Original Article

Effect of sickle cell diseases on height and weight

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ABSTRACT

Objectives: We tried to understand what are the effects of the sickle cell diseases (SCD) on metabolic parameters, especially the body weight and height in the study.

Methodology: The study was performed in the Hematology and Internal Medicine Polyclinics on SCDs and routine check up patients.

Results: The study included 122 patients with SCDs (58 females) and 176 control cases. Mean age of the SCDs cases was 28.6 years. When we compared the patients and control groups, mean body weight and body mass index (BMI) were significantly reduced in the SCDs cases (71.6 vs. 57.8 kg and 24.9 vs. 20.7 kg/m2, p= 0.000 for both), whereas the mean heights were similar in both groups (166.1 vs. 168.5 cm, respectively, p>0.05). Similar to the decresed mean body weight and BMI, mean values of the low density lipoprotein cholesterol and high density lipoprotein cholesterol were significantly lower in the patients group (p= 0.000 for both), whereas the fasting plasma glucose and triglyceride values were unchanged between the groups (p>0.05). Additionally, probably parallel to the reduced mean body weight and BMI, mean values of the alanine aminotransferase (34.9 vs. 56.7 U/L, p= 0.000) and systolic and diastolic blood pressures were also significanly lower in the patients group (113.3 vs. 118.8 and 72.3 vs. 83.6 mmHg, respectively, p<0.01 for both), all of which can be explained by definition of the metabolic syndrome.

Conclusion: Although the body weight can significantly be reduced by SCDs, the body height may strongly be determined by heredity.

KEY WORDS: Heredity, Height, Sickle cell diseases.

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INTRODUCTION

Human growth is probably under the influences of many hereditary and environmental factors, and optimal growth can be achieved by working on them. Genes may be more significant in human growth[1], and there is a common agreement that parents' heights affect the stature of the children.[2] On the other hand, external factors may play a major role in the body weight. For example, it was shown that only urban and rural living conditions may cause up to a 12% difference in height and a 30% difference in weight,[3] but there is still little known about genetic and environmental control of body mass.

Sickle cell diseases (SCDs) are chronic hemolytic anemias including sickle cell anemia (Hb SS) and sickle cell-hemoglobin C, sickle cell-beta thalassemia,

and sickle cell-alpha thalassemia diseases. They are characterized by sickle-shaped erythrocytes which are caused by homozygous inheritance of the hemoglobin S (Hb S). They are especially common in malaria-stricken areas of the world including Africa, Mediterranean, India, and Middle East. The responsible allele is autosomal recessive located on the short arm of the chromosome 11.

Glutamic acid is replaced with a less polar amino acid, valine, in the sixth position of the beta chain of the Hb S. Under various stressful conditions including cold, exercise, pregnancy, infections, emotional distress, and hypoxia, presence of a less polar amino acid promotes polymerisation of the Hb S, which distorts erythrocyte into a sickle shape and decreases its elasticity. The decreased elasticity of the erythrocytes is the central pathology of the disease, since the normal erythrocytes can deform to pass through capillaries easily. Vascular occlusions induced ischemia and infarctions are the final consequences of the disease, so the life expectancy the homozygotes is decreased by 25 to 30 years.[4] In the present study, we tried to understand what are the effects of the SCDs on metabolic parameters, especially the body weight and height.

METHODOLOGY

The study was performed in the Hematology and Internal Medicine Polyclinics of the Mustafa Kemal University on SCDs and random check up patients with a required number between March 2007 and April 2010. Only the SCDs patients on silent phase but not on the painful crisis were included into the study. SCDs were diagnosed by the hemoglobin electrophoresis performed via high performance liquid chromatography method, and an additional genetic testing was performed just for the suspected cases from the combination of thalassemias, especially the alpha-thalassemias. The control cases were chosen from the healthy check up cases, and they were age and sex-matched cases with the SCDs patients.

The medical history of all cases including already used medications was recorded, and a routine check up procedure including fasting plasma glucose (FPG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglyceride (TG), and alanine aminotransferase (ALT) values was performed. Body weight and height were measured, and body mass index (BMI) of each case was calculated by the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared to calculate BMI.[5] Systolic and diastolic blood pressures (BP) were checked after a 5-minute of rest in seated position with the mercury sphygmomanometer (ERKA, Germany), and no smoking was permitted during the previous 2-hour. Eventually, the mean weight, height, BMI, FPG, LDL-C, HDL-C, TG, ALT, and systolic and diastolic BP values were detected in both groups, and compared in between. Mann-Whitney U Test, Independent-Samples t Test, and comparison of proportions were used as the methods of statistical analyses.

RESULTS

The study included 122 patients with SCDs (58 females) and 176 control cases (84 females). The mean age of the SCDs cases was 28.6 years, and there were 107 patients with Hb SS, 11 patients with sickle cell-beta-thalassemias, and four cases with sickle cell-alpha-thalassemias. Additional genetic testing was required just for the alpha-thalassemia cases. Characteristic features of the study cases are summarized in Table-I. When we compared the patients and control groups, the mean body weight and BMI were significantly reduced in the SCDs cases (71.6 vs. 57.8 kg and 24.9 vs. 20.7 kg/m2, p= 0.000 for both), whereas the mean heights were nearly similar in both groups (166.1 vs. 168.5 cm, respectively, p>0.05).

The mean values of the FPG were unchanged between the patients and control groups (93.9 vs. 94.7 mg/dL, respectively, p>0.05), and the mean value of the TG was higher in the patient's group, but the difference was nonsignificant (120.1 vs. 112.1 mg/dL, p>0.05). Similar to the retarded mean body weight and BMI, the mean value of the LDL-C was significantly lower in the patients group (74.0 vs. 109.6 mg/dL, p= 0.000).

On the other hand, the mean value of the HDL-C was also lower in the patients group as (24.4 vs. 42.6 mg/dL, p= 0.000). Additionally, probably parallel to the retarded mean body weight and BMI again, mean values of the ALT (34.9 vs. 56.7 U/L, p= 0.000) and systolic and diastolic BPs were also significanly lower in the patients group (113.3 vs. 118.8 and 72.3 vs. 83.6 mmHg, respectively, p<0.01 for both). On the other hand, six patients (three females and three males with mean ages of 32.3 and 29.3 years, respectively) were lost to follow up due to infections induced sepsis, and there were pulmonary hypertension in two, cirrhosis in two, and cirrhosis plus chronic renal disease in one of them.

DISCUSSION

SCDs include a group of genetic disorders characterized by the presence of Hb S, which is the firstly discovered hemoglobinopathy, and is known for 100

Table-I: Characteristic features of the study cases.

Variables	*Sickle cell cases*	*Control cases*	*p-value*
Number	122	176	
Female ratio	47.5% (58)	47.7% (84)	ns*
Mean age (years)	28.6 ± 10.2 (14-59)	28.6 ± 8.2 (15-58)	ns
Mean weight (kg)	57.8 ± 11.0 (31-83)	71.6 ± 14.4 (43-111)	0.000
Mean height (cm)	166.1 ± 9.1 (145-188)	168.5 ± 10.0 (137-195)	ns
Mean BMI† (kg/m2)	20.7 ± 2.9 (14.7-29.9)	24.9 ± 4.3 (17.3-41.2)	0.000
Mean FPG‡ (mg/dL)	93.9 ± 13.8 (56-119)	94.7 ± 12.0 (63-160)	ns
Mean LDL-C§ (mg/dL)	74.0 ± 29.8 (24-164)	109.6 ± 29.6 (43-231)	0.000
Mean HDL-CQ% (mg/dL)	24.4 ± 7.8 (9-45)	42.6 ± 11.0 (24-91)	0.000
Mean triglyceride (mg/dL)	120.1 ± 63.9 (31-348)	112.1 ± 65.0 (27-388)	ns
Mean ALT¶ (U/L)	34.9 ± 20.5 (11-125)	56.7 ± 26.6 (20-168)	0.000
Mean systolic BP** (mmHg)	113.3 ± 14.9 (80-150)	118.8 ± 16.6 (80-170)	0.008
Mean diastolic BP (mmHg)	72.3 ± 9.9 (60-100)	83.6 ± 10.7 (60-110)	0.000

*Nonsignificant (p>0.05) †Body mass index ‡Fasting plasma glucose
§Low density lipoprotein cholesterol Q%High density lipoprotein cholesterol
¶Alanine aminotransferase **Blood pressure

years.[6] Together with the hemoglobin E, it is the most commonly seen hemoglobinopathy in the world. Hb S causes erythrocytes to change their normal biconcave disc shape to a crescent or sickle shape during various stresses of the body. The erythrocytes can take their normal shapes after normalization of the stressful conditions, but after repeated cycles of sickling and unsickling, they are damaged permanently, and hemolysis occurs. So lifespan of the erythrocytes decreases from the normal 120 days to 15-25 days. This hemolysis is responsible for the anemia that is the hallmark of the SCDs. For example, all of the SCDs cases were anemic, and had received erythrocyte suspansions before in the present study.

Painful crises are the most common and disabling symptoms of the disease. Although some authors reported as opposite[7], pain itself may not be directly life threatening, but as also seen in our experience infections are the most common triggering factors of the crises. So the risk of mortality is significantly higher during the crises. On the other hand, pain is the result of a complex and poorly understood interaction between erythrocytes, endothelium, leukocytes, and platelets. Whether leukocytosis contributes to the pathogenesis of the painful crises, perhaps by releasing cytotoxic enzymes is unknown. The adverse actions of neutrophils on endothelium are of particular interest with regard to the stroke and cerebrovascular diseases in SCDs. For example, leukocytosis in the absence of infections was an independent predictor of the severity of the disease in a previous study[8], and it was associated with the risk of stroke in a cohort of Jamaican patients.[9] Occlusions in vasculature of the bone marrow, bone infarctions, inflammatory mediators, and activation of afferent nerves may take role in the pathophysiology of the pain. Hospital admissions for acute painful crises typically last for 4-10 days, but the time varies greatly. Because of the severity of the pain, narcotic analgesics are usually required to control them.[10] In our practice the painful crises are the most significant problems for patients, for families, and even for health workers due to the severity and prolonged nature of the episodes.

Because of the repeated infarctions and subsequent fibrosis, the spleen is commonly very small in adults. Eventually, a functional and anatomic asplenism develop due to the decreased antibody production, opsonization, and reticuloendothelial functions. Terminal consequence of the asplenism is increased risk of infections with Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis like encapsulated bacteria. Thus, infections, especially pneumococcal infections, are common in early childhood, and are associated with a high mortality rate. The causes of death were infection in 56% of infants in a previous study.[8] In another study, the peak incidence of death among children with SCDs occured between 1 and 3 years of age, and the deaths among patients less than 20 years of age were predominantly caused by pneumococcal sepsis.[11] Adults, even those who appear relatively fit, are susceptible to acute multiorgan failure, and may die during acute crises, probably due to the associated infections on the grounds of immunosuppression.

SCDs can affect nearly all organ systems of the body.[12-14] Aplastic crises, sequestration crises, hemolytic crises, acute chest syndrome, avascular necrosis of the femoral and humeral heads, priapism

and infarction of the penis, osteomyelitis, acute papillary necrosis of kidneys, chronic renal failure, occlusion of retinal arteries and blindness, pulmonary hypertension, bone marrow necrosis induced dactilitis in children, chronic punched-out ulcers around ankles, hemiplegia, and cranial nerve palsies are only some of the presentation of the disease. Eventually, the median age of death was 42 years for males and 48 years for females in the literature[4], whereas it was 29.3 and 32.3 years, respectively, in the present study. The great differences between the survival should be searched with further studies. As a result of such a great variety of clinical presentation, it is not surprising to see that the mean body weight and BMI were significantly reduced in the SCDs cases in the present study. On the other hand, as an opposite finding to some other reports[15-16], the mean heights were nearly similar in the SCDs and control cases in the present study. Probably due to the significantly lower mean body weight and BMI, mean values of the LDL-C, ALT, and systolic and diastolic BPs were also significantly lower among the patients, which can be explained by definition of the metabolic syndrome.[17-19]

Normally the BMI may be determined by a complex network of hormonal, nutritional, physical, and genetic factors. For example, it was reported that approximately 70 genes may take role in the regulation of bone mass[20], and some genes were shown to affect both the BMI and bone geometric parameters.[21] The same results were also shown even in animals that the results indicate substantial additive genetic control of Brahman body weight to hip height ratio.[22] For example, leptin is an adipose hormone produced mainly by adipocytes, and it acts centrally to control body weight.[23] Leptin is also expressed on osteoblasts,[24] and acts as a skeletal growth factor[25] and promotes bone mineralization.[24] The pleiotropic effect of leptin on BMI and bone geometry may also be supported by the evidence of the genetic correlation of leptin with BMI and bone geometry.[26] On the other hand, the body length growth velocity was found not to be affected by genes in some studies.[27] Whereas we detected that although the significantly retarded mean body weight and BMI in the SCDs cases (p= 0.000 for both), the mean body heights were similar in the patients and control groups in the present study (p>0.05). In conclusion, although the body weight can significantly be retarded by SCDs, the body height may strongly be determined by heredity.

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