ROLE OF UTRASONOGRAPHY IN NEONATAL JAUNDICE

THESIS

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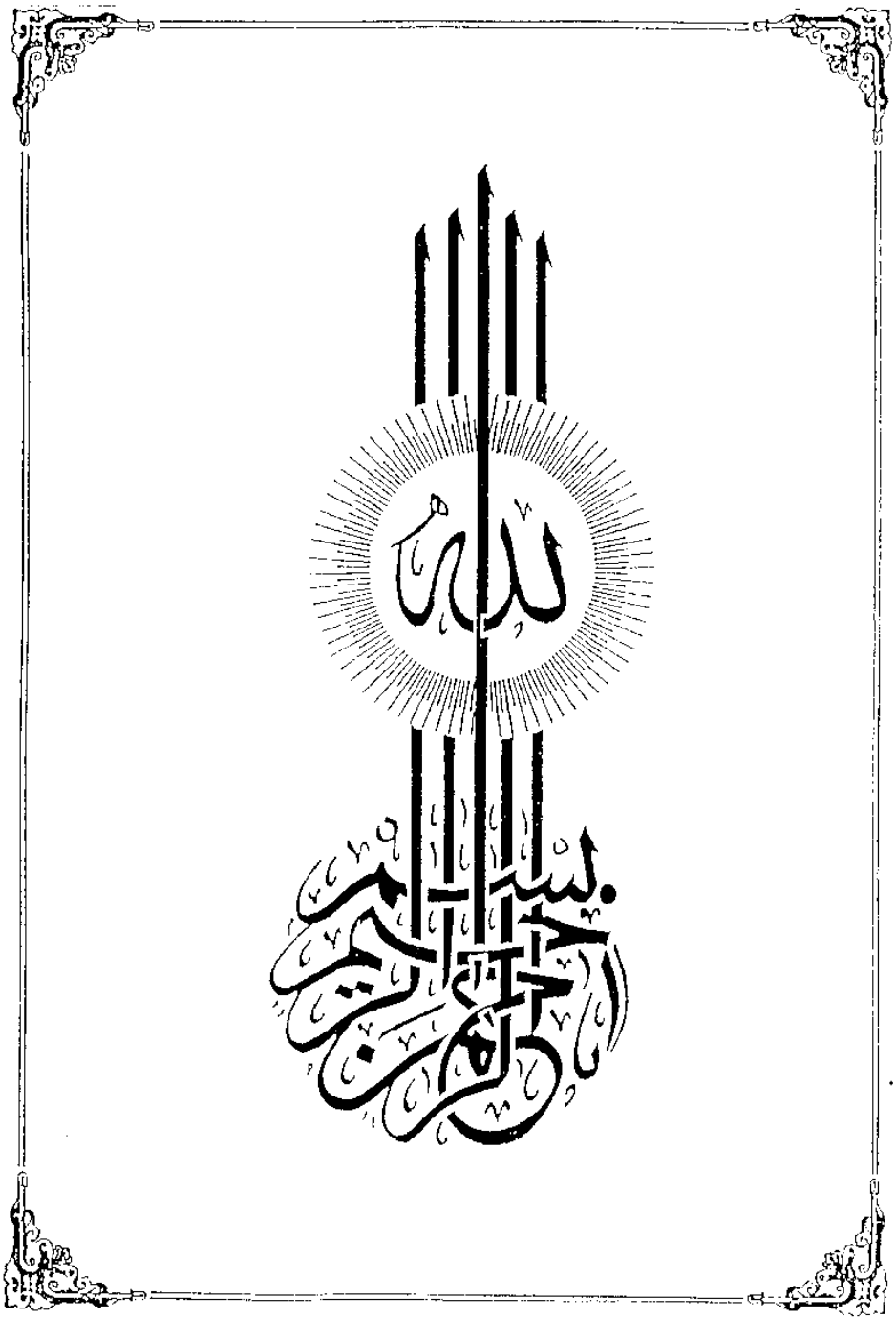

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Ultrasonography is one of the most valuable diagnostic tools of preferable use in paediatrics. It is painless, non invasive, non ionizing, safly repeatable and requires the least prepration of the patient.

Jaundice is one of the commonest neonatal problems and according to *[Nelson, 1987]* : it is observed during the first week of life in approximately 60% of term infants and 80% of preterm infants.

Ultrasonography can provide much valuable information in the jaundiced patients. The classification of the etiology on obstructive and non obstrctive babis is curcial since this will often determine whether surgical or me dical management respectively will be indicated.

The aim of this study is to evaluate the diagnostic role of ultrasonography in cases of neonatal jaundice.

PATHOGENESIS

Jaundice is the visible manifestation of chemical hyperbilirubinemia. Most adults are visibly jaundiced when serum bilirubin concentrations exceeds 2.0mg per 100ml. Where as neonatal is rarely perceptible untill the serum bilirubin concentrations exceed 7.0 mg per 100ml .

Chemical hyperbilirubinemia, a serum bilinrubin of 2.0mg per 100ml or more, is virtually universal in newborn infants during the first week of life. Although some degree of jaundice may be considered a normal physical finding in both term and preterm infonts. ***[Avery & Taeusch, 1984]***.

Almost all infants with mild elevation in bilirubin level either are not investigated or their jaundice is dismissed as physiologic. A good understanding of the mechanisms that contribute to normal bilirubin metabolism is important in considering both physiologic and pathologic jaundice. Such considerations are probably second infrequency only to consideration of respiratory difficulty ***[A.Philip, 1987]***.

Bilirubin matabolism :

Bilirubin is produced by the catabolism of hemoglobin in the reticuloendothelial system. The tetrapyrol ring of heme is cleaved by heme oxygenase to form equivelant quantities of biliverdin and carbon monoxide. Biliverdin is converted to bilirubin by biliverdin reductase.

One gram of hemoglobin produces 35 mg of bilirubin. Sources of bilirubin other than circulating hemoglobin represents 20% of bilirubin production; these sources include ineffecient (Shunt) hemoglobin and lysis of precursor cells in the bone marrow. Compared with adults, new born infants have a 2 to 3 fold greater rate of bilirubin production (6-10mg/kg/24hr. Vs. 3mg/kg/24hr. This due, in part, to an increased red blood cell mass (higher hematocrit) and ashortened erythrocyte half-life of 70 to 90 days compared wih the 120 day erythrocyte half-life in adults ***[Behrman and Kliegman, 1990].***

Bilirubin occurs in plasma in four forms

1. unconjugated bilirubin tightly bound to albumin
2. Free or unbound bilirubin (presumably the form responsible for kernicterus, since it can cross cell membranes).
3. Conjugated bilirubin (the only raction to appear in urine).

4. Delta fraction (bilirubin covalently bounda to albumin), which appears in serum when hepatic excretion of conjugated bilirubin is impaired in pateints with hepatobiliary disease. The delta fraction permits conjugated bilirubin to persist in the circulation and delays resolution of jaundice.

Measurement of serum bilirubin is ususally via the van den Bergh diazo reaction. The term "direct-reacting" and "indirect-reacting" bilirubin correspond roughly to conjugated and unconjugated bilirubin, respectively ***[Nelson, 1987]***.

The bilirubin that gives an indirect reaction with the van den Bergh reagents is carried in the plasma bound to albumin. In the liver it is mostly conjugated to glucuronic acid to form bilirubin diglucornide, which is then excreted into the intercellular bile canliculi. Congjugated bilirubin is not normally present in the blood in significant amounts, but reflux into the circulation occurs if there is an obstruction in the biliary system or sever damage to liver parenchymal cells. It will then give a direct van den Bergh reaction and it is called "direct bilirubin".

The conjugation of free or indirect bilirubin to glucuronic acid to form conjugated or direct bilirubin takes place in the liver parenchyma by a series of enzyme

reactions. It is now known that the final step is dependent on two distinct enzymes. The microsomal enzyme uridine diphosphate glucuronate glucuronyl transferase, catalyses the formation of bilirubin monoglucuronide from unconjugated bilirubin and uridinediphosphate glucuronic acid (UDPGA), where as the formation of bilirubin diglucuronide from bilirubin monoglucuronide requires the activity of a second enzyme, bilirubin glucuronide glucuronosyl transferase. (UDPGA) is the only form in which glucuronic acid is available for congujation several other substances imporant in medicine and inculding steroids, salirylotes, aniline and chloramphenicol are excreted along the same pathway. It should be noted also that the various steps in bilirubin conjugation involve bath nucleotide and carbohydrate metabolism. The availability of glucose is therefore of importance in bilirubin excretion. There is furthermore, evidence that other ways of bilirubin excretion exist besides glucuronation. One of these is by conjugation to sulphate but the newborn is apparently unable to use this pathway to compensate for defective glucuronation .

From the point of view of the newborn infant the importance of the conjugation of bilirubin to glucuronic acid lies in the change in the solubility of bilirubin which this process brings about. Free or indirect bilirubin is insoluble in water so that it can not be excreted by the kidneys or in the bile. Because it is fat soluble, however,

it can enter the brain or the subcutaneous adipose tissue especially if high serum level exist. As the premature infant lacks subcutaneous tissue fat there may be greater danger of "indirect" bilirubin entering the nervous system where it is highly toxic (kernicterus). Conjugated or direct bilirubin is, on the other hand, soluble in water and so readily excreted in the urine or bile, and as it is not soluble in fat it is not toxic to the nervous system.

An abnormally high level of indirect bilirubin may develop in the blood of the new born under two conditions. Firstly, a deficiency in the liver of the activity of glucuronyl transferase will result in a high serum indirect bilirubin, derived from the normal rate of red cells breakdown. Such a deficiency or immaturity of this enzyme system is common, especially in premature infant. The situation in the premature infants may be further complicated by a lack of available glucose for the formation of UDPGA. Secondly, a raised serum indirect bilirubin level can arise from increased production due to haemolytic anaemia. In some cases both factors are operative for example, dangerous levels of indirect bilirubin are rare in the adult with haemolytic anaemia because the liver has an enormous reserve capacity for glucuronation whereas a similar degree of haemolysis in the newborn is quite beyond the capacity of the enzyme system concerned. The danger of a high serum indirect bilirubin level is of course, that this

fat-scluble pigment may gain entry to the cells of the central nervous system. It should be realized however, that only indirect bilirubin which is not bound to serum albumin is free to enter the central nervous system and other tissues and the risks of hyperbilirubinaemia are therefore influenced by the bilirubin-binding capacity of the serum albumin. Kernicterus consequent upon hyperbilirubinaemia will only develop when the serum albumin is unable to bind further indirect bilirubin. Several factors may influence the bilirubin-binding capacity in an adverse direction and so increase the risks of brain damage. These include a low level of serum albumin and metabolic acidosis, both of which are common in premature infant, and displacement of the bilirubin from its albumin-binding sites by other organicions, which have an affinity for albumin, such as sulphafurazol, salicylates, heparin, fatty acids, and haematin which may be released during haemolysis. On other hand an abnormally high level of direct or conjugated bilubin bilirubin may develop in the blood of the biliary obstruction or sever hepatocellular damage. There is however no danger of the water-soluble direct bilirubin entering the nervous system *[Hutchison 1986]*.

Before, we proceed in the pathogensis, classification is necessary to highlight the pathogensis related to each type of jaundice and hence method of investigation and the required managment accordingly.

Kelnar and Harvey (1986) for example classified jaundice into three categories; these are prehepatic, hepatic and post hepatic, and that classification is irrespective of state of conjugation of bilirubin.

However, ***Nelson et al. (1987)*** classified jaundice into two main classes; conjugated and unconjugated type and furthermore, the possible underline cause which may be metabolic, infective genetic etc.

Hutchison and Cocburn (1986) said in this context" the type of jaundice due to a high level of " indirect" bilirubin is called non-obstructive, whereas that involving reflux into the blood from the liver of "direct" bilirubin is obstructive. Of course, it is possible for both types to coexist."

As for ultrasonography as an imaging modality the last classification may be siutable and preferable to others. So we can consider it in our study.

Obstructive jaundice:

There are many causes of obstructive jaundice or that of mainly conjugated type of bilirubin. also the authors differ in their tabulation of these causes. ***Behrman and***

Kliegmon (1990) gave a table according to diagnostic and frequency of occurrence of each group. They devide these causes into common and uncommon ones. Table (1).

Table (1) :

Causes of obstructive jaundice.

Common

Hyperalimentation cholestasis.

CMV infection. (cyto megalo virus infection).

Other perinatal congenital infection.

Inspissated bile from prolonged haemolysis.

Neonatal hepatitis.

Sepsis.

Uncommon

Hepatic infarction.

Inborn errors of metabolism (galactosemia, tyrosinosis)

Cystic fibrosis

biliary atresia.

Choledochal cyst.

Alpha-1-Anti-trypsin deficiency.

Hepatitis β.

Alagille syndrome (arteriohepatic dysplasia).

Byler disease.

[Behrman and Kliegman, 1990]

Nelson (1987) described the raised level of conjugated bilirubin as neonatal cholestasis that is due to functional impairment of bile secretion that may result from damage to liver cells or to the biliary secretory appratus, and that the neonates with cholestasis may be devided into those with extrahepatic and those with intrahepatic disease (Fig. I)