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A biochemical study of the effect of Neonatal Jaundice on bilirubin concentration level in newborns

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الخلاصة:

تم تصميم هذه الدراسة للتحقق في تأثير مرض اليرقان الولادي على مستوى تركيز البيليروبن الكلي والغير مقترن في مصل الأطفال ألحديثي الولادة المصابين باليرقان الولادي (أبو صفار). ولتحقيق هذا الهدف تمت الدراسة على 60 طفل مريض, وقد دلت النتائج على زيادة معنوية ملحوظة ($p< 0.005$)في مستوى تركيزي البيليروبن الكلي والمقترن لدى الاطفال المصابين باليرقان الولادي لدى مقارنتهم مع نتائج فحص البيليروبن لدى الأطفال حديثي الولادة نفسهم وبعد العلاج . لم يظهر تقويم الفرو قات الجنسية تأثير لفروق معنوية في مستوى تركيزي البيليروبن لدى الأطفال المصابين باليرقان الولادي. العمر, العلاج اظهرت النتائج تأثيرات واضحة في مستوى تركيز البيليروبن للأطفال الذين تمت دراستهم.

Abstract:

The present study was conducted to verify the effect of neonatal jaundice in infants newborns on serum bilirubin concentration level, to achieve this aim, 60 infants patients complained of neonatal jaundice were subjected to the study. The results showed significant ($p< 0.005$) increase of total and unconjugated bilirubin concentrations in infants patients when compared with those of the healthy infants (after treatment). The evaluation of the sex differences did not exhibit effect significant variation in serum bilirubin concentration of infants patients. The age and treatment, were found to have effect on serum bilirubin concentration level in infants patients of neonatal jaundice.

Introduction:

Neonatal jaundice is yellowing of the skin and other tissue of new born infants caused by the accumulation of indirect unconjugated bilirubin in the skin due to an overall increase in the total bilirubin in the blood [1]. Neonatal jaundice is of two types: physiological and non-physiological (pathological). Physiological jaundice, which is usually harmless, is often seen in infants around the second day after birth, lasting till day 8 in normal births, or to around 14 in premature births. In physiological jaundice, serum bilirubin normally drops to allow level with out intervention, this type of jaundice is presumably a consequence of metabolic and physiological adjustments after birth [2]. Under normal circumstances, the level of indirect reacting bilirubin in umbilical cord serum is 1-3 mg/dl and rises at a rate of less than 5 mg/dl /24 hr, thus jaundice becomes visible on the 2 nd – 3 rd day [3].

Pathological jaundice appears on the first day of life, with bilirubin usually higher than 15 mg/dL and not resolve on its own [2]. Jaundice and its underlying hyperbilirubineamia are considered pathologic if their time of appearance, duration, or pattern of serially determined serum bilirubin concentrations varies significantly from that of physiologic jaundice or if the course is compatible with physiologic jaundice but other reasons exist to suspect that infant is at special risk from the neurotoxicity of unconjugated bilirubin [4].

Jaundice is observed during the 1 st week of life in approximately 60% of term infants and 80% of preterm infants [5].

Bilirubin : bilirubin is produced when red blood cells break down as part of a normal process [6], Bilirubin is transported in the blood bound to albumin; the binding process is the first step in bilirubin catabolism. It is transported across the hepatocyte by four steps, hepatic uptake of

bilirubin, binding of bilirubin to intracellular binding proteins (ligandin), conjugated of bilirubin with glucuronic acid, and secretion of bilirubin glucuronides into bile. In the gut, bilirubin is converted by bacterial action into urobilinogen. Some of the later compound is absorbed from the gut into the portal blood, hepatic uptake of urobilinogen is incomplete, and a small quantity reaches the systemic circulation and is excreted in the urine. Most of the urobilinogen in the gut is oxidized in the colon to the brown pigment urobilin, which is excreted in the stool [6, 7].

In neonatal jaundice a blood test that will measure the different types of bilirubin, these types are:

Indirect bilirubin: this is the type that is usually increased in infants with neonatal jaundice and in patients who have increased destruction of red blood cells.

Direct bilirubin: this is the type that is usually associated with liver disease.

New born infant's metabolism of bilirubin is transition from the fetal stage, during which the placenta is principal route of elimination of the lipid-soluble conjugated from is excreted from hepatic cells into the biliary system and then into the gastrointestinal [8].

Treatment: The treatment varies based on the cause of jaundice and the bilirubin level, usually in normal neonatal jaundice, the process will be self –limiting and the does not need to be treated [9]. The infant may be able to be discharged home within 48 hours of life with out problems, the infant will need to be followed up by the pediatrician to ensure that the bilirubin level is gowing down [9,10].

Treatment might include: Holding breast-feeding temporarily, phototherapy, exchange transfusions [10].

Materials and Methods:

Sixty infants complained from neonatal jaundice were included in this study. The range of their age was 2-7 days. The infants patients were admitted to General Infants Hospital/Karballa for treatment. Jaundiced new born infants was diagnosed by physicians. The information was included name, sex, age(day), treatment, duration(hr).

The total and unconjugated bilirubin concentrations in sera of neonatal jaundice in infants patients were estimated according to the method of Van Den Bergh [11].

The results were expressed as mean ± SD and analyzed statistically. The differences between the results of infants patients of neonatal jaundice and control were assessed by student's t test. Significant variation was considered when the P value was less than 0.05, the linear regression analysis was used for examinations of the relationships between the serum total bilirubin concentration and age of infant patient.

Results:

The results of serum total and unconjugated bilirubin concentrations measurements revealed significant ($p< 0.005$) elevation in new born patients with neonatal jaundice when compared with those of the healthy infants or new born after treatment, table (1).

To evaluate the influence of sex on serum total and unconjugated bilirubin concentrations levels of jaundiced new born infants, the individuals were classified into male new born patient and female new born patients. There were 30 male infant patients and 30 female new born patients, when male and female patients were evaluated in regards to total and unconjugated bilirubin concentrations significant difference could not be obtained, table (2).

To understand the difference in total bilirubin between new born patients of neonatal jaundice were treated with only breast feeding and new born patients who treated with breast feeding and phototherapy, the infants patients of neonatal jaundice were classified into two group according to the treatment. Group 1 included 20 new born patient who complained from neonatal jaundice were treated with only breast feeding and group 2 consist of 38 new born patient who complained from neonatal jaundice were treated with breast feeding and phototherapy, there results were showed in (table 3), the estimation of serum bilirubin concentrations indicated significant (p

<0.005) elevation of total and unconjugated bilirubin in new born patients were treated of breast feeding and phototherapy, when compared with the infants patients were treated of only breast feeding.

To verify the impact of age (day) of new born patient on serum total bilirubin, the linear regression analysis illustrated significant positive correlation for serum total bilirubin concentration with age (day) of infant patient ($r = 0.23$, $p < 0.05$) fig 1.

Table.1: Serum total and uncojugated bilirubin concentrations in infants patients of neonatal jaundice and with new born patients after treatment.

Parameter	Subject	Number	Mean ± SD	P value
Total bilirubin (mg/dl)	new born Patients	60	15.63 ± 3.72	<0.005
	Patients after treatment	60	8.68 ± 3.18	
Unconjugated bilirubin (mg/dl)	new born Patients	60	9.79 ± 2.12	<0.005
	Patients after treatment	60	5.57 ± 2.17	

Table.2: Sex differences in serum total and uncojugated bilirubin concentrations in new born patients of neonatal jaundice.

Parameter	Subject	Number	Mean ± SD	P value
Total bilirubin (mg/dl)	Male new born Patients	30	15.13 ± 2.09	*N.S
	Female new born Patients	30	14.68 ± 2.38	
Unconjugated bilirubin (mg/dl)	Male new born Patients	30	10.29 ± 2.12	*N.S
	Female new born Patients	30	10.07 ± 2.17	

*: N.S: Non significant

Table.3: Relationship between the different treatment on Serum total and uncojugated bilirubin concentrations levels in new born patients of neonatal jaundice.

Parameter	Subject	Number	Mean ± SD	P value
Total bilirubin (mg/dl)	new born patients with treatment of breast feeding	20	10.93 ± 2.72	<0.005
	new born patients with treatment of breast feeding and photo	38	15.39 ± 2.12	
Unconjugated bilirubin (mg/dl)	new born patients with treatment of breast feeding	20	8.58 ± 1.67	<0.005
	new born patients with treatment of breast feeding and photo	38	11.64 ± 1.97	

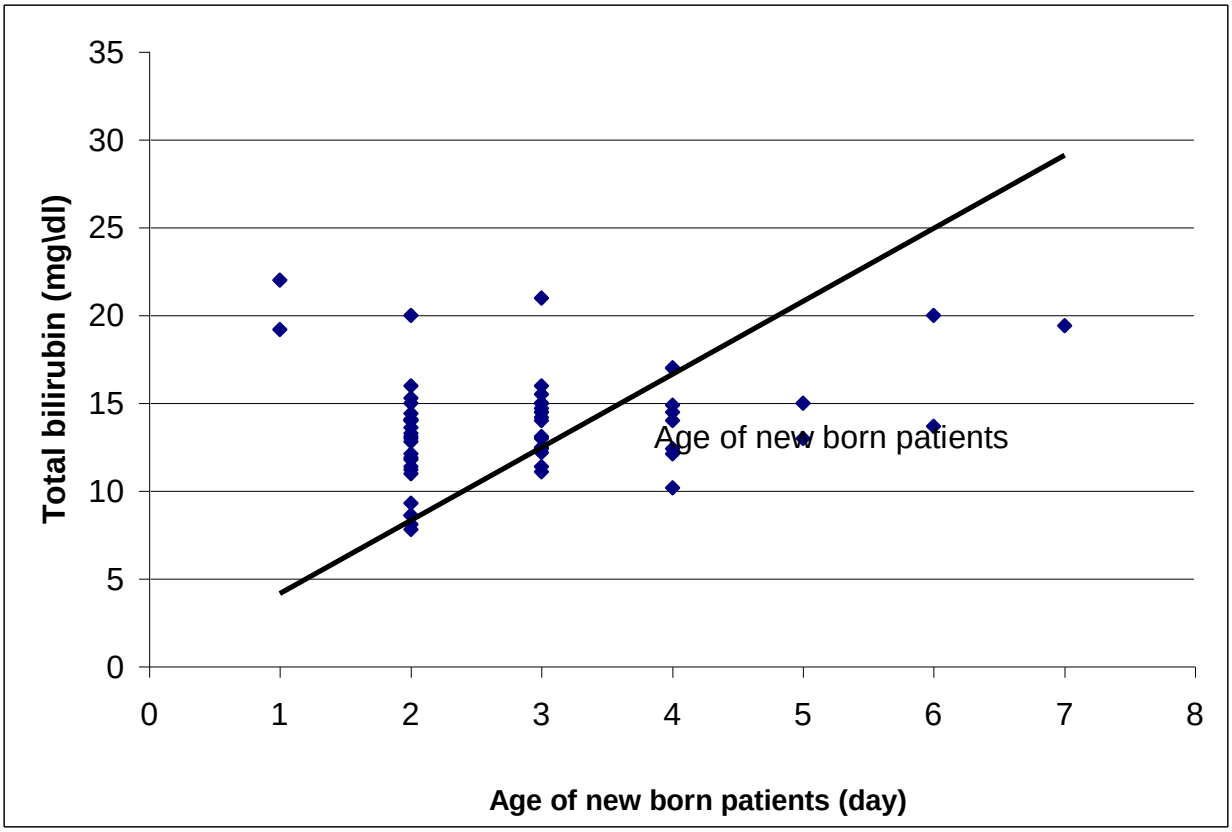

Fig.1: Correlation between serum total bilirubin concentration level and age of new born patient of neonatal jaundice.

Discussion:

In the present study, serum total and unconjugated bilirubin concentrations was found to be elevated significant in the infants patients of neonatal jaundice, these results indicated that total bilirubin elevation is essentially belonged to the neonatal jaundice, that first appears on the 2 nd or 3 rd day is usually " physiologic" but may represent a more severe form [1]. Neonatal jaundice is usually a normal condition resulting from destruction of old red blood cells, after red blood cells are broken down, bilirubin is made, bilirubin is pigment that causes jaundice One of the jobs of the liver is to clear bilirubin from the body [12].

The liver of the baby in the first 1-2 weeks of life is immature and may not be able to handle disposal of all the bilirubin made. The extra bilirubin will then be deposited in the skin, causing the skin to look yellow, other factors such as poor feeding (decreased breast feeding or formula volume or frequency), if the baby is underweight, diabetes in the mother, or drugs may also cause an increased bilirubin level [13].

Hemolysis is suggested by a rapid rise in serum bilirubin (>0.5 mg/dl/hr), anemia, pallor reticulocytosis, hepatosplenomegaly, and a positive family history. Familial nonhemolytic icterus (Crigler- Najjar syndrome) and early-onset breast feeding jaundice are seen initially on the 2nd or 3rd day, jaundice appearing after the 3rd day within the 1st wk should suggest bacterial sepsis or urinary tract infection it may be due to other infection, notably syphilis, toxoplasmosis, enter virus [14].

Jaundice that is noted initially after the 1st wk of life suggests breast milk jaundice, septicemia, congenital, atresia or paucity of the bile ducts, hepatitis, galactosemia, hypothyroidism, possibly the crises of other hemolytic anemia (such as pyruvate kinase and other glycolytic enzyme deficiencies, hemolytic anemia related to drugs [15]. Persistent jaundice during the 1st month of life suggests

inspissated bile syndrome (which may follow hemolytic disease of new born), hyperalimentation-associated cholestasis, hepatitis and cytomegatic inclusion disease [14].

We can expression the result around the age in the table.3 and fig.1 during the studies of under normal circumstances, the level of indirect-reacting bilirubin in umbilical cord serum is 1-3 mg/dl and rises at a rate of less than 5 mg/dL/24 hr; thus, jaundice becomes visible on the 2nd-3rd day, usually peaking between the 2nd and 4th days at 5-6mg/dl and decreasing to below 2 mg/dL between the 5th and 7th days of life [16]. Jaundice associated with these changes designated physiological and is believed to be the result of increased bilirubin production after break down of fetal red blood cells combined with transient limitation in the conjugation of bilirubin by the liver [17].

Overall, 6-7% of full-term infants have indirect bilirubin levels greater than 12.6 mg/dl, and less than 3% have levels greater than 15 mg/dL risk factors for indirect hyperbilirubinemia include maternal diabetes, breast feeding, weight loss, dehydration [16]. A family history of neonatal jaundice, exclusive breast-feeding, bruising, cephalohematoma, and maternal age older than 25 yr identify approximately 60% of cases of extreme hyperbilirubinemia, in infants without these variables, indirect bilirubin levels rarely rise above 12 mg/dl, whereas infants with several risk factors are more likely to have higher bilirubin levels (1 mg/dl) by 10-14 days of life [18]. Prediction of which neonatal infants are at risk for exaggerated physiologic jaundice can be based on hour-specific bilirubin levels in the 1st 24-72 hr of life [19].

The rise in serum bilirubin tend to be same or a little shower than that in term infants, but it is longer duration, which generally results in higher levels, the peak being reached between the 4th and 7th days; the pattern depends on the time required for the development of mature mechanisms for the metabolism excretion of bilirubin. Peak levels of 8-12 mg/dl are not reached until the 5th-7th days, and jaundice is infrequently observed after the 10th day, in general, a search to determine the cause of jaundice should be made if: (1) it appears in the 1st 24-36hr of life, (2) serum bilirubin is rising at a rate faster than 5 mg/dl/hr, (3) serum bilirubin is greater than 12 mg/dl or 10-13 mg/dl preterm infants, (4) jaundice persists after 10-14 days of life [20].

A bout the treatment of neonatal jaundice some infants have a significant increase in the unconjugated bilirubin levels due to breast feeding. Holding breast feeding and supplementing with infant formula for 48 hours may in some cases decrease the bilirubin in infants with "breast milk jaundice"[21]. Phototherapy is a treatment that allows the bilirubin under the skin to be broken down by a special light that illuminates the baby's body. These lights are usually blue-green, they are placed about 4 inches above the baby, the more skin that exposed to the lights the better they work to break down bilirubin, the lights do not prevent the baby from eating and/or from drinking formula or being breast feeding [22]. If the bilirubin level remains high or is increasing, the new born infant may need treatment to decrease the bilirubin level, these treatment include: holding breast-feeding, phototherapy and exchange transfusions, according to the case of new born by the level of bilirubin [23].

In some cases the level of the bilirubin can be very high, the doctors are concerned if the bilirubin levels are more than 20-25mg/dl, when it is above 25mg/dl, there is a risk that bilirubin can cause irritation in some areas of the brain, if this lasts, the baby may develop a change in how his or her behaves and develops [22].

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