates with jaundice requiring phototherapy.(Mutlu et al., 2013).

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