Total Serum Bilirubin and Related Anemia in Thalassemic Patients

البيليروبين الكلي في المصل وصلته بفقر الدم في مرضى الثلاسيميا

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الخلاصة

هدفت الدراسة الحالية لتقييم مستوى البيليروبين الكلي(بنوعيه المباشر وغير المباشر) في المصل ودراسة نوع العلاقة بين مستوى الهيموغلوبين مرضى الثلاسيميا لدى Indirect SBوغير المباشر Direct SB المباشر TSB

غير المباشر)) والعمر لنفس المرضى لتحقيق هذا الغرضSB المباشر و TSB (SB والبليروبين الكلي Hb

تم دراسة ٤٣ من مرضى الثلاسيميا (١٩ اناث و٢٤ ذكور) معدل اعمارهم ١٢.٦١±٤.٥٤وبمدى عمر ٤-٢٢ سنة تضمنت الدراسة ايضا ٣١ شخصا من الاصحاء (١٢ اناث و١٩ ذكور) معدل اعمارهم ٥.٣٦± ١١.٥٥

قيس مستوى البلروبين الكلي في المصل (المباشر وغير المباشر) بالطريقة اللونية اخذت كمجموعة سيطرة

للمرضى مقارنة بالاصحاء (مجموعة TSB) قي مستوى البلروبين الكلي P<٠.٠٠١ بينت النتائج زيادة معنوية

اظهر تحليل الارتباط (P<٠.٠١)بصورة ملحوظة Hb الهيموغلوبين انخفضت مستويات السيطرة) بينما

Direct SB٤٨Indirect SB, (r= ٠. علاقات ارتباطية معنوية طردية متزايدة P< ٠.٠١) مع العمر لكل من

, ٥٣, (٠.Direct SB (r= -٠.٣٣, P< ٠.٠٥), لكل من بينما العلاقة الارتباطية سالبة وعكسية P< ٠.٠١)

مع مستوى الهيموغلوبين. الاستنتاج: ان ارتفاع مستوى البيلروبين (r= -٠.٧٥, P< Indirect SB ٠.٠٠٠١) الكلي في مرضى الثلاسيميا وعلاقته العكسية مع مستوى الهيموغلوبين تعتبر دليل جيد على وجود فقرالدم .

Abstract: The aim of present study was to evaluate total serum bilirubin TSB (direct and indirect SB) for thalassemic patients and to verify the correlation between Hb level, age and TSB level (direct and indirect) for the same patients. To achieve this aim, Forty-three thalassemic patients (١٩ females & ٢٤ male) with mean ages of ١٢.٦١±٤.٥٤ with a range of ٤-٢٢ years were enrolled. Thirty one healthy individuals (١٢ females & ١٩ males) of ages ١١.٥٥± ٥.٣٦ were enrolled as control group. The total serum bilirubin, (direct and indirect) levels in sera of patients and control group were measured by a colorimetric method. The results show a highly significant increase for TSB (P<٠.٠٠١), for patients in compared with healthy control while Hb levels were decreased

significantly (P<٠.٠١) for the same patients. The linear regression analysis exhibited strong positive significant correlations for direct SB (r= ٠.٤٨, P< ٠.٠١), indirect SB(r= ٠.٥٣, P< ٠.٠١) with age while its negative significant relationship for direct SB (r= -٠.٣٣, P< ٠.٠٥), indirect SB(r= -٠.٧٥, P< ٠.٠٠٠١) with Hb levels in thalassemic patients. Conclusion, elevation of TSB in thalassemic patients and its inverse correlation with Hb consider the best indicator of the presence of anemia.

Key words: TSB, Thalassemia, Anemia

Introduction:

Thalassemia (from Greek, thalassa, haima, blood; British spelling, "thalassemia") is an inherited autosomal recessive blood disease. In thalassemia, the genetic defect results in synthesis of one of the globin chains that make up hemoglobin. Thalassemia syndromes are a heterogeneous group of single gene disorders, inherited in an autosomal recessive manner, prevalent in certain parts of the world [١].

Approximately ٤ mg/kg body weight of bilirubin is produced daily from haem-containing proteins from erythroid and non-erythroid sources. Haemoglobin, released by the breakdown of senescent red blood cells, is the major erythroid source, but there is a significant contribution from free haem and haemoglobin that is produced but not incorporated into mature red cells (ineffective erythropoiesis). Approximately ٢٠% of the total daily bilirubin production is normally contributed by other haemoproteins, primarily in the liver, such as cytochromes, catalase, peroxidase and tryptophan pyrrolase. Bilirubin is potentially toxic but is

normally rendered harmless by tight binding to albumin and rapid conjugation and excretion by the liver [٢].

It is a naturally as antioxidant and has a role in protecting lipid and lipoproteins against oxidation and against plaque formation in human beings [٣].

Bilirubin is found in two forms; direct reacting bilirubin found in the bile and indirect found in the blood [٤].

Unconjugated bilirubin is water insoluble, so it is not excreted in the bile or urine and partially reabsorbed and undergoes enterohepatic circulation. Conjugated bilirubin is water-soluble and is not absorbed across the small intestinal epithelium [٥].

Within hepatocytes, the solubility of bilirubin is increased by the addition of one or two molecules of glucuronic acid forming, Bilirubin monoglucuronide and diglucuronide metabolites which were actively transported into the bile [٦, ٧]. The heterozygous state of thalassemia is characterized by chronic, low _grade ineffective erythropoiesis and variable levels of serum bilirubin level [٨].

Some studies revealed that patients with thalassemia major and intermedia show a marked variability of serum indirect bilirubin levels [٩].

Aim of the study: To evaluate total serum bilirubin TSB (direct and indirect SB) for thalassemic patients and to verify the correlation between Hb level, age and TSB level (direct and indirect) in the same patients.

Patients & Methods:

Forty-three thalassemic patients (١٩ females & ٢٤male) were enrolled randomly, in this study. The patients routinely visited the thalassemic center in Ibn-Al-Balady Hospital during September – December ٢٠٠٩. Their mean ages were ١٢.٦١±٤.٥٤ with a range of ٤-٢٢ years. The control group consist of ٣١ healthy individuals (١٢ females & ١٩ males) mean ages ١١.٥٥± ٥.٣٦ with a rang ٧-٢٢ years. The serum bilirubin level (total & direct) was determined by a colorimetric method ((Randox assay kit) [١٠, ١١].

Statistical analysis:

Data analyses were carried out using the statistical package for social sciences (SPSS version ١٠). The results were expressed as (mean ± SD) and analyzed by the use of independent t-test was done for the comparison of two groups and the differences were considered significant when P was <٠.٠٥. Pearson's correlation analysis of the data was made using the statistical program**.**

Results& Discussion:

The results show highly significant increase (p<٠.٠٥-٠.٠٠١) in the level of TSB (direct and indirect) in thalassemic patients when compared with those of control group while Hb levels were decreased significantly (P<٠.٠١) for the same patients (table ١). The linear regression analysis exhibited strong positive significant correlations for direct SB (r= ٠.٤٨, P< ٠.٠١), indirect SB(r= ٠.٥٣, P< ٠.٠١) with age while its negative significant relationship for direct SB (r= -٠.٣٣, P< ٠.٠٥), indirect SB(r= -

٠.٧٥, P< ٠.٠٠٠١) with Hb levels in thalassemic patients (table ٢ and Fig ١, ٢).

Mean Hb level was (٨.٠٤± ١.١g/dl) in thalasemic patients compared to the mean value of (١٣.٥± ٠.٩ g/dl) in the controls subject. This indicates suboptimal blood transfusion at least partially because by low health education of the parents and their knowledge about the disease is very limited and transfusion used only when the patients showed clinical symptoms caused by sever anemia and simply to sustain life [١٢, ١٣]. In addition, it may be caused by the difficulties in reaching the center for blood transfusion.

This was in contrast to reported values from other countries were patients are treated in favor of a supertransfusion programme maintaining Hb level above ١٢ g/dl or hypertransfusion programme where the Hb value never allowed dropping below ٩ g/dl [١٤, ١٥]. The increase in serum bilirubin obtained in our study may be interpreted by several probabilities i.e., the less severe of thalassemia patients are less registered in Ibn – Albalady center because they are less aware about seriousness of cases. Other contributing causes may include higher incidence of viral hepatitis and hemochromatosis.

In the present study direct and indirect serum bilirubin found to be significantly increase compared to control these increases may be result from impairment of the necessary bilirubin conjugation in the hepatocyte. This problem may occur before bilirubin has entered the hepatocyte or within the liver cell. Excessive heme metabolism from hemolysis or re-absorption of a large hematoma, results in significant increases in

bilirubin, which may overwhelm the conjugation capacity and lead to a state of unconjugated hyperbilirubinemia [١٦].

On other hand this study revealed, that there is a significant correlation between TSB and patients age. This finding is consistent with other finding reported by [١٧, ١٨]. This correlation may be related to the amount of total blood transfused at any age, with expected increase in viral hepatitis [١, ١٩]

Table ١: Serum bilirubin total, direct and indirect and Hb levels in thalassemic patients & the control group.

Parameter	group	Mean±SD	Range	P-value
Hb (g/dl)	Control	١٣.٥ ± ٠.٩	١١.٤-١٥.٧	P<٠.٠١
	Patient	٨.٢ ± ١.٢	٤.٦-١٠.٦	P<٠.٠٠١
		١٢.٨٣±٥.٠٣	١.٧-٢٥.٠	
		٣٠.٠٥±١٦.٤١	٧.٤٠-٧٨	
TSB (µ mol/L)	Control	٢.٠± ٠.٩		P<٠.٠٥
		٧.٥٨ ± ٣.٨٩	٠.١-٤.٠	

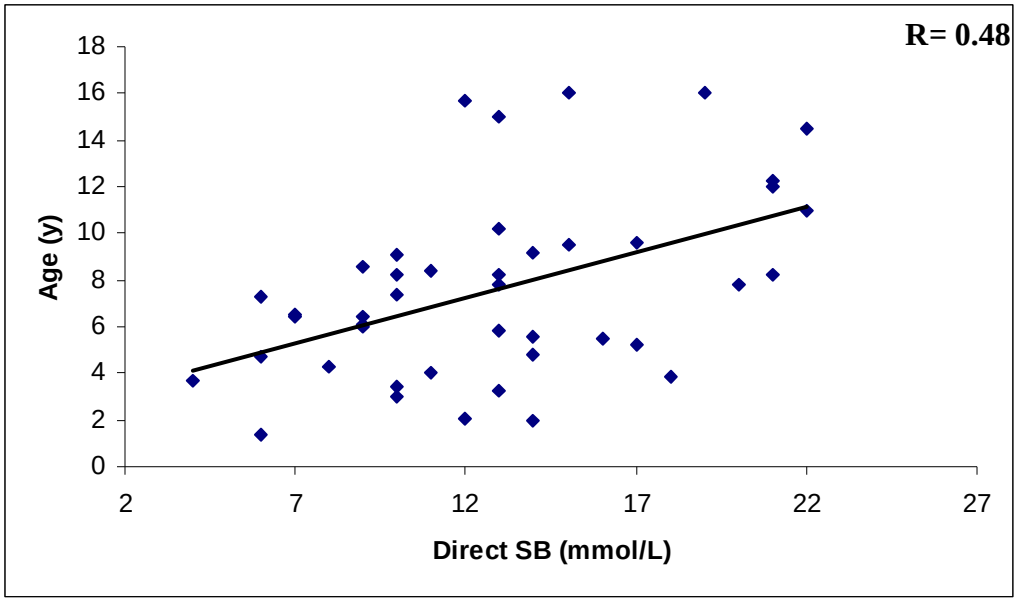
Direct SB (µ mol/L)	Patient	٩.٧٦±٢.٩	١.٤-١٦.٠	P<٠.٠٠١
	Control	٢٢.٣٨±١٤.٦٥	٢-١٦.٠	
Indirect SB (µ mol/L)	Patient		٤.١-٦٢.٠	
	Control			
	Patient			

Table ٢: The correlation of Hb and age with Direct SB and Indirect SB levels in thalassemic patients.

Parameter	**Hb**		**Age**	
	r	**P- value**	**r**	**P- value**
Direct SB (mmol/L)	-٠.٣٣	P<٠.٠٥	٠.٤٨	P<٠.٠١
Indirect SB	-٠.٧٥	P<٠.٠٠٠١	٠.٥٣	P<٠.٠١

(mmol/L)				

Fig ١:The correlation of Hb with Direct SB and Indirect SB levels in thalassemic patients


R= 0.48
Age (y)
Direct SB (mmol/L)
0
2
4
6
8
10
12
14
16
18
2
7
12
17
22
27

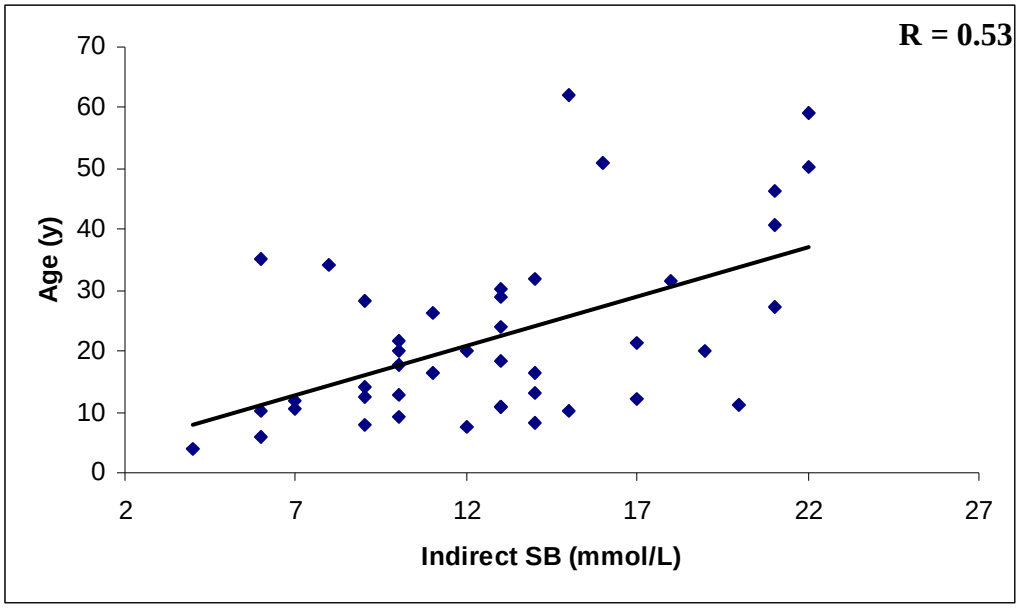


Fig ٢: The correlation of age with Direct SB and Indirect SB levels in thalassemic patients

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