Evaluation of cholecystokinin levels and some biochemical variables in children with neonatal jaundice

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Abstract

Jaundice is a natural phenomenon that recurs constantly and then gradually disappears. A large percentage of newborns suffer from yellowing of the skin and eyes, which is called neonatal jaundice. This research study was conducted in the laboratory department of Tikrit Teaching Hospital in Salah al-Din Governorate, as well as in some private laboratories affiliated with Tikrit city, from March 15, 2025, to September 15, 2025. The study groups included (60) samples of children aged between (1-7) days and were distributed into two groups. The first group included 30 blood samples from healthy children, and 30 blood samples from children with jaundice after confirming that they had a bilirubin level of (15.5-30) mg/dl after conducting tests for the disease and referring them to the doctor. Then, blood was taken from both groups, and separated by centrifugation, and then the biochemical parameters were estimated, which included (bilirubin, C-reactive protein-CRP, glucose, Cholecystokinin-CCK, Potassium-K, Calcium-Ca, Glutathione-GSH, Malondialdehyde-MDA). The results of the present study showed that significant changes occurred in each of the studied variables in the blood serum of children with jaundice compared to the healthy subjects, at a $P \leq 0.05$.

Keywords: **cholecystokinin , biochemical , neonatal jaundice.**

Introduction

Neonatal jaundice is one of the common diseases in newborns. It is called neonatal hyperbilirubinemia, as bilirubin, which is the yellow pigment, accumulates in the extracellular fluids, in the conjunctival membranes of the eye, and in other membranes. It usually appears during the first days after birth, as the skin color turns yellow and appears on the face and sometimes extends to the lower chest (1). It is one of the diseases that causes concern for doctors and parents, as it causes critical complications for newborns and

increases the length of their stay in the hospital and the possibility of them being readmitted to it again (2). Jaundice has many negative effects that require both children and their families to admit newborns to the hospital or to readmit them again during the first month, especially in the first week of the newborn's life. Since maternal and child-related variables during labor and environmental factors affect the course and severity of neonatal jaundice, which are related to the perinatal period and are linked to the occurrence of neonatal hyperbilirubinemia, these factors can be managed and modified (3,4). The bile in the liver collects in the gallbladder in a greater proportion than necessary, and it often affects newborns and premature infants born before the 36th week of pregnancy. It results from the breakdown of red blood cells, especially hemoglobin in the blood, which turns into bile, called bilirubin (5).

The most important causes of jaundice are high levels of bilirubin resulting from the breakdown of a large number of red blood cells, blockage of the bile ducts, deficiency in the representation of liver cells responsible for secreting bilirubin into bile, low levels of the enzyme G6PD (glucose-6-phosphate dehydrogenase), and infection with the hepatitis C virus (6).In addition to factors related to the child, such as congenital trauma (birth injury), low birth weight, birth asphyxia, G6PD deficiency, males being more affected than females, hyperemia, and sepsis (blood poisoning).Congenital hepatitis (neonatal hepatitis), congenital diseases, rubella and hypothyroidism, hereditary syndromes, cholestasis syndrome, in addition to blood group or Rh factor (Rh) incompatibility between mother and child (7,8). Children with jaundice are accompanied by a group of symptoms such as discoloration of their bodies and visible mucous membranes, a change in the skin color to yellow, constant drowsiness, weakness and lethargy, the child's urine is dark, in addition to the yellowing of the whites of their eyes, and the child's stool is light in color. In addition to swelling of their legs and distension of their abdomen due to fluid accumulation, high fever, and weight loss, newborns with severe hyperbilirubinemia are at risk of neurological dysfunction when bilirubin crosses the brain barrier to reach the cerebellum and hypothalamic nuclear bodies. It causes neurotoxicity through acute programmed cell death, which manifests as acute encephalopathy leading to cerebral palsy, seizures, and sensorineural hearing loss (9,10).

Sufficient maternal knowledge and early awareness to avoid jaundice and seek health care are among the most important basic components of effective and correct management in controlling neonatal jaundice (11). The treatment of jaundice depends on the concentration of

bilirubin in the blood for the correct diagnosis of hyperbilirubinemia in newborns (12). Several methods have been used to treat cases of neonatal jaundice among children, including non-medical and traditional methods that have been circulated and used by many mothers and grandmothers. It was found that many families use these methods, which consist of giving the sick newborn water mixed with sugar or cumin, and attaching a piece of gold jewelry or a garlic plant around the child's neck. They also use some precious stones and beads (13).

C-reactive protein (CRP) is a diagnostic marker for neonatal jaundice. It is an acute-phase protein belonging to the Pentraxin family, which is produced at low concentrations by liver cells and plays a key role in innate and adaptive immunity. This index can be used in conjunction with WBC as an effective indicator in the diagnosis of pathological jaundice and early clinical intervention caused by bacterial infection in newborns, which can reduce the risk of clinical complications in newborns and help in assessing the disease, guiding treatment, and predicting the desired effectiveness of treatment (14,15).

Cholecystokinin is a peptide hormone responsible for the digestion of fats and proteins. This hormone is produced by the first section of the small intestine in response to the presence of partially digested food in the duodenum, causing the gallbladder to contract and thus secrete bile into the intestine. It is also a neurotransmitter. The main function of the smooth muscle in the digestive tract is to mix and push the contents and nutrients into the intestine in a coordinated manner (16). Cholecystokinin acts directly on smooth muscles, where its effect is always contractile, while the nerve-mediated effect is either contractile or relaxing, depending on the nature of the nerve impulse responsible for the action of cholecystokinin (17).

Electrolytes are considered one of the essential elements that are important for prolonging life and maintaining good human health, as human blood contains 0.9% of various salts, and these electrolytes enter into the composition of many vital compounds in the body such as enzymes, hormones and vitamins, or combine with another chemical composition such as iron in the heme compound or calcium phosphate in the bones (18).In addition, the diffusion of electrolytes between the fluid inside and outside the cells depends on their ionization into positive and negative ions, which play an important role in maintaining and controlling various physiological activities, such as maintaining water balance and its distribution within the body. It contributes to controlling the level of osmotic pressure and acid balance in the body, and the rise and fall of its level plays a fundamental role in newborn patients

(19).Through the increase in some special indicators in neonatal jaundice and the hyperbilirubinemia in their bodies, the current research aimed to investigate the effect of high bilirubin on some biochemical and mineral variables in children with neonatal jaundice in the city of Tikrit.

Material and Methods

Sample Collection

This research study was conducted in the laboratory department of Tikrit Teaching Hospital in Salah al-Din Governorate and some private laboratories affiliated with Tikrit city for a period from 3/15/2025 to 9/15/2025. The study groups included (60) samples of children aged between (1-7) days and were distributed into two groups. The first group included 30 blood samples from healthy children, and 30 blood samples from children with jaundice after confirming that they had a bilirubin level of (15.5-30) mg/dl after conducting tests for the disease and referring them to the doctor. Then, blood was taken from both groups and separated by a centrifuge, then the biochemical markers were assessed, which included (bilirubin, CRP, F.B.G, CCK, K, calcium, GSH, MDA).

Estimation of total serum bilirubin

The amount of Total Serum Bilirubin in blood serum was measured by the Sulfanilic Acid Method using a ready-made kit supplied by the French company BIOLABO.

Estimation of Serum C-reactive protein

C-reactive protein concentration was measured by the AFIAS CRP device. 0.5 ml of blood serum from each child was placed in the device, which operated according to the manufacturer's instructions. After providing the patient's personal information, such as name, gender, and age, 200 µL is automatically drawn from the tube, and the required readings are completed accurately. The device gives the result within 5 minutes and is automatically printed and withdrawn on paper.

Estimation of serum glucose level

The serum glucose level of jaundiced children was estimated using the colorimetric enzyme method and according to the Dingeon method (20).

Estimation of serum levels of (CCK, GSH, MDA)

The Concentrations of (CCK, GSH, MDA) were determined based on the Fin Test-China kit.

Statistical analysis

The results were analyzed using SPSS and using the F-test to analyze the results between sick and healthy children at a probability level of ($P \leq 0.05$).

Result and Desiccation

Table (1) shows the mean ± S.D. of the diagnostic indicators and biochemical parameter in the two study groups.

Groups Parameter	Mean ± SD Control No=30	 NNJ No=30	P-Value
TSB (mg/dl)	6.12 ± 1.93	15.81 ± 4.71	P ≤ 0.001
CRP (mg/L)	1.81± 1.21	4.01± 3.19	P ≤ 0.001
Glucose (mg/dl)	101.01± 29.19	106.01± 30.13	P ≤ 0.001
CCK (Pg/ml)	98.01 ± 4.87	215.14 ± 17.61	P ≤ 0.001
K^{+} (µmol/L)	4.43 ± 0.67	3.03 ± 0.87	P ≤ 0.001
Ca^{++} (µmol/L)	8.93 ± 0.97	9.51 ± 1.17	P ≤ 0.001
GSH (ng/ml)	10.11±7.31	3.01±0.49	P ≤ 0.001
MDA (nmol/ml)	10.51 ± 0.51	18.76 ±0.62	P ≤ 0.001

The results of the present study showed significant changes in all of the studied variables in the blood serum of children with jaundice compared to the healthy group at a $P \leq 0.05$, as shown in the following figures:

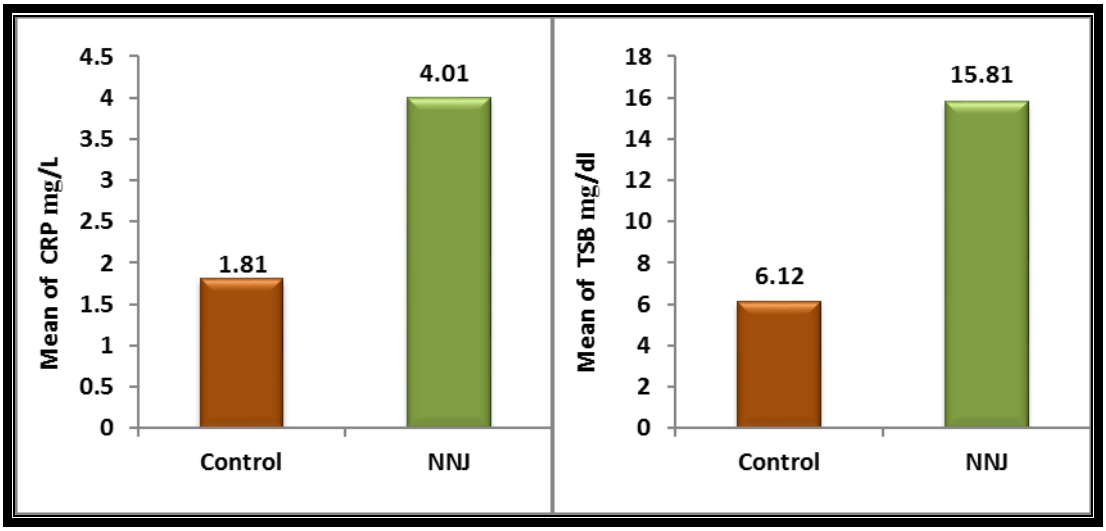

Fig (1,2): CRP and TSB in the blood serum of the samples under study

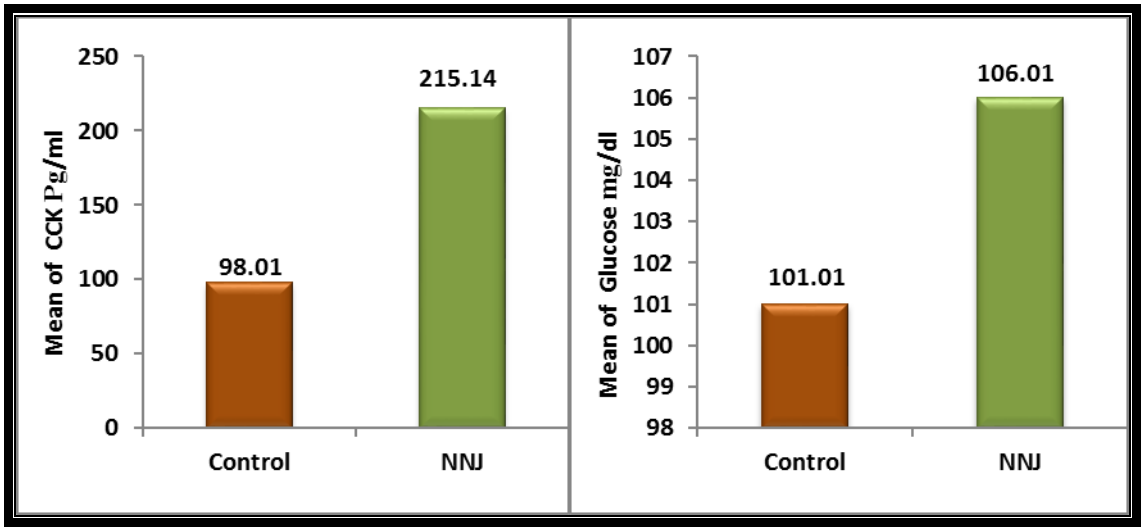

Fig (3,4): CKKP and glucose in the blood serum of the samples under study

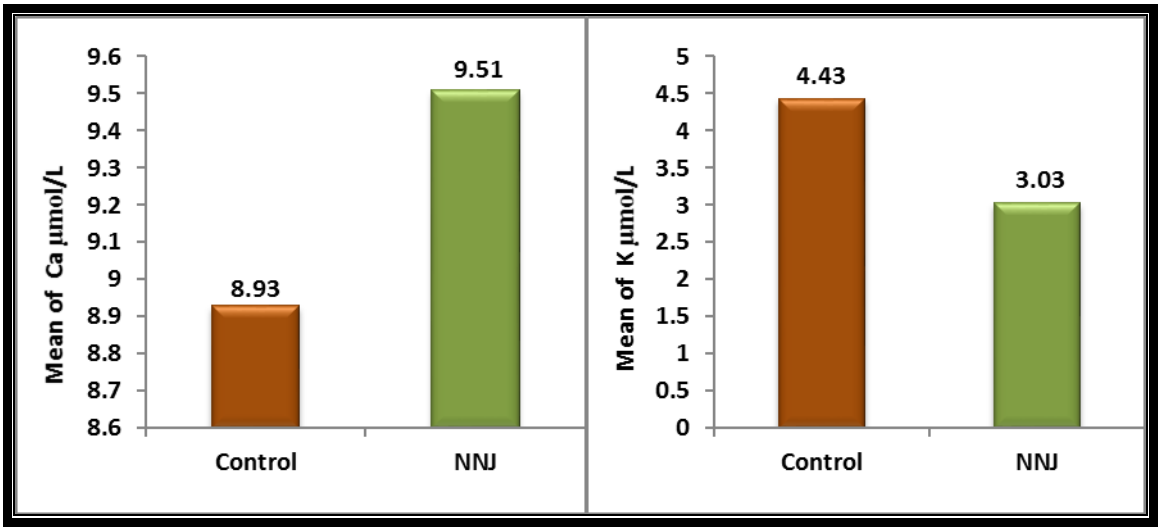

Fig (5,6): Ca and K in the blood serum of the samples under study

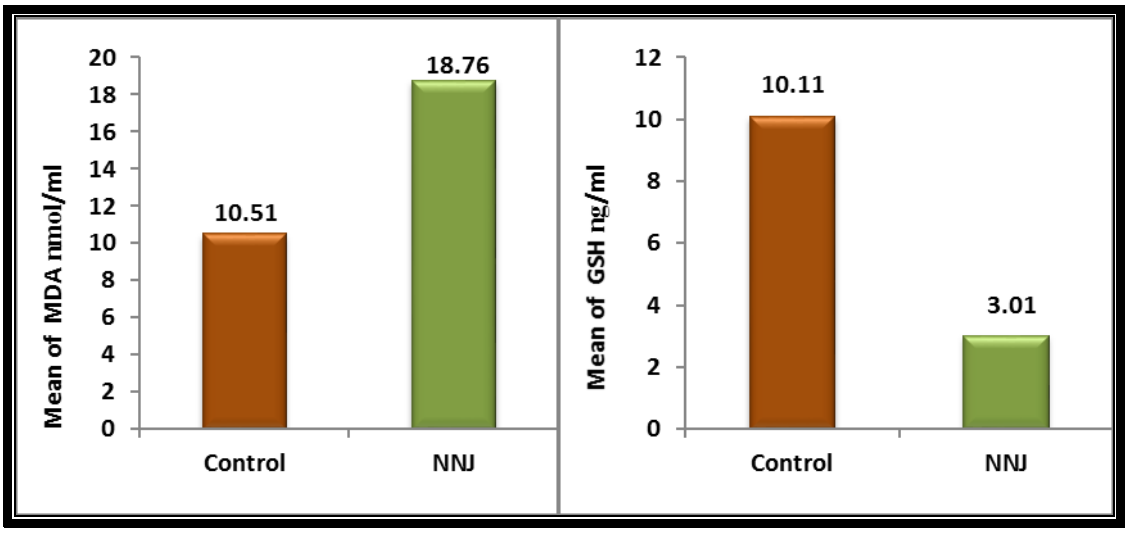

Fig (7,8): MDA and GSH in the blood serum of the samples under study

Dissection

Jaundice is caused by an increase in the level of bilirubin in the body due to the accelerated breakdown of red blood cells, the decreased ability of the liver to deal with bilirubin, and the increase in enterohepatic circulation (21). The result of high bilirubin levels in children with jaundice was agree with Suneja et al. (22) and Olatubi (23). The reason for the increase is that the livers of these children do not produce enough of the enzyme UGT and the liver is unable to quickly remove bilirubin from the blood due to the appearance of high levels of IDB in the blood. Exposure to light converts bilirubin into water-soluble isomers that can be easily eliminated through the digestive system or excreted in urine. In addition, liver failure leads to its inability to conjugate unbound bilirubin with glucuronic acid and store it as bound bilirubin in the gallbladder, or sometimes high bilirubin occurs due to damage and explosion in liver tissue (24,25).

The result of the current study showed a significantly elevated in CRP in G1 compared control group. C-reactive protein is considered one of the strongest proteins used as a diagnostic indicator for jaundice, because this protein is produced at a low concentration by liver cells and plays a fundamental role in immunity. Therefore, it is affected by fungal and adaptive diseases. Therefore, it is affected by neonatal jaundice and its concentration increases in the blood, as in other liver enzymes (26, 27).

Also, the result showed a significant rise in glucose for patients compared to healthy children. The result of high glucose levels in children with jaundice was consistent with the result of Volosivska et al (28). The reason for the increase is due to metabolic disturbances that occur in the glucose concentration in newborns with jaundice, which may be due to breastfeeding and the infant's inability to maintain balance, or the increase occurs as a result of the ambiguous interaction process that occurs between weak liver function and hormonal stress, in addition to therapeutic factors. This increase may represent a compensatory metabolic response rather than an independent disease symptom, but it may require careful and continuous monitoring to avoid metabolic complications that may occur in the future (22).

On the other hand the present study showed increase in CCK hormone in patinates children compered healthy children, The result of the high level of CCK in children with jaundice was agree with Al-Hatemi (29).It is believed that the reason for the rise in the level of the CCK hormone is due to the fatty acids that are present in high quantities in breast milk, which ultimately leads to stimulating the cells - located in the lining of the duodenum - to increase the secretion of the CCK hormone into the bloodstream. Then it moves and binds to the hormone receptors in the gallbladder, which works to contract the gallbladder and open the Oddi valve. This leads to the excretion of bilirubin accumulated in the gallbladder into the intestines and its disposal through the feces. Therefore, most doctors advise increasing the number of times of breastfeeding for children with jaundice to get rid of the largest amount of bilirubin concentration through the feces (30).

As for the result of the insignificant difference in the level of minerals, which included potassium and calcium), the result of the significant decrease in potassium was in agreement with the results of both Gozetici et al. (31) and Mohamed (32). As for the result of the insignificant increase in calcium, it was in agreement with the results of both Asl et al. (33) and Rozario (34). All of the reasons for these fluctuations in electrolyte levels are due to hyperbilirubinemia in newborns. However, electrolyte levels such as K, Na, and Ca must be monitored because disturbances in their levels and imbalance in newborns are a cause for concern and require continuous monitoring (22, 35). Phototherapy used for jaundice can reduce the concentration of electrolytes in the blood serum, such as Ca, K, and Na (36). This is because blood electrolyte levels can decrease significantly during phototherapy and are affected by the duration of exposure to light, as electrolyte imbalance leads to severe and harmful effects that are short- to long-term (37).

The result of the low GSH concentration in children with jaundice agrees with Turgut (38); the reason for the decrease is due to the accumulation of reactive oxygen species, which leads to a decrease in the level of GSH in newborn children with jaundice. This may also be because glutathione is found in high concentrations within red blood cells, and their breakdown and decomposition release glutathione into the bloodstream. This leads to an increase in its concentration in the serum of children with congenital jaundice.

The reason for the high level of MDA in children with jaundice is attributed to hemolysis in these children, because hemolysis can be explained by its effect on oxidative stress, as hemolysis itself leads to an increase in oxidative stress, which leads to an increase in the concentration of bilirubin. The oxidative effect on membrane lipids may cause an increase in MDA due to elevated generation of ROS, due to excessive oxidative damage in these patients. These oxygen species can, in turn, oxidize many other important biomolecules, including membrane lipids. Elevated MDA concentration in infants with severe G6PD deficiency reflects oxidative injury due to neonatal hyperbilirubinemia, which may be attributed to the formation of free radicals that remove hydrogen atoms from lipoproteins, causing lipid peroxidation, of which MDA is the major product (39).

Conclusion:- In infants with neonatal jaundice, elevated bilirubin is a key symptom. High levels of the hormone cholecystokinin are also observed in infants with neonatal jaundice. High bilirubin levels may indicate serious problems, including hemolysis and liver problems. High levels of C-reactive protein indicate a concurrent infection in patients. As for mineral levels, normal levels were observed among patients and healthy individuals, while low glutathione levels increase liver damage due to oxidation, and high levels of malondialdehyde indicate damage to the liver and other cells as a result of bilirubin accumulation and oxidation.

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