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REVIEW ARTICLE

A Mini-Review on Biochemical Aspects of Albumin in Jaundice

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ABSTRACT
The a-fetoprotein (AFP) and vitamin D binding protein homologous genes are located near the albumin gene on chromosome 4. (Ge-globulin). The white precipitate that developed during the boiling of acidic urine from people with proteinuria gave rise to the name albumin (albus = white). From the prenatal stage onward, albumin is typically the most prevalent plasma protein, making up roughly half of the plasma protein content. The majority of bodily fluids, such as interstitial fluid, CSF, urine, and amniotic fluid, contain significant amounts of it. The extravascular space has more than half of the total albumin pool.
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INTRODUCTION

Of a predicted molecular weight of 66,438 Da, albumin contains a non-glycosylated polypeptide chain with 585 amino acids. It features a three-dimensional structure in the form of a heart supported by 17 intrachain S-S bonds [1]. It is a relatively stable protein that can withstand temperatures greater than those at which most plasma proteins would denature [2]. Because it contains a lot of charged amino acids, albumin is very soluble and, at pH 7.3, has a net negative charge of roughly -12 [3]. Therefore, for normal albumin concentrations of 0.5 to 0.8 mmol/L and lower albumin concentrations, albumin contributes between 6 and 10 mmol/L to the amon gap [4]. Albumin has a net charge of roughly 25 at a pH of 8.6 for alkaline electrophoresis, resulting in strong mobility toward the anode. It acts as a crucial plasma transporter for free sulfhydryl substances [5]. Hepatocytes manufacture albumin. Colloidal osmotic pressure (COP) and protein intake regulate the synthesis rate. Albumin has a typical plasma half-life of 15 to 19 days. As the main component of colloid osmotic pressure and as a transporter for a wide range of substances, including fatty acids and other lipids, bilirubin, foreign substances like drugs, thiol-containing amino acids, tryptophan, calcium, and metals, albumin serves two of its most clearly defined purposes [5].

ROLE OF ALBUMIN IN BILIRUBIN METABOLISM

Due to unconjugated bilirubin's extremely poor water solubility in the absence of a carrier molecule, albumin is a crucial aid in facilitating transport to the liver or other sites of metabolism. Both a high-affinity and a low-affinity location for bilirubin appear on albumin. About 25 mg of bilirubin can be bound by the high-affinity site per 100 mL plasma [6]. Two molecules of bilirubin can be bound by one albumin molecule. There is a second site that is less affine to bilirubin. Only under extremely elevated bilirubin levels does it connect to this low-affinity spot. Bilirubin is bound loosely by albumin. Bilirubin binding is dynamic, with

some unbound and bound bilirubin constantly in balance [7]. Aspirin, penicillin, etc., can bind to the albumin binding sites for bilirubin. Therefore, such medications may divert albumin away from bilirubin. Hence, care should be taken while administering such drugs to newborn babies to avoid kernicterus.

PLASMA ALBUMIN IN INFANTS:

The albumin level depends on the gestation age. So more premature babies lower albumin levels. The average concentration of term neonates is 3.5 - 5.0 g/dl. When the bilirubin levels increase, the albumin binding sites become saturated, and the amount of unbound bilirubin increases. The amount of unbound bilirubin doubles when the total bilirubin is 15 - 20 mg/d l, quadruples at 25 mg/dl and increases eightfold at 30 mg/dl. Plasma albumin level increases in the first few days of life, resulting in a mean increase over the first seven days of almost 30%. Adult levels reach only by five months [8]. The tight binding capacity of albumin for bilirubin may be diminished in the newborn period. Low pH may have a direct effect on the binding of bilirubin to albumin and is known to increase the movement of bilirubin into the tissue, altering the equilibrium between the bound and the unbound, thereby promoting the dissociation of bilirubin sites [9]. Such an effect might occur because of the change in pH in the neonate, changing the solubility of bilirubin. Neonates have a lower pH when compared to adults. As pH decreases, the solubility of free bilirubin decreases, and bilirubin moves out of the solution and enters cells more easily than bound bilirubin. Bilirubin binding may be further suppressed in premature infants, whose course 1s are frequently complicated by hypoalbuminemia, hypoxia, hypoglycemia, acidosis, hypothermia, hemolysis and septicemia. The resulting increase in free bilirubin is implicated in neurotoxicity at relatively low serum bilirubin levels in premature infants [10].

PHYSIOLOGICAL JAUNDICE

Within the first week of life, breastfed newborns are more likely than bottle-fed babies to acquire physiological jaundice, but the onset of jaundice is not a cause to quit nursing. Jaundice that is prevalent, primarily innocuous, and for which newborns have no underlying reason during the first few weeks of life is referred to as physiological jaundice [11]. Although the causes of the link between breastfeeding and neonatal jaundice are not fully understood, they may include factors in breast milk that are unknown, insufficient breastfeeding support that causes a reduction in intake, or sluggish gut action that causes an increase in enter hepatic circulation of bilirubin. Last but not least, it's possible that the relative decrease in bilirubin levels in newborns who are given formula is the result of enhanced bilirubin clearance from the stomach. The chance to determine if effective lactation has been established and to give proper breastfeeding support and guidance is diminished by the current NHS practice of early postnatal discharge, which frequently occurs within 24 hours [12].

BREASTFEEDING JAUNDICE:

This is a result of inadequate or decreasing feeding frequency. The reduced frequency could make physiological jaundice worse. Avoiding or treating this kind of jaundice is feasible by encouraging women to breastfeed as frequently as possible. Breast milk jaundice (BMJ) was initially described by Arias in 1963 [13]. Neonatal jaundice that is linked to nursing is known as breast milk jaundice. Unconjugated hyperbilirubinemia in a breastfed infant is what defines it. It appears after the first 4–7 days of life, lasts longer than normal jaundice, and has no other known causes. Although the cause of this "breast milk ja und ice" is yet not fully known, the ailment seems typically benign. The following elements have been proposed as contributing factors: Unusual progesterone metabolite that inhibits uridine-diphosphoglucuronic acid (UDPGT) glucuronyl transferase in breast milk (pregnane-3-alpha 20 beta-diol). Delayed development of enteric flora in breastfed neonates and increased enterohepatic circulation of bilirubin due to enhanced beta-glucuronidase activity in breast milk and, therefore, the intestines of the breastfed newborn [14]. Individuals with breast milk jaundice have higher levels of inflammatory cytokines in their milk, particularly interleukin (IL)-1 beta and IL-6, which are known to be cholestatic and lower bilirubin uptake, metabolism, and excretion. Jaundice in these newborns may be brought on by breast milk containing excessive amounts of epidermal growth factor (EGF) [15], [16]. The GIT in newborns grows, multiplies, and matures due to EGF, which is also essential for the GIT's adaptability after birth. Patients with breast milk jaundice had higher amounts of EGF in their blood and breast milk. Infants with breast milk jaundice were found to have increased serum levels of alpha-fetoprotein [17],

[18]. Breast milk is an essential source of bacteria for developing an infant's gut flora. However, in recent research, persistent jaundice may be a sign of underlying liver illness and must be carefully examined [19].

PATHOLOGICAL JAUNDICE:

Anti-D antibodies can cross the placenta and assault the blood of Rh-positive babies in subsequent pregnancies in Rh-negative women who have grown sensitized to the D-antigen in an Rh-positive foetus. This results in the disorder known as erythroblastosis fetalis, newborn hemolytic disease, and rhesus isoimmunization. Red blood cells are largely hemolyzed before and after delivery in this disease. Fetal anaemia can develop in severe instances and lead to congestive heart failure. The bilirubin produced from enhanced hemolysis is greater than the liver's capacity to conjugate it. The placenta removes bilirubin, protecting the foetus, but the newborn is in danger of kernicterus after birth due to the rapidly rising bilirubin levels [20].

ABO incompatibility:

ABO incompatibility is most frequently observed when the mother belongs to group O and the infant to A or B. It seldom affects the foetus and is milder than Rhesus disease. They typically have jaundice that becomes apparent on day 1 or 2 but responds well to phototherapy. Rarely is an exchange transfusion necessary when an otherwise healthy, term newborn has an ABO incompatibility. The diagnosis is simple when the Direct Coombs Test is positive, and the blood groups are correct [21]. When the Direct Coombs Test is negative, yet the evidence suggests ABO, it might be challenging. Suppose anti-A or anti-B IgG antibodies are present in the mother's plasma and the baby's RBCs. In that case, the diagnosis in this circumstance is likely to be a lack of glucose-6-phosphate dehydrogenase. A cytoplasmic enzyme called G6PD creates reduced glutathione and catalyzes the first stage of the hexose monophosphate pathway, resulting in NADPH. By doing this, the red blood cell membrane is shielded from the harmful effects of oxidation. Infants with severe jaundice, families with a history of considerable jaundice, or those from regions where G6PD deficiency is common should all be investigated. In neonates with G6PD deficiency, decreased bilirubin conjugation caused by variations in the UGTlAl and OATP2 genes is crucial to developing hyperbilirubinemia.

SUMMARY

Visible jaundice typically emerges between 24 and 72 hours after birth. TSB levels typically increase in term newborns, reaching a peak level of 12 to 15 mg/dl by three days of life before declining. The highest TSB in preterm newborns occurs between 3 and 7 days of life and can increase by more than 15 mg/dl. Weeks may pass before the TSB levels in both terms and preterm babies fall below 2 mg/dl. When TSB concentrations are outside the "physiological jaundice" range, it is indicated that "pathological jaundice" occurs.

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