
Sex- and Age-Related Differences in Bilirubin Concentrations in Serum Among Population in El-Beida City

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Abstract: Bilirubin (BR) is a yellow compound that occurs in the normal catabolic pathway that breaks down heme in vertebrates. The relation between age and sex and the concentration of bilirubin in serum among population in El-Beida City was evaluated in 75 (39%) was female and 118 (61%) male. Results from distribution of cases upon age groups in each gender separately (as each group consist of 10 years intervals); Age of the subjects was varied between less than 6 months to more than 75 years. The highest prevalence of the subjects was found in the age group less than six months with 25%. Rest age groups were found almost similar in term of distribution in both genders. Results from distribution of cases upon months in each gender separately; distribution of the subjects was varied between 12 months. The highest prevalence of the subjects was found in the July and August with 40% and 20% respectively. Rest months were found almost similar in term of distribution in both genders. Results found that 60-80% of cases had high level of direct and total bilirubin that significantly differences compared with normal values. .

Key words: Age, Sex, Bilirubin, El-Baida City, Gender

Introduction

Bilirubin is one of the end products of hemoglobin catabolism, and its deposition in the skin and mucous membranes can result in icterus (Srinivas et al., 2016). In case of brain bilirubin deposition and its lack of early diagnosis and treatment, it can lead to major complications such as kernicterus. This condition can be fatal during the first months of life or might cause mental retardation, movement and balance disorders, seizure, high-frequency hearing loss, and speech disorders in survivors (Wankaew et al., 2013). Therefore, early diagnosis and treatment of neonatal jaundice is vital to prevent such serious complications (Tamook et al., 2005). One-fourth of neonates with icterus had predisposing maternal factors. The most important parameters were hypertension followed by vaginal bleeding, diabetes, urinary infection, and premature rupture of membranes, maternal diabetes, East Asian race, prematurity, drug consumption, living in highlands, polycythemia, male gender, trisomy 21, cyanosis, cephalohematoma, oxytocin injection for delivery, breast feeding, weight loss (dehydration or calorie deprivation), delay in bowel movements, and history of neonatal jaundice in the siblings (Olusanya and Slusher, 2015). In term neonates, the indirect bilirubin level reaches adult values normally within 10-14 days (Finn et al., 2016).

Bilirubin (BR) is a yellow compound that occurs in the normal catabolic pathway that breaks down heme in vertebrates. This catabolism is a necessary process in the body's clearance of waste products that arise from the destruction of aged or abnormal red blood cells (Braunstein, 2019). First the hemoglobin gets stripped of the heme molecule which thereafter passes through various processes of porphyrin catabolism, depending on the part of the body

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in which the breakdown occurs. For example, the molecules excreted in the urine differ from those in the feces. The production of biliverdin from heme is the first major step in the catabolic pathway, after which the enzyme biliverdin reductase performs the second step, producing bilirubin from biliverdin (Mosqueda et al., 2005).

Bilirubin is excreted in bile and urine, and elevated levels may indicate certain diseases (Smith and Morton, 2011). It is responsible for the yellow color of bruises and the yellow discoloration in jaundice. Its subsequent breakdown products, such as stercobilin, cause the brown color of feces. A different breakdown product, urobilin, is the main component of the straw-yellow color in urine. It has also been found in plants (Pirone et al., 2009). Bilirubin consists of an open chain tetrapyrrole. It is formed by oxidative cleavage of a porphyrin in heme, which affords biliverdin. Biliverdin is reduced to bilirubin. After conjugation with glucuronic acid, bilirubin is excreted. Bilirubin is structurally similar to the pigment phycobilin used by certain algae to capture light energy, and to the pigment phytochrome used by plants to sense light. All of these contain an open chain of four pyrrolic rings. Like these other pigments, some of the double-bonds in bilirubin isomerize when exposed to light. This isomerization is relevant to the phototherapy of jaundiced newborns: the E,Z-isomers of bilirubin formed upon light exposure are more soluble than the unilluminated Z,Z-isomer, as the possibility of intramolecular hydrogen bonding is removed (McDonagh et al., 1980).

Bilirubin is created by the activity of biliverdin reductase on biliverdin, a green tetrapyrrolic bile pigment that is also a product of heme catabolism. Bilirubin, when oxidized, potent antioxidant activity of bilirubin (Stocker et al., 1987), has led to the hypothesis that bilirubin's main physiologic role is as a cellular antioxidant (Barañano et al., 2002). Total bilirubin = direct bilirubin + indirect bilirubin (Tietze, 2011). Elevation of both alanine aminotransferase and bilirubin is more indicative of serious liver injury than is elevation in ALT alone, as postulated in Hy's law that elucidates the relation between the lab test results and drug-induced liver injury (Gwaltney-Brant, 2016). Therefore this study was aimed to find out sex- and age-related differences in bilirubin concentrations in serum among Population in El-Baida City.

Methodology

The study was designed and performed from January 2019 to December 2020 at Al-Raze Lab with chemistry department at Omar Al-Mukhtar University. One hundred and ninety three subjects were enrolled in the study. Plasma total bilirubin was measured using the method of (Walters and Gerarde, 1970). Total bilirubin reacts with diazotized sulfanilic acid forming a colored complex that can be measured spectrophotometry at 540 nm. Bilirubin is degraded by light (Sofronescu et al., 2012). Blood collection tubes containing blood or (especially) serum to be used in bilirubin assays should be protected from illumination. For adults, blood is typically collected by needle from a vein in the arm. In newborns, blood is often collected from a heel stick, a technique that uses a small, sharp blade to cut the skin on the infant's heel and collect a few drops of blood into a small tube. Direct bilirubin is any form of bilirubin which is water-soluble and is available in solution to react with assay reagents; direct bilirubin is often made up largely of conjugated bilirubin, but some unconjugated bilirubin (up to 25%) can still be part of the "direct" bilirubin fraction. Likewise, not all conjugated bilirubin is readily available in solution for reaction or detection (for example, if it is hydrogen bonding with itself) and therefore would not be included in the direct bilirubin fraction

The bilirubin level found in the body reflects the balance between production and excretion. Blood test results should always be interpreted using the reference range provided by the laboratory that performed the test. Data was presented as number and percentage, statistical significance in the bilirubin levels were assessed using ANOVA analysis with Tukey multiple comparison test.

Results

This study concluded about 193 samples of patient's serum; these samples were analyzed for direct and total bilirubin. According to this study, of the 193 subjects 75 (39%) was female and 118 (61%) male. Age distribution relating to these subjects established cases that analyzed for two different measurements were shown in (Figure 1). Results from distribution of cases upon age groups in each gender separately (as each group consist of 10 years intervals); Age of the subjects was varied between less than 6 months to more than 75 years.

The highest prevalence of the subjects was found in the age group less than six months with 25%. Rest age groups were found almost similar in term of distribution in both genders. Distribution relating to these subjects established cases among a month of study that analyzed for two different measurements were shown in (Figure 2). Results from distribution of cases upon months in each gender separately; distribution of the subjects was varied between 12 months. The highest prevalence of the subjects was found in the July and August with 40% and 20% respectively. Rest months were found almost similar in term of distribution in both genders. Distribution relating to these subjects established cases among a month of study that analyzed for two different measurements were shown in (Figure 2). Results from distribution of cases upon months in each gender separately; distribution of the subjects was varied between 12 months. The highest prevalence of the subjects was found in the July and August with 40% and 20% respectively. Rest months were found almost similar in term of distribution in both genders. Table 1 illustrated the results obtained upon different levels of direct and total bilirubin. Result found that significantly differences compared to normal values that had high level of direct and total bilirubin.

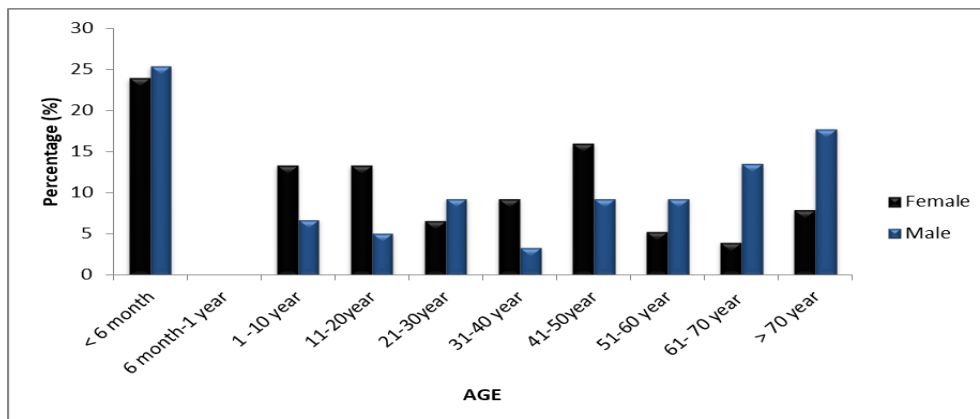


Figure 1: Age distribution among 193 subjects.

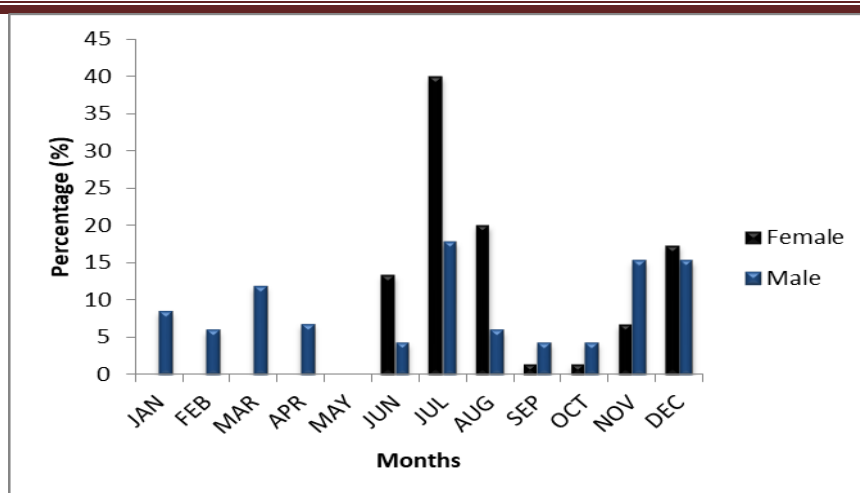


Figure 2: Distribution of subjects among a year.

Table 1: Levels of direct and total bilirubin among all subjects.

Three categories upon level of direct and total bilirubin		Number of cases (%)	Level of direct/total bilirubin (mg/dl) Mean \pm SD
Direct bilirubin	Low < 0.2 mg/dl	6 (3.11)	0.1 \pm 0.00 ^b
	Normal 0.2-0.3 mg/dl	14 (7.25)	0.236 \pm 0.0497 ^b
	High 0.3- 0.5 mg/dl	126 (65.3)	1.079 \pm 0.434 ^b
	Very high >0.5 mg/dl	47 (24.4)	5,174 \pm 3.11 ^a
-	-	-	-
Total bilirubin	Low < 0.3 mg/dl	1(0.52)	0.2 ^c
	Normal 0.3-1.9 mg/dl	55 (23.5)	1.204 \pm 0.518 ^c
	High 1.9-4 mg/dl	47 (24.4)	3.04 \pm 0.92 ^b
	High > 4 mg/dl	90 (46.6)	11.54 \pm 4.97 ^a

Data are expressed as mean \pm SD of direct/total bilirubin. Within each row number (%) and means with different superscript (^a, ^b or ^c) were significantly different at $p < 0.05$.

Discussion

This study was show the means for bilirubin within each age group and the normal range of values for each group as determined from the 39 and 61 percentiles. Slightly elevated bilirubin could induce a stress response to the endoplasmic reticulum, resulting in a decreased proliferative and metabolic activity of hepatocytes (Müllebner et al., 2015).

The discordance in serum bilirubin levels between men and women does not appear to be attributable to gender differences in the Gilbert polymorphism, because several studies have

demonstrated a similar genotype distribution between men and women (Borlak et al., 2000). Because the gender disparity in serum bilirubin does not manifest prior to age 10 year, it has been postulated that hormonal changes commencing at puberty cause altered bilirubin metabolism (Madhavan et al., 1997). In the present study, the mean bilirubin level was marginally higher in male compared to female, while it may become significant in a larger population. Similarly, Boskabadi et al. (2014) reported higher bilirubin level among boys. In another study, higher bilirubin level was significantly associated with male gender (Gale et al., 1990).

In the present study, investigation of the relationship between maternal age and bilirubin level revealed that the highest level was obtained from the 60-70 year age group. Similar results were reported by Boskabadi et al. (2014). Moreover, Gale et al. (1990) asserted that high bilirubin levels were remarkably associated with increased maternal age. Whereas, in another study no significant correlation was found between bilirubin level and maternal age (Garosi et al., 2016).

الفروق المرتبطة بالجنس والعمر في تراكيز البيلوروبين في مصل الدم بين عينة من السكان في مدينة البيضاء

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المستخلص: البيلوروبين (BR) هو مركب أصفر يحدث في المسار التقويضي الطبيعي الذي يكسر الحديد في الفقاريات. تم تقييم العلاقة بين العمر والجنس وتركيز البيلوروبين في المصل بين السكان في مدينة البيضاء في 75 (39%). إناث و 118 (61%) ذكور. النتائج من توزيع الحالات على الفئات العمرية في كل جنس على حدة (حيث تتكون كل مجموعة من 10 سنوات) ؛ كان عمر الأشخاص متفاوتاً بين أقل من 6 أشهر إلى أكثر من 75 عامًا. تم العثور على أعلى معدل انتشار في الفئة العمرية أقل من ستة أشهر بنسبة 25%. بينما باقي الفئات العمرية متشابهة تقريباً من حيث التوزيع في كلا الجنسين. النتائج من توزيع الحالات على الأشهر في كل جنس على حدة ؛ تفاوت توزيع الحالات بين 12 شهراً. تم العثور على أعلى معدل انتشار كان في شهري يوليو وأغسطس بنسبة 40% و 20% على التوالي. بينما باقي الأشهر متشابهة تقريباً من حيث التوزيع في كلا الجنسين. ووجدت النتائج أن 60-80% من الحالات كان لديها مستوى عالٍ من البيلوروبين المباشر والكلبي والذي كان به اختلافات معنوية مقارنة بالقيم الطبيعية.

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