

A STUDY OF RELATION BETWEEN CONGENITAL JAUNDICE AND SOME BIOCHEMICAL PARAMETERS IN NEWBORNS IN NINEVEH GOVERNORATE

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Abstract

The research was conducted at Al-Kahlaa Educational Hospital, which specializes in obstetrics and pediatrics and is located in Nineveh Governorate. The researchers carried out the study from August 1, 2022, to March 30, 2023. The study included a follow-up of newborns, comprising males (54) and females (26), aged between one day and ten days who had neonatal jaundice. After classifying the cases based on gender, the researchers compared these groups based on gestational age and weight. The analysis of the research data revealed a statistically significant difference ($p < 0.05$) in the incidence of congenital jaundice between males (67.5%) and females (32.5%). Additionally, there was a notable variation with a statistical significance level below 0.05 in the total bilirubin levels in males. The results indicate a significant increase ($p \leq 0.05$) in the incidence of neonatal jaundice among groups with a gestational age of at least 36 weeks (52.5%). These groups (28–31) and (32–35) weeks of gestation recorded incidence rates of 12.5% and 40%, respectively, compared to the (36–39) weeks group, which recorded an incidence rate of 47.5%. However, there was no significant difference in total bilirubin levels between the (32–35) weeks group and the (28–31) and (36–39) weeks groups, with concentrations of (4.07 ± 18.13) , (3.64 ± 15.12) , and (3.12 ± 15.81) , respectively. Statistics revealed a significant decline in weight among individuals with a certain gestational age, specifically 28–31 weeks, with a value of (0.45 ± 1.92) . When compared to the gestational age groups of 32–35 and 36–39 weeks, the weight decline was greater, with values of (0.48 ± 2.62) and (0.58 ± 2.78) , respectively. The incidence rates of jaundice in these groups were 15% and 48.75%, respectively, compared to 36.25% in the group weighing over 3 kg. Statistical analyses also showed a significant increase in total bilirubin concentration in the group weighing 2–2.9 kg (4.14 ± 17.20) compared to the 1–1.9 kg and over 3 kg groups (3.40 ± 15.40 and 3.28 ± 16.44 , respectively). The results showed a significant increase in the activity level of collagen peptide-III (PIIINP) at a probability level ($p \leq 0.05$) in females (0.01 ± 18.51) compared to males (0.08 ± 10.32).

Keyword: congenital jaundice, bilirubin, procollagen-III peptide.

Introduction

Congenital jaundice is an increase in the level of a substance in the baby's blood called bilirubin. Naturally produced by the human body as a result of the breakdown of red blood cells, then the liver picks up and excretes them through Stool, and this type of jaundice usually occurs between the second and fifth days, and it can be said that neonatal jaundice is It is a natural phenomenon that recurs frequently and continuously and appears in more than 42% of newborns during the first week of pregnancy. Their lives and then gradually and automatically disappear without



any other symptoms such as heat and vomiting & Kaplan (Hammerman, 2004). Almost all newborns have elevated bilirubin values during the week.

The first age, but the case goes undiagnosed because of the slight increase in bilirubin values, and a large percentage is infected of newborns with yellowing in the color of the skin and eyes so that the parents or the doctor can distinguish it by examining the child and it is what is called jaundice or Abu yolk (Dennerly *et al.*, 2001). The occurrence of jaundice is the result of several causes the most important of them is: an increase in the child's hemoglobin values, and when the child's body tries to get rid of the amount of blood cells the extra red blood cells are caused by the breakdown of bilirubin, which is responsible for jaundice, in addition to the immaturity of the liver in the child, so that the liver cannot get rid of the excess amount of bilirubin in the blood as well as increase the production and absorption of bilirubin at this early stage in a child's life, which leads to the appearance of yellow color in the skin and eyes and the first thing that appears the yellow color on the face of the child, then the chest, abdomen, and finally the feet (Alan, 2002) does not constitute the continuation of jaundice a real danger in itself, but the problem may be in its cause, unlike the case in severely elevated bilirubin values.

In the first ten days, when the brain can be affected, jaundice becomes very serious and leads to the accumulation of this substance in the body, the child's brain and injury to a serious condition called kernicterus (Carceller *et al.*, 2009), and may suffer as a result of this). With mental retardation and motor paralysis (Atkinson *et al.*, 2003), and the values of bilirubin vary, at which jaundice becomes dangerous to the child, according to the weight and age of the child, and the presence of complex diseases related to the liver and ducts biliary tract (AAP, 2004). Therefore, this study aimed to know the changes in the rate of jaundice congenital and its relationship to health and physiological causes of the newborn child during pregnancy and after birth. Jaundice divides there are several types, namely: Physiologic jaundice and Breast milk jaundice pathologic jaundice Jaundice haemolysis and jaundice (Maisels, 2005; Golonka, 2010).

Procollagen-III peptide (PIIINP) is produced by the synthesis of collagen III or the degradation of pre-existing collagen III fibres. It is secreted into the circulatory system during the process of collagen degradation (Sugimoto *et al.*, 2016). Skeletal muscle and other soft tissues, such as skin, exhibit high prevalence of PIIINP, while bone contains small quantities of this protein, where as PIIINP levels serve as a reliable diagnostic biomarker for assessing the extent of liver inflammation and fibrosis in individuals with alcoholic liver disease. (Mcpherson *et al.*, 2017). Additionally, the PIIINP levels have been demonstrated to indicate effective synthesis of collagen in the body (Nielsen *et al.*, 2013).

Materials and methods:

Preparing sick conditions: This study was conducted in Al-Khansa Teaching Hospital for Maternity and Children in Nineveh Governorate from the beginning of the month August 2020 until the end of October 2020, and the study included a follow-up of (82) cases of newborns for both sexes (males 45 and females 26) aged (1 to 12 days) with premature neonatal jaundice and those lying in the home preterm division. Knowing that children do not suffer from any disease such as liver disease, severe anemia, and others.



The cases were divided into two groups according to gestational age as follows:-

The first group: Newborns with a gestational age of less than 36 weeks, and their number is 42, and this, in turn, was divided into Two secondary groups included _: newborns with a gestational age ranging from (28-31 weeks), their number was 10 newborns Births with a gestational age ranging between (32-35) their number 32.

The second group: includes newborns with a gestational age of (36-39) weeks and their number 38.

Were also divided according to Weight to:-

The first group: Newborns with a weight of less than <3 kg and included two categories (1-1.9) and (2-2.9) their number 51

The second group: Newborns with a weight of more than >3 kg their number 29.

Collecting blood samples: Capillary blood samples were drawn using special medical syringes. Each sample was divided into two sets of tubes: -

The first group: placing blood in tubes containing an anticoagulant to perform the tests for measuring blood masses.

The second group: The samples were placed in tubes free of anticoagulant and left at laboratory temperature for a period of time (15-20) minutes, then centrifuged at 3000 revolutions per minute for the purpose of separating the blood from its components Separation of serum for tests for measuring total bilirubin.

Methods and Materials: included:

1- Calculating the gestational age:

The gestational age was calculated by asking the mother about the date of the last menstrual period and the first day of childbirth, then Extract the gestational age according to the following equation:

Gestational age = 12 days of the menstrual cycle + first day of Situation. (Sadler, 1990)

2- Laboratory tests:

A - Measuring the percentage of total bilirubin, a blood sample was drawn on the first day of the onset of jaundice. By means of a capillary tube with open ends, then one end was closed using a rubber stopper. Then it was separated using centrifuge at 5000 rpm for five minutes for obtaining blood serum Bilirubin meter at a factor value of 10.1 the device whistles using distilled water, the device is read on Concentration which is the final focus of the model in units (Ahlfors, 2000) mg/dl to determining the concentration of procollagen-III peptide in the blood serum.

Using the Kit from the Chinese company (Sunlongbiotech) and relying on Enzyme linked immune sorbent assay, ELISA, technique(Ram Sarup Singh, 2019).

B- Hematopoietic measurement Packet cell volume, Capillary tubes and a Heamatocriteceer micro centrifuge were used fuge to measure the percentage of hematopoietic mass (Brown, 1976). The examination process was carried out by making the blood flow into the tube.



capillary by capillary action, leaving approximately 15 mm of the tube unfilled and then closing one of the tubes its ends were covered with artificial clay, and then placed in the microcentral device, and the device was run for 5 minutes at a speed of 11000. Cycle / minute, then extract the tubes from the device and read the percentage of blood volume P.C.V % using a ruler. Hematocrit reader pcv.

Statistical Analysis: The statistical program Spss V.10 version (2010) was used to calculate the results by extracting the mean Arithmetic and standard deviation (Mean $\pm$ SD), percentage, as well as using T-test to analyze differences found between the major and minor aggregates and their comparison with the tabular under the probability level (0.05).

Results and discussion

1- Effect of sex on total bilirubin and procollagen III peptide (P3NP) concentration, hematocrit, weight and gestational age in patients with jaundice. The data of the statistical analysis in Table (1) indicated a significant substantial rise (p less than 0.05).in the concentration of Bilirubin in males when compared with females reached (3.19 ± 18.75) and (4.63 ± 15.42), respectively. As The results showed in the same table that there were no significant differences (p less than 0.05) in blood mass, weight and age.

Pregnancy in both sexes. Figure (1) shows an increase in the incidence of congenital jaundice in males 67.5% compared to with females. (32.5 %) the blood of a fetus while in its mother's womb contains numbers of red blood cells that reach about 6.5 million red blood cells/mm³, which contain a type of hemoglobin called fetal hemoglobin f type where up to 90% is the normal hemoglobin of the fetus, after birth this type is replaced by hemoglobinIn the blood of adults, in addition to this, this number of corpuscles decreases significantly, up to about 4.5 million red blood cells / mm³, through a rise in the rate of red blood cell breakdown and the outcome of that process an increase in the concentration of bilirubin, causing congenital jaundice; The gender of the newborn may have an effect on increasing the incidence of infection Jaundice, as males suffer from jaundice more than females, and this is due to the number of red blood cells in males more Of which in females, the current results are consistent with what was indicated by (Behrman *et al.*, 2000) and (Clemons, 2000).

The data shown in Table 1 demonstrates a statistically significant rise in the activity level of procollagen III peptide (P3NP) in the blood serum of patient's male (0.08 ± 10.32) compared to the activity level of P3NP in the females (0.01 ± 18.51) at a probability of ($P \leq 0.05$). This is because elevated levels of this substance in the blood se hepatitis and serve as a diagnostic biomarker for assessing the extent of liver inflammation and cirrhosis (McPherson, S. et al., 2017).

2- Effect of gestational age on total bilirubin and procollagen III peptide concentration, hematocrit and weight in patients with congenital jaundice.

The data presented in Figure 2 indicate a rise in the prevalence of congenital jaundice across different gestational age groups. The highest incidence was observed in the gestational age group of less than 36 weeks, which encompassed both the (28–31) and (32–35) week subgroups, with rates of 12.5% and 40%, respectively. In comparison, the incidence of congenital jaundice

in the gestational age group of 36–39 weeks was 47.5%. The results in the table (2) showed that there is a statistically significant increase ($p < 0.05$) in the level of total bilirubin at gestational age (32–35) compared to gestational age (28–31) and (36–39), with measurements of (4.07 ± 18.13), (3.64 ± 15.12), (3.12 ± 15.81), (0.09 ± 8.23), (0.07 ± 5.45) and (0.08 ± 4.68) respectively. Figure (3) demonstrates that Table (2) reveals no statistically significant distinction ($p \leq 0.05$) in blood clotting between the two groups. However, the table does indicate a noteworthy reduction in weight among individuals within the same age categories. The pregnancy had a gestational age between 28 and 31 weeks, with a mean value of 0.45 ± 1.92 . In comparison, pregnancies with gestational ages between 32–35 and 36–39 weeks had mean values of (0.48 ± 2.62 and 0.58 ± 2.78), respectively. respectively, but there was no significant difference between the last two groups, Fig (4), result from the accumulation of unconjugated bilirubin, which is elevated in it. Excessive levels of bilirubin in the blood, which may lead to brain paralysis, hearing loss and some problems it is necessary to distinguish between pathological jaundice and unsatisfactory jaundice known as physiological jaundice Which goes away on its own, but the problem lies when bilirubin concentrations rise more than 14 mg/dL (Ahdab, 2007), especially in children who are born prematurely, as stated in the results of the current study, which showed the presence of an increase in the total bilirubin concentration ranged between (15.12– 18.13) mg/dL, and the reason may be attributed to These children are born with suffocation from lack of oxygen due to lack or lack of surfactant Due to immaturity of the pulmonary alveoli (small air sacs), and lack of oxygen cause an increase in the lysis of red blood cells (Watchko, 2000) Also, the incomplete maturity of the digestive system, especially The liver, where its ability to process excessive bilirubin is limited, as well as an increase in the size and number of blood cells red erythrocytes and increase their breakdown and production of bilirubin and consequently a decrease in the liver's ability to absorb free bilirubin from the plasma is converted to bound bilirubin, due to a lack of activity of the hepatic enzyme glucuronyl transferase in addition, the turnover of bilirubin in the small intestine is very slow due to the lack of activity of the natural flora this result is consistent with what was stated by (Cashore, 2000). Thor et al, 2011 indicated that there is A relationship between the incidence of congenital jaundice and the increase in the rate of premature births, it was consistent with the results of this study It showed a significant increase in the incidence of congenital jaundice in children born at the age of Pregnancy less than 35 weeks, the reason for this increase is attributed to an increase in the rate of premature births, which amounted to 52.2% as In Figure (2), the causes are due to weak structure, general exhaustion, and nutritional deficiencies due to social status and the economic and lack of health conditions and the incidence of internal diseases such as high blood pressure and albuminuria Diseases of the glands, kidneys, etc..., taking drugs, repeated abortions, and the occurrence of pregnancy immediately after the abortion the results in the table indicate that there is a significant increase in the level of activity procollagen III peptide with increasing age for the patient group (0.08 ± 13.52), (11 ± 78), (0.03 ± 9.61) compared to the control group (0.01 ± 2.87), (0.09 ± 3.22), (0.06 ± 3.55) for all age groups. The reason may be attributed to acute inflammation that leads to abnormal formation of collagen, the accompanying soft tissue fiber, which leads to higher levels P3NP with age ((Shin et al., 2021).

3-Effect of weight on total bilirubin concentration and hematocrit in patients with congenital jaundice.

The results in Figure (5) showed an increase in the incidence of congenital jaundice among weight groups, and it was higher in the group less than (<3 kg), which included both Individuals (1-1.9) and (2-2.9), it amounted to (15% and 48.75%).when compared with the group ((>3), where it amounted to (36.25%), as the results showed in the table (3) There was a significant increase ($p < 0.05$) in the concentration of total bilirubin, and it was the highest in the group (2-2.9), as it reached (4.14 ± 17.20) in comparison to group members (1 -1.9) and, (> 3), where it reached (3.40 ± 15.40) and (3.28 ± 16.44), respectively, and the table did not show any significant differences ($p \leq 0.05$) in the blood mass of the same groups. Studies have indicated that newborns with low birth weight are more susceptible to infection congenital jaundice, where the incidence of (Maisels *et al*, 2003) was 63.75%. These results came Similar to the results of this study, which showed a significant increase in the concentration of total bilirubin and the incidence of infection neonatal jaundice in children with a weight less than 2.9 kg as shown in the figure, and this increase is attributed to an increase in the proportion of premature births in which the newborn suffers from immaturity and a decrease in the concentration of ligand in protein In the blood, it is a binding protein that transports bilirubin to liver cells (Ahlfors and Wennberg, 2004) and a decrease in In the activity of the hepatic enzyme, which causes an increase in the concentration of bilirubin in the blood, and the reason may be due to factors related to the mother such as smoking, diabetes, use of certain medications, or delayed removal or clamping of the umbilical cord to the newborn, which increases infection rates) (Maisels and McDonagh, 2008).

Table (1): Effect of sex on total bilirubin procollagen-III peptide concentration, hematocrit, weight and gestational age in patients with jaundice neonatal;

Sex	Number	Mean $\pm$ SD				
		Total bilirubin (mg/dl)	procollagen-III peptide (ng/ml)	blood stack (%)	Weight (kg)	gestational age (week)
Male	54	3.19 ± 18.75	0.08 ± 10.32	0.08 ± 55	0.63 ± 2.72	35.55 ± 2.18
Female	26	15.42 ± 4.63	0.01 ± 18.51	0.06 ± 56	2.58 ± 0.51	35.15 ± 3.29

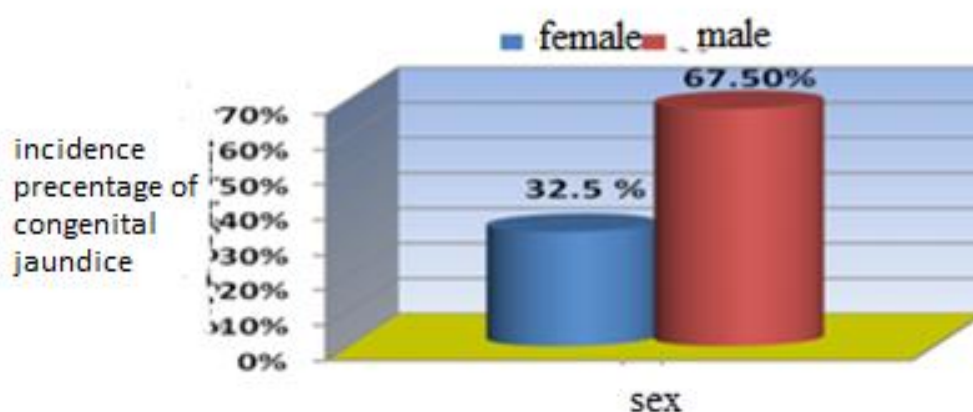
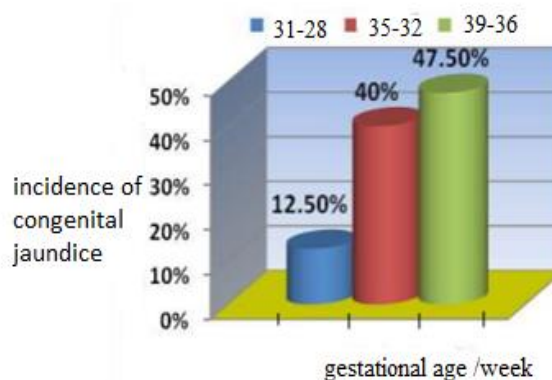
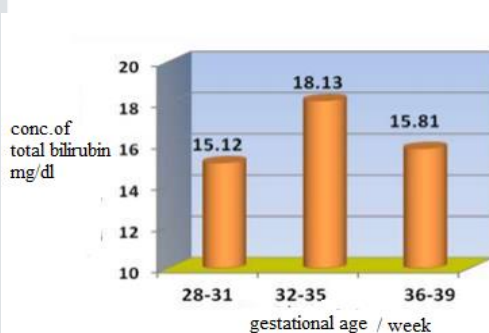


Figure (1) the effect of sex on the incidence of congenital jaundice.

Table (2): Effect of gestational age on total bilirubin and procollagen-III peptide concentration, hematocrit and weight in patients with congenital jaundice

Standards gestational age	Number	SD $\pm$ Mean			
		Total bilirubin (mg/dl)	Procollagen-III peptide (ng/ml)	Blood stack (%)	Weight (kg)
28-31 week	10	3.64 $\pm$ 15.12	0.08 $\pm$ 4.68	6.45 $\pm$ 57.00	0.45 $\pm$ 1.92
32-35 week	32	4.07 $\pm$ 18.13	0.07 $\pm$ 5.45	6.38 $\pm$ 58.41	0.48 $\pm$ 2.62
36-39 week	38	3.12 $\pm$ 15.81	0.09 $\pm$ 8.23	8.66 $\pm$ 52.84	0.58 $\pm$ 2.78



Significant difference between the groups below the level of significance ($P < 0.05$)

Table (3): Effect of weight on total bilirubin and procollagen-III peptide concentration and hematocrit in people with congenital jaundice

Standards Weight kg	Number	SD $\pm$ Mean		
		Total bilirubin (mg/dl)	procollagen-III peptide (ng/ml)	blood stack (%)
1-1.9	12	3.40 $\pm$ 15.40	0.03 $\pm$ 9.61	7.46 $\pm$ 53.17
2-2.9	39	4.14 $\pm$ 17.20	0.04 $\pm$ 11.78	8.37 $\pm$ 56.15
<3	29	3.28 $\pm$ 16.44	0.08 $\pm$ 13.52	7.60 $\pm$ 55.83

- Significant difference between the groups below the level of significance ($P \leq 0.05$).

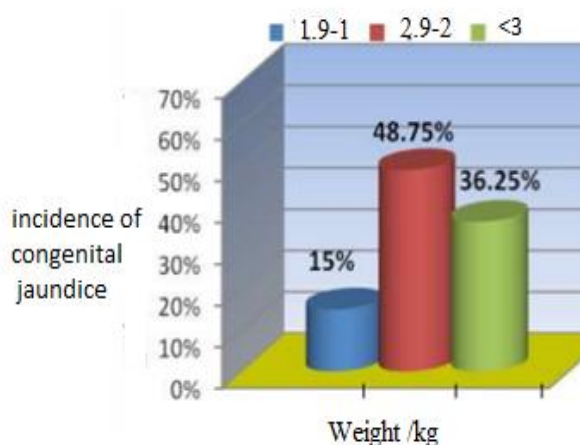


Figure (5): Effect of weight on the incidence of congenital jaundice

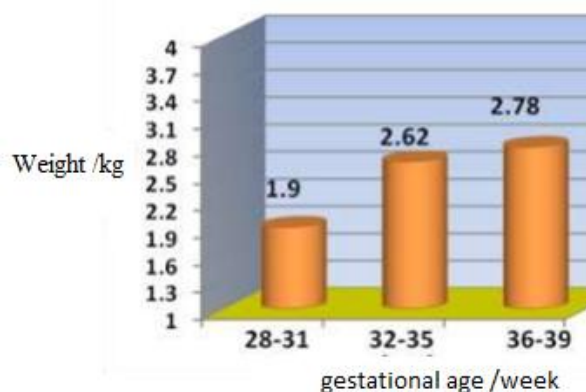


Figure (4): Effect of gestational age on weight in patients with jaundice neonatal

Conclusion:

The study results indicate a clear relationship between gender and gestational age with the incidence of congenital jaundice in newborns. The data showed a higher rate of congenital jaundice among males compared to females, reflecting the impact of gender on this condition. It was also found that there is a significant increase in jaundice incidence among infants with a gestational age of at least 36 weeks, highlighting the importance of gestational age as a contributing factor. Furthermore, the study showed that weight also affects bilirubin levels, as there were significant differences in bilirubin concentration across various weight categories, indicating that lower-weight infants are more susceptible to jaundice. An increase in the activity level of collagen peptide-III (PIIINP) was observed in females compared to males, which may indicate differences in biological responses between genders. Overall, the findings emphasize the importance of considering gender, gestational age, and weight when assessing the risks associated with congenital jaundice in newborns.

References:

1. (AAP) American Academy of Pediatrics. (2004) . Subcommittee on Hyperbilirubinemia. "Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation". Pediatrics; 114 (1): 297–316.
2. Ahdab-Barmada M. (2000) . Neuropathology of kernicterus: definitions and debate. In: Maisels MJ, Watchko JF, eds. Neonatal jaundice. Amsterdam: HarwoodAcademicPublishers,75–88.
3. Ahlfors CE and Wennberg RP. (2004). Bilirubin-albumin binding and neonatal jaundice. Seminars in Perinatology; 28:(5)334-9.
4. Ahlfors CE. (2000). Measurement of plasma unbound unconjugated bilirubin. Analytical Biochemistry; 279:(2)130-5.
5. Alan Creene . (2002) . in Medline Plus Medical Encyclopedia : Jaundice Yellow skin , ADAM , Inc ; P . P : 1 – 4.
6. Atkinson LR, Escobar GJ, Takayama JI (2003).Phototherapy use in jaundiced newborns in a large managed care organization: do clinician adhere to the guideline? Pediatrics.111(5 Pt 1):e555-61.
7. Behrman, R. E., Kliegman R.M., Jenson H.B. (2000). Nelson Textbook of pediatrics . 16 th ed , Philadelphia , Saunders; P . P : 511 – 28 .
8. Carceller-Blanchard A, Cousineau J, and Delvin EE. (2009) . Point of care testing: transcutaneous bilirubinometry in neonates. Clinical Biochemistry; 42:(3)143-9. Cashore WJ. (2000). Bilirubin and jaundice in the micropremie. Clin Perinatol . 27:171-9.
9. Clemons R . M . (2000) . Issues innew born care . prim car. 27 : 251 – 67. Dennery PA, Seidman DS, Stevenson DK. (2001). Neonatal hyperbilirubinemia. N Engl J Med; 344 : 581 – 90.
10. Golonka, Debby. (2010). Digestive Disorders Health Center: Bilirubin. WebMD .pp. 3.
11. Kaplan M, Hammerman C.)0225(. Understanding and preventing severe neonatal hyperbilirubinemia:is bilirubin neurotoxicity really a concern in the developed world? Clin Perinatol.-01:444.

12. Kaplan M, Muraca M, Hammerman C. (2020) .Imbalance between production and conjugation of bilirubin: A fundamental concept in the mechanism of neonatal jaundice. *Pediatrics*. 110(4):e47.
13. Maisels MJ, Watchko JF. (2003) .Treatment of jaundice in low birth weight infants. *Arch Dis Child Fetal Neonatal* Ed.88:F459–63.
14. Maisels MJ. (2005). Jaundice. In Avery's Neonatology Pathophysiology & Management of Wilkins, Philadelphia. pp775.
15. Maisels, M.J. and McDonagh, A.F. (2008). Phototherapy for Neonatal Jaundice. *New England Journal of Medicine*, volume 358, number 9, February 28, p: 920-928 Sadler T.W. (1990) . *Langman's medical embryology*. 1ed ; p 142.
16. McPherson, S. *et al.* Age as a Confounding Factor for the Accurate Non-Invasive Diagnosis of Advanced NAFLD Fibrosis. *Am. J. Gastroenterol.* 112, 740–751 (2017).
17. Nielsen, M.J.; Nedergaard, A.F.; Sun, S.; Veidal, S.S.; Larsen, L.; Zheng, Q.; Suetta, C.; Henriksen, K.; Christiansen, C.; Karsdal, M.A. The neo-epitope specific PRO-C3 ELISA measures true formation of type III collagen associated with liver and muscle parameters. *Am. J. Transl. Res.* 2013, 5, 303–315.
18. Ram Sarup Singh, ... Ashish Kumar Singh, in *Advances in Enzyme Technology*, 2019.
19. Sugimoto, M., Saiki, H., Tamai, A. Ventricular fibrogenesis activity assessed by serum levels of procollagen type III N-terminal amino peptide during the staged Fontan procedure. *J Thorac Cardiovasc Surg.* (2016);151:1518-1526.
20. Shin, H.E., Kim, M., & Won, C.W. (2021). Association between plasma procollagen type III N-terminal peptide (P3NP) levels and physical performance in elderly men: The Korean Frailty and Aging Cohort Study (KFACS). *Experimental Gerontology*, 154, 111523.
21. Watchko JF. (2000). The clinical sequelae of hyperbilirubinemia. In: Maisels MJ, Watchko JF, eds. *Neonatal jaundice*. Amsterdam: Harwood Academic Publishers. 115–35.

