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The Determination of Hepatic Enzymes Level in Children with Sickle Cell Anemia and Correlation with Age, Gender, HbS and HbF Variables

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ABSTRACT: sickle cell anemia is an autosomal recessive hematologic and genetic disorder which is due to a variant of Hb, named HbS. presents with impaired liver function test, chronic hepatomegaly. The aim of this study was to determine hepatic enzymes level in children with sickle cell anemia and correlation with age, gender, HbS, HbF variables using them for earlier diagnosis of hepatic injuries in this patients. Methods: This descriptive – analytic cross- sectional study was done on children with sickle cell anemia aged 2 months to 18 years old who attended in the Bandar Abbas Pediatric Hospital in 2011. After assessment of CBC and Hb electrophoresis and hepatic enzyme measurement (SGOT, SGPT, and ALKP) and record these, statistical analysis was done using SPSS20 and descriptive statistics (Mean and standard deviation and t-test, analysis Pearson's univariate). A total of 53 patients, 32 males and 21 females, enrolled the study. The most genotype was SB+ (25 cases, 47.1%) and the least genotype was SC (2 cases, 3.7%) cut of point of SGOT, SGPT and ALKP was 45.4 and 1200 respectively. Liver function test was normal in 18 cases (33.9%) and in 35 cases (66.1%) was increased. There was no statistical significant difference in liver enzyme between gender and genotypes and HbF. Univariate analysis revealed that there is no correction between ages and hepatic enzyme but Pearson's correlation test showed decreasing SGOT with increase of age. Increasing HbS with increase of HbS which is statistically significant (p=0.045). The results of this study revealed that physicians and careers need to be more attentive to liver function in children with sickle cell anemia.

Keywords: Sickle Cell Anemia, Hepatic Enzymes, Transaminase

ORIGINAL ARTICLE

INTRODUCTION

Sickle cell disease (SCD) is a common genetic disorder which is the result of a single base-pair change thymine for adenine, at the sixth codon of the beta globin gene. In the United States, sickle cell disease is the most common genetic disease identified through the state – mandated newborn screening program, occurring in 1:2, 647 births (Michael ET AL., 2011). Life expectancy is shortened in 1994, in the US; the average life expectancy of persons with this condition was estimated to be 42 years in males and 48 years in females (Platt et al., 1994). But today, thanks to better management of the disease, patients can live into their 50s or beyond. Sickle-cell disease occurs more commonly in people from parts of tropical and sub-tropical sub-Saharan regions where malaria is or was common. In areas where malaria is common, there is a fitness benefit in carrying only a single sickle-cell gene (sickle cell trait). Those with only one of the two alleles of the sickle-cell disease, while not totally resistant, are more tolerant to the infection and thus show less severe symptoms when infected (Wellems et al., 2009). According to WHO statement in 2011, 300,000 children are born with hemoglobin disorders worldwide-annually that around 200,000 of them have sickle cell anemia that occur in Africa. Sickle cell disease is prevalent in many parts of India, where the prevalence has ranged from 9.4 to 22.2% in endemic areas (Awasthy et al., 2008). Three quarters of sickle-cell cases occur in Africa. A recent WHO report estimated that around 2% of newborns in Nigeria were affected by sickle cell anemia, giving a total of 150,000 affected children born every year in Nigeria alone. The carrier frequency ranges between 10% and 40% across equatorial Africa, decreasing to 1–2% on the North African coast and <1% in South Africa. It is characterized by chronic hemolytic anemia and vaso-occlusive crises, which can lead to widespread vascular occlusion by sickled red blood cells leading to multiple organ infarctions. In this respect, SCD can be considered as a

multisystem disease for example: painful crisis, acute chest syndrome, fever and bacteremia, priapism, Stroke, splenic sequestration (Meshikhes et al., 1998). The sickle cell anemia can be diagnosed by clinical manifestation, PBS and hemoglobin electrophoresis. The most commonly used procedures for newborn diagnosis include thin layer/isoelectric focusing and high-performance liquid chromatography (HPLC) (Michael et al., 2011). Hydroxyurea was the first approved drug for the causative treatment of sickle-cell anemia, was shown to decrease the number and severity of attacks in a study (Charache et al ., 1995) and shown to possibly increase survival time in a study (Steinberg et al ., 2003). This is achieved, in part, by reactivating fetal hemoglobin production in place of the hemoglobin S that causes sickle-cell anemia. Hydroxyurea had previously been used as a chemotherapy agent, and there is some concern that long-term use may be harmful, but this risk has been shown to be either absent or very small and it is likely that the benefits outweigh the risks (Platt, 2008). The aim of this study was to determine hepatic enzymes level in children with sickle cell anemia and correlation with age, gender, HbS, HbF variables using them for earlier diagnosis of hepatic injuries in this patients.

METHODS AND MATERIALS

This descriptive – analytic cross- sectional study was done in the Bandar Abbas Pediatric Hospital from March 2011 to March 2012. The study was conducted on children with sickle cell anemia aged 2 months to 18 years old who admitted to Bandar Abbas Pediatric Hospital. Children with HbS fewer than 50% excluded from study. At first, CBC and Hb electrophoresis determined with 2 ml venous blood in citrated tubes in the basis of standard methods in the Bandar Abbas laboratory. The measurement of AST (2 IU/Lit), ALT(4 IU/Lit) and ALKP(3 IU/Lit) were determined and evaluated in 2 ml venous blood in clog tube collected in Bandar Abbas Pediatric Hospital laboratory using quantitative diagnostic kits. Variables were age, gender, genotype, HbS and HbF levels in patients Electrophoresis. After assessment of Liver function tests level and Hb electrophoresis, all data were collected through questionnaires, encoded forms and finally imported to the SPSS20 statistical software. Afterwards data were analyzed with descriptive statistics methods (Mean and Standard deviation), T-test and Pearson's unvariate and multivariate analysis of variance and then the collection data was depicted as tables. p.value<0.05 was considered as significance level.

RESULTS

A total of 53 patients with sickle cell anemia who enrolled the study were 32 males (60.3%) and 21 females (39.6%). The most age group of population were 2-5 years old (15 cases, 60.3%) and the least age group were under 2 years old (6 cases, 11.3%) in this study. the most genotype was SB+(25 cases, 47.1%) and the least genotype was SC (2 cases, 3.7%). Cut of point of SGOT, SGPT and ALKP was 10-45 IU, 10-40 IU and 160-1200 IU respectively. Liver function test was normal in 18 cases(33.9%), abnormal in 35 cases(66.1%)(abnormal SGOT(85.7%), SGPT(34.2%) and ALKP(2.8%)) and 7 cases have increased SGPT and SGOT.The T-tests showed that there is no statistical significant difference in liver enzymes(SGOT, SGPT, ALKP) between two sexual groups(p.value>0.05)(table 1).Univariate analysis(ANOVA) revealed that there is no significant difference between liver enzymes(SGOT, SGPT, ALKP) in different age groups but Pearson's correlation test showed decreasing SGOT with increasing age(table 2).

Variance analysis showed that there is no significant difference between liver enzymes level in different level of genotypes (p.value >0.05) (table 3).Pearson's correlation tests revealed that there is statistically correlation between ALKP and HbS(p = 0.045) but not between SGOT and SGPT with Hbs. Increasing ALKP with increase of HbS. Multivariate correlation test also showed that correlation level between three liver enzymes(SGOT, SGPT, ALKP) and HbS is medium (R2 = 0.011, R= 0.33)(table 4). Pearson's correlation tests showed that there is no correlation between HbF and liver enzymes, Multivariate correlation test also revealed that correlation level between three liver enzymes and HbF is low (R2 = 0.073, R= 0.27)(table 5).

Table 1. Liver enzymes level in different gender

Liver enzymes	Gender	N	Standard Deviation ± Mean	t	P.value
SGOT	Male	32	60.7±27.7	1.679	0.99
	Female	21	48.5±22.4		
SGPT	male	32	35.1±20.6	0.198	0.844
	female	21	36.9±23.9		
ALKP	male	32	475.7±397.57	0.763	0.449
	female	21	407.3±121.9		

Table 2. Liver enzymes level in different age groups

Liver enzymes	Age groups (year)	N	Standard Deviation ± Mean	P.value
SGOT	<2	6	67.8±24.4	0.242
	2-5	15	63±35	
	5-8	13	47.4±19.7	
	9-12	11	24.9±58.3	
	>12	8	10.4±43.8	
	Total	53	55.9±26.1	
SGPT	<2	6	41.1±18.1	0.844
	2-5	15	38.7±27.3	
	5-8	13	35.3±24.1	
	9-12	11	30.1±13.3	
	>12	8	33.3±21.4	
	Total	53	35.5±21.8	
ALKP	<2	6	731.1±825.8	0.207
	2-5	15	452.5±150.9	
	5-8	13	409.2±204.5	
	9-12	11	408.2±154.6	
	>12	8	349.3±164.7	
	Total	53	448.6±317.9	

Table 3. Liver enzymes level in different genotypes

Liver anzymes	Genotype	N	Standard Deviation± Mean	P.value
SGOT	SB^+	25	52.83±20.6	0.779
	SS	11	54.8±34.8	
	SD	11	65.2±32.9	
	SB^0	4	54.5±12.3	
	SC	2	51.5±27.5	
	Total	53	55.9±26.1	
SGPT	SB^+	25	34.5±23.5	0.621
	SS	11	32.5±18.9	
	SD	11	44.5±24.5	
	SB^0	4	31±11.4	
	SC	2	25.5±14.8	
	Total	53	35.5±21.8	
ALKP	SB^+	25	488.1±145.4	0.897
	SS	11	440.8±145.4	
	SD	11	417.09±27.1	
	SB^0	4	382.5±156.2	
	SC	2	297.5±45.9	
	Total	53	448.6±317.9	

Table 4. The significant levels of HbS correlation with different liver enzymes

HbS	SGOT	SGPT	ALKP
P value	0.295	0.417	0.045

Table 5. The significant levels of HbF correlation with different liver enzymes

HbF	SGOT	SGPT	ALKP
P value	0.447	0.876	0.74

DISCUSSION

A total of 53 children, 66.1% have abnormal liver enzymes due to increasing SGOT (85.7%) during one year in this study. ALKP, SGPT and SGOT level didn't affect by any of variables including gender, genotype and HbF. There was only significant difference between increasing HbF and ALKP, also with increasing age, SGOT decreased. Regarding to small blood sample volume, there was a significant difference. Such that more than half of Volunteers were male (60.3%) and half of them had SB+ genotype. The results of our study is similar to Maha (2009) and Taiwo (2005) in terms of percent of liver enzymes (our study=33.9%, Maher's study=31%, Kolita's study=25%). There was no correlation between gender and AST level just like two other studies. Unlike Mahera and Kolita's study, there was statistically significant correlation between age and liver enzymes in our study. Our findings were consistent with Isichei's study (1980) in 1-11 years old age group and SGOT level was higher in 1-5 years old age group (increasing age and decreasing SGOT). There was no significant difference between AST level and genotype in contrast to Saha's study in 1982[14] and Samperi's study (1996).

The results of this study revealed that physicians and carers need to be more attentive to liver function in children with sickle cell anemia.

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