

## ESTIMATION THE LEVEL OF CREATININE OF NEONATAL HYPERBILRUBINEMIA

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### ABSTRACT

This study is intended to asses serum level of creatinine in neonates suffering from hyperbilirubinemia. In this study 60 of neonatal patients(35 male, 25 female) were collected from prematurity unit(PU) in Al-Zahra Educational Hospital/Al-Najaf Al-Ashraf during the period from August,2014to February,2015. A group of 20 randomly(12male, 8female) selected apparently healthy group. After diagnosis of hyperbilirubinemia, the patients were divided into three groups according to age (1-3),(4-7) and (7-9) days, and blood groups of babies and mother's. The result of the current study shows

significant increase( $p < 0.05$ ) in serum level of creatinine in hyperbilirubinemia patients ( $3.802 \pm 0.221 \text{ mg/dl}$ ) in comparison with control group( $1.217 \pm 0.0328 \text{ mg/dl}$ ) . And shows a significant differences( $p < 0.05$ ) between male( $3.788 \pm 0.281 \text{ mg/dl}$ ) and female( $2.865 \pm 0.296 \text{ mg/dl}$ ) in serum levels of creatinine. While the result manifests there is a significant increase( $p < 0.05$ ) in serum levels of Cr in neonatal with N (O+) M(O-) when compared with another blood groups.

**KEY WORDS:** hyperbilirubinemia, creatinine.

### INTRODUCTION

Neonatal hyperbilirubinemia is known as icterus neonatorum, neonatal jaundice and infant jaundice is a very common phenomenon but poorly understood problem and it is in many cases of uncertain clinical significance despite the seriousness of this disease.<sup>[1,2]</sup> Neonatal jaundice expose underlying skin and subcutaneous tissue can be detected with pressure applied by a finger for blanching the skin, so, jaundiced newborns have yellow color of the face that extending down onto the chest and yellowing the white part of the eye as well as this disease can make the newborn sleepy and interfere with feeding. <sup>[3]</sup> Creatinine is a product of

chemical waste, creatine metabolite, which is produced by the muscle metabolism, from three amino acids termed as glycine, methionine, arginine and the liver produced creatine so it arrives to the muscles via the blood then phosphocreatine is produced from creatine, during the muscles activity, a reaction occurs between phosphocreatine and ADP to produce ATP that is necessary for the muscles energy, then creatine is released.<sup>[4]</sup>

#### Aims of the study

1. Evaluation of serum level of creatinine as biomarkers of neonatal hyperbilirubinemia.
2. Estimating the level of total serum bilirubin of infants compared with serum level of creatinine.
3. Determining the blood groups of the neonate and mother's that could contribute to disease.

## MATERIALS AND METHODS

### Samples

The study was conducted on 60 neonates patients (25female , 35male). The patient's age was ranging from 1 to 9 days . The study was carried out from August, 2014 to February, 2015, samples were collected from the prematurity unit(PU)in Al-Zahra Educational Hospital/Al-Najaf Al-Ashraf. Hyperbilirubinemia was diagnosed by pediatricians. The information of patients was obtained through data that included the name, gender, age, blood group and the mother's blood group. Whereas, all neonatal patients under the study had no heart disease, kidney disease ,lung disease and any of viral and bacterial disease. A group of 20 randomly(12male, 8female) selected apparently healthy group(the bilirubin level is normal), has been used as a control group. Their age range was similar to that of neonates patients. Neonates hyperbilirubinemia patients are divided into subgroups according to blood group, gender and ages.

### Measurement of Creatinine

This was done by a method based on Kinetic test, carried out with specific kit for test, processed by(cypress diagnostic, Belgium, catalog number HB0080) by a semi-automatic biochemistry analyzer( Cyan-Start Cy-004, cypress, diagnostic, Belgium, SN: BISIBQ123E).

### Measurement of Blood group test

This was done by a method based on agglutination method, carried out with specific kit for this test, proceed by (Expert diagnostics FZC, UAE WM-27).

### Statistical Analysis

Statistical analysis of comparison between the patients and healthy groups were tested by one way ANOVA test, while the comparison between subgroups was analyzed by t-test. It carried out the correlation between the parameters correlation coefficient of Pearson. A level of statistically significant determination by P-value < 0.05.

### RESULTS

Result of table (1) showed bilirubin, creatinine serum levels of neonatal hyperbilirubinemia to three neonatal ages (1-3) (4-6) (7-9) days. This result observed significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $14.205 \pm 0.368$  mg/dl), creatinine ( $1.815 \pm 0.134$  mg/dl) of neonatal hyperbilirubinemia with age (1-3) days. Whereas, the result of neonatal hyperbilirubinemia with age (4-6) appeared significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $17.19 \pm 0.177$  mg/dl), creatinine ( $3.885 \pm 0.142$  mg/dl), While the result of neonatal hyperbilirubinemia with age (7-9) days, revealed significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $20.49 \pm 0.364$  mg/dl), creatinine ( $5.708 \pm 0.127$  mg/dl).

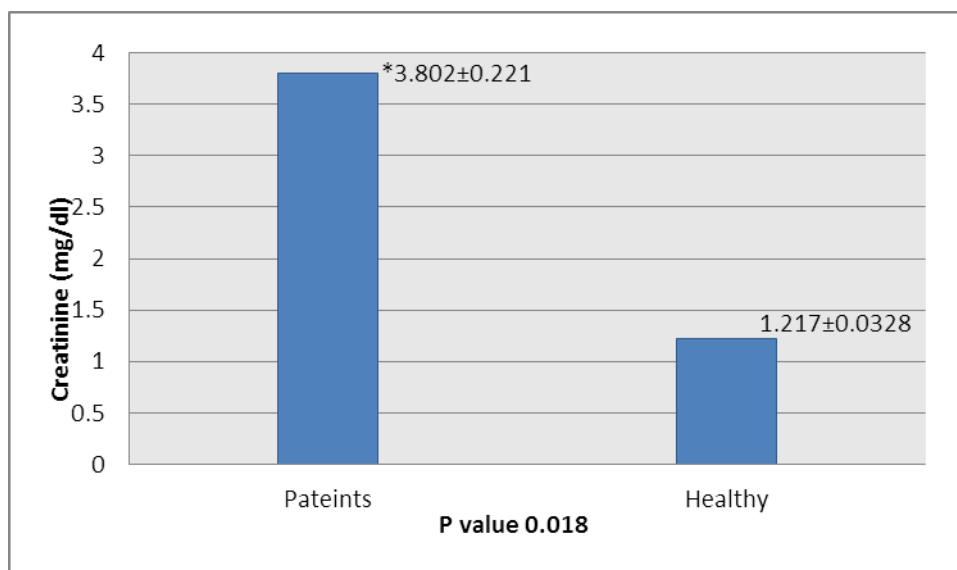
**Table(1): Comparison of Neonatal Hyperbilirubinemia at different ages.**

Clinical setting	<i>Hyperbilirubinemia</i>		
	<i>(1-3) Days</i>	<i>(4-6) Days</i>	<i>(7-9) Days</i>
Bilirubin(mg/dl)	$14.205 \pm 0.368$	$**17.19 \pm 0.177$	$*20.49 \pm 0.364$
P value	<b>0.011</b>	<b>0.092</b>	<b>0.041</b>
Creatinine(mg/dl)	$1.815 \pm 0.134$	$**3.885 \pm 0.142$	$*5.708 \pm 0.127$
P value	<b>0.094</b>	<b>0.047</b>	<b>0.022</b>

\*Statistically significant differences ( $p < 0.05$ ) between (7-9) days, (4-6) days and (1-3) days.

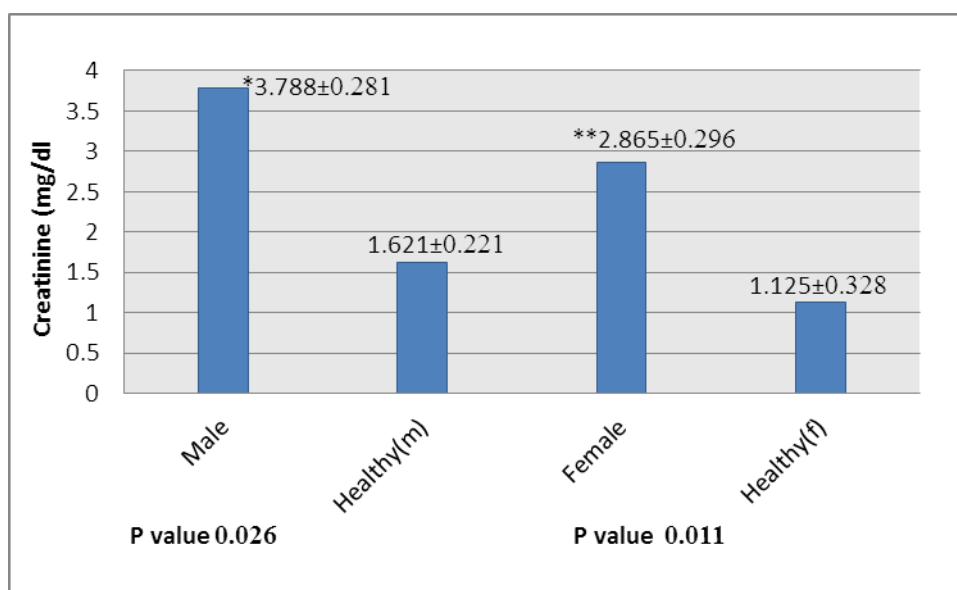
\*\* Statistically significant differences ( $p < 0.05$ ) between (4-6) days, (1-3) days.

The result in figure (1) appeared significant elevation ( $p < 0.05$ ) of serum creatinine concentration in neonatal hyperbilirubinemia ( $3.802 \pm 0.22$  mg/dl) when compared with healthy group ( $1.217 \pm 0.0328$  mg/dl), and indicated significant increase ( $p < 0.05$ ) in creatinine concentration of male ( $3.788 \pm 0.281$  mg/dl) as compared with healthy male ( $1.621 \pm 0.221$  mg/dl), and also scored significant increase ( $p < 0.05$ ) in female ( $2.865 \pm 0.296$  mg/dl) in comparison with healthy female ( $1.125 \pm 0.328$  mg/dl) and male ( $3.788 \pm 0.281$  mg/dl) as presented in figure (3-2).



\*Statistically significant differences ( $P < 0.05$ ) between patients and healthy group.

**Figure(1):serum level of Creatinine in neonatal hyperbilirubinemia comparison with healthy group.**

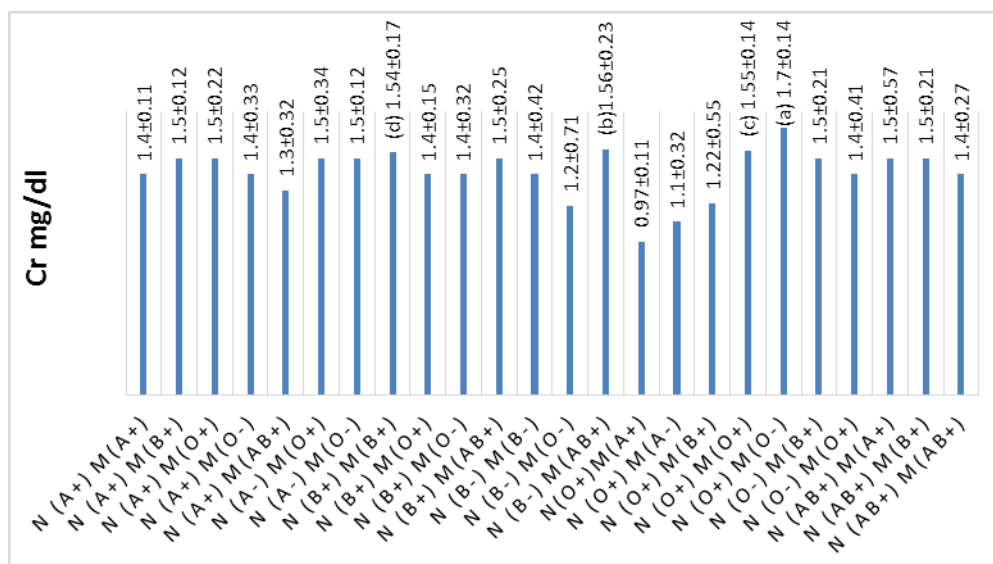


\*Statistically significant differences ( $P < 0.05$ ) between male, female, and Healthy (m).

\*\*Statistically significant differences ( $P < 0.05$ ) between female, and Healthy (f).

**Figure(2):serum level of Creatinine in neonatal hyperbilirubinemia (male, female) comparison with healthy group.**

In figure(3) the result scored significant elevation ( $p < 0.05$ ) in serum levels of Cr in neonatal with N (O+) M(O-) ( $1.7 \pm 0.14$  mg/dl) when comparison with other blood groups.



(a) Statistically significant differences ( $P < 0.05$ ) between N (O+) M(O-) and the other blood groups.

(b) Statistically significant differences ( $P < 0.05$ ) between N (B-) M(AB+) and the other blood groups.

(c) Statistically significant difference ( $P < 0.05$ ) between N (O+) M(O+) and the other blood groups.

(d) Statistically significant differences ( $P < 0.05$ ) between N (B+) M(B+) and the other blood groups.

**Figure(3):serum level of Creatinine in neonatal hyperbilirubinemia comparison between different babies and mother's blood group**

## DISCUSSION

The results in the current study shows that there are significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $14.205 \pm 0.368$ mg/dl), at the age(1-3)days. Whereas, the result of neonatal hyperbilirubinemia with age (4-6)days appears significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $17.19 \pm 0.177$ mg/dl), with age(7-9)days indicates significant differences ( $p < 0.05$ ) in serum level of bilirubin ( $20.49 \pm 0.364$ mg/dl). The result of the current study in accordance with the results of the study Zhang *et al.*,<sup>[5]</sup>; Hung *et al.*,<sup>[6]</sup> showed that the total serum bilirubin level(TSB) rises with age, they documented in their study, the reference intervals of total bilirubin for apparently healthy elderly should be established according to different age and sex groups. The present study reveals significant differences ( $p < 0.05$ ) in serum level of creatinine at different age stage in neonatal. At the age(1-3)days, creatinine ( $1.815 \pm 0.134$ mg/dl). Whereas, the result of neonatal hyperbilirubinemia with age(4-6) indicates

significant differences ( $p < 0.05$ ) in serum level of creatinine ( $3.885 \pm 0.142$  mg/dl), while at (7-9) days the result creatinine ( $5.708 \pm 0.127$  mg/dl). According to reports of previous studies that the rise in the level of creatinine observed in the first days of life, and then gradually began to decline. Manzar *et al.*,<sup>[7]</sup> showed in their study dropped in the level of creatinine from 0.64 mg/dl to 0.44 mg/dl, which was higher at birth 0.75 mg/dl, Miall *et al.*,<sup>[8]</sup> showed there was a significant increase in serum creatinine among premature infants in the first 48 hours of life, which supported results of previous studies. While, the study of Le *et al.*,<sup>[9]</sup> documented that there were many factors, including gender, age, drug, diet, muscle Mass and metabolic rate, can affect creatinine level in the serum, Which leads to inexact estimation of kidney impairment.

In the current study results scored significantly increase in the serum levels of creatinine in neonatal with hyperbilirubinemia as compared with healthy neonatal group as in figure (1). Creatinine is a terminal metabolite of creatine, is a very useful indicator of kidney function, although it is extremely important for the evaluation of renal function, but is not sensitive to early renal function decrease.<sup>[10]</sup> Production of creatinine is affected by muscle mass, age, and gender and is also related by tubular secretion. So, there are a lot of constraint associated with relying upon as an indicator for dialysis patients.<sup>[11,12]</sup>

In the agreement with the present study Zhang *et al.*,<sup>[5]</sup> observed in their study, the serum levels of creatinine increased in synchronization with increasing age, Cr was related to the total muscle mass in the body, so men's was obviously higher than women's. The current study compatible with the study of Liu *et al.*,<sup>[13]</sup> creatinine presented a significant increase in the newborns with different severity of Hypoxic- Ischemic Encephalopathy (HIE) only on first day after birth. Qiang *et al.*,<sup>[14]</sup> showed to compare the sensitivity of Cys-C and Scr in valuation the renal function impairment at early stage of shock. Serum level of creatinine provides estimates of glomerular filtration (eGFR) rate, which is strong risk factors for a wide range of outcomes.<sup>[15]</sup> The result of the present study revealed significant increase in the level of serum creatinine between male and female neonates with hyperbilirubinemia as in figure (2). Hans *et al.*,<sup>[16]</sup> found the inability to distinguish the level of creatinine in serum between male and female term and preterm neonatal to the lack of full information in the database. The results were excessive increase in the level of serum creatinine in neonatal, especially in the early days of delivery. There were differences in level of serum creatinine between males and females at different age groups, in male serum creatinine much higher than level of

serum creatinine in female.<sup>[17]</sup> A study by Zhang *et al.*,<sup>[5]</sup> proved that the high level of creatinine associated with an increase in age, it is clear that males have the highest level of serum creatinine than in females.

The results in the current study, have shown a significant increase ( $p < 0.05$ ) in serum levels of Cr in neonates with N (O+) M(O-) as compared with other blood groups as in figure(3). Etemadi *et al.*,<sup>[18]</sup> observed in their study 5.9% due to deaths for medical reasons, 8.9% deaths from cardiovascular associated with non-O blood groups. these blood groups also connected with elevated risk of gastric cancer. These results support the clinical importance and reduce risks in determining the blood group in the transfusion medicine. Wang *et al.*,<sup>[19]</sup> confirmed that the risk of gastric cancer in blood type of A was significantly higher than in other blood groups non-A, While it was lower in O blood group subjects.

## CONCLUSIONS

Creatinine is important as biomarker in the detection and diagnosis of neonatal hyperbilirubinemia. There is a relationship between age and the high level of biomarkers as a result of severe systemic damage. The difference in ABO between the mother and the neonate is considered one of the main reasons behind the progress of the disease.

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