RELATIONSHIP BETWEEN DEPRESSION, ANXIETY, QUALITY OF LIFE AND VASO-OCCLUSIVE CRISIS IN ADOLESCENTS WITH SICKLE CELL DISEASE

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ABSTRACT

***Aims**: To explore the relationship between frequency of pain episodes and depression, anxiety, and health related quality of life (HRQOL) in adolescents with sickle cell disease (SCD).*

***Materials and methods**: Ten males and twelve females, between the ages of 12 and 19, selected during admittance to pediatric hematology outpatients of city hospital with a vaso-occlusive crisis in the period between September 2012 and February 2013, were included in the study. Beck Depression (BDI) and Anxiety Inventories (BAI), and Short Form Health Survey (SF-36) were used to evaluate depression, anxiety and HRQOL.*

***Results**: Nine (40.9%) of the adolescents with SCD had BDI scores higher or equal to 17. In the whole group, 3 (13.6%) patients did not have anxiety, while 14 (63.6%) of them had mild and 4 (18.2%) had moderate anxiety. Physical and mental components of HRQOL were not correlated to BDI and BAI scores. Patients with frequent pain episodes (>10 annually) were found to have tendency to depression and anxiety while their mental and physical components of HRQOL were lower than patients with infrequent pain episodes (<5 annually).*

***Conclusion**: Depression and anxiety in adolescents with SCD was found relatively high, while Physical and Mental components of HRQOL were relatively low. However, Physical and Mental Health of the patients was not affected from depression and anxiety presence. Pain episode frequency might be the main determinant of higher depression and anxiety and lower HRQOL component scores.*

***Key words**: Sickle cell disease, adolescent, depression, anxiety, quality of life.*

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Introduction

Sickle cell disease (SCD) is an autosomal recessive genetic disorder of hemoglobin structure manifested with acute episodes of ischemic pain crisis due to obstruction of blood vessels by sickled red blood cells. This episode is a complex process of varying frequency and severity[1]. On average, children and adolescents with SCD experience five to ten episodes per year, although most of the children experience a painful episode over a 2-week period[2].

Children and adolescents with SCD face many challenges associated to living with a chronic condition that requires lifelong medical management. Vaso-occlusion is also a major contributor to morbidity and mortality.

Recurrent, acute pain that often requires emergency management is the hallmark of vaso-occlusion and negatively affects quality of life. Palermo previously documented that pain may lead to impairment in performing age-appropriate physical, mental, and social activities in daily life in children with SCD[3]. A number of studies have shown that the frequency of neuropsychiatric problems in adolescents with SCD is higher than normal controls[4,5]. Among the neuropsychiatric problems, depression, anxiety disorders, learning problems, and attention deficit disorders are commonly reported(6). Current literature has shown that adolescents with SCD have a higher risk of depression and anxiety[7,8].

HRQOL in adolescents with SCD have also been studied previously. The majority of these stud-

ies have reported a lower HRQOL when compared to the normal controls[9].

SCD is highly prevalent among African, Caribbean, Asian and Mediterranean populations and it is also common in Turkey. The prevalence of sickle cell anemia trait, was found to be 0.5% in Turkey while it was 0.4% in Eastern Mediterranean Region[10]. Despite its high prevalence no study has examined the impact of pain episodes on comorbid psychological complications and HRQOL in Turkey. In this study the relationship between frequency of pain episodes and depression, anxiety, and HRQOL in adolescents with SCD was explored.

Methods

Twenty two Turkish adolescents, 10 male and 12 females, between the ages of 12 and 19 with SCD were included in the study. They were selected during admittance to pediatric hematology outpatients of city hospital with vaso-occlusive crisis between September 2012 and February 2013. Informed consents of the patients and their parents were obtained by researchers. The study was carried out with the approval of the Human Medical Ethics Committee of the Mustafa Kemal University Faculty of Medicine in Hatay.

Questionnaire form

Form consisted of questions addressing demographics including age, gender, educational status, monthly income and clinical characteristics including history of splenectomy or psychiatric disorder. Patients were grouped according to the frequency of pain episodes they suffered in last year. Annual attack frequency lower than 5 was named group 1, while 5 to 10 attacks group 2, and more than 10 attacks in a year was included in group 3.

Beck anxiety inventory (BAI)

It is a self-assessment tool used to determine frequency of anxiety symptoms experienced by an individual, which was developed by Beck et al. in 1988. It includes 21 items, which are rated by a 3-points Likert type scale. Turkish reliability and validity studies were performed by Ulusoy et al. in 1998[11]. In this tool, 8-15 points is considered as mild anxiety while 16-25 points and 26-63 points are considered as moderate and severe anxiety, respectively.

Beck depression inventory (BDI)

This tool measures physical, emotional, cognitive and motivational symptoms observed in depression. It includes 21 items, which are rated by a 3-points Likert type scale. Higher total scores indicate increased severity of depression[12]. Turkish adaptation, validation and reliability studies were performed by Hisli et al. who reported cut-off point as 17[13].

Short form Health Survey (SF-36)

It is a self-assessment tool used to measure quality of life in individuals with a physical disease, which was developed by Ware and Sherbourne in 1992[14]. Turkish validity study was performed by Koçyiğit et al. 1999[15]. It has 8 subscales including physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). The first five scales are summarized into the physical health dimension (PHCS) and the last three scales into the mental health dimension (MHCS). Each subscale is rated between 0 and 100 points.

Statistical analysis

The data were analyzed using the SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Fischer's test was used for comparisons between categorical variables. Continuous variables which were not normally distributed were compared between groups using The Kruskal-Wallis and Mann-Whitney U tests. Spearman correlation coefficients were used to assess relationships among depression, anxiety, physical health dimension and mental health dimension scores of patients. $p<0.05$ was considered as statistically significant in all analysis.

Results

Most of the patients live in rural area and reported low income (Table 1).

Of the patients 12 (%54.5) were female, while 10 were (%45.5) male. Both were similar in age ($p=0.762$). Median age of the females was 15.5 (range; 12-18), while it was 15.5 (range; 12-18) in males.

Nine (40.9%) of the adolescents with SCD had BDI score higher or equal to 17. Median BDI score was 13 (min-max;6-26) in males, while it is 9.5 (min-max;2-38) in females ($p=0.689$). Median score of BDI was 10.5 (min-max;2-20) in males, 12 (min-max; 8-40) in females ($p=0.247$).

Table 2 shows BDI scores and BAI results according to gender.

Of the 22 patients with SCD, 3 (13.6%) patients did not have anxiety. All of them were males. Fourteen (63.6%) of them had mild anxiety. Eight (36.4%) of them were female while 6 (27.3%) were male. Only four (18.2%) patients had moderate anxiety. Three of them were female. Only one female (4.5%) patient had severe anxiety. However no difference was found in anxiety rate between male and females.

	n(%)
Education	
Primary school	12 (54.5%)
Secondary school	10 (45.5%)
Economic class	
Low income	17 (77.3%)
Moderate	3 (13.6%)
High	2 (9.1%)
Residence	
Rural	12 (54.5%)
Suburban	3 (13.6%)
Urban	7 (31.8%)
Maternal education	
Illiterate	1(4.5)
Primary school	20 (91%)
Secondary school	1(4.5)
Paternal education	
Illiterate	1 (4.5)
Primary school	19 (91%)
Secondary school	2 (9.1)
History of psychiatric disorder	3 (13.6%)
History of suicidal thoughts	1 (4.5%)

Table 1: Some socio-demographic parameters of patients with SCD.

Median PHCS of the males was 51.5 (32.4-68.8), while it was 44.3 (31.4-69) in females. Median MHCS of the males was 53.2 (37-74.3), while it was 54.6 (15.3-83.6) females. Both components of HRQOL were similar according to gender (p=0.509, p=0.742, respectively). Scores of Health-Related Quality of Life of the Adolescents with SCD was shown in table 3.

PHCS of the patients was not correlated to BDI and BAI scores (p=0.591, p=0.203, respectively). Likewise MHCS of the patients was neither correlated to BDI nor BAI scores (p=0.236, p=0.439 respectively).

	Male (n=10)	**Female (n=12)**	**p**
History of surgery	3 (30%)	1 (8.3%)	0.293
Family History of Blood Disorders	7 (70%)	9 (75%)	1
Family History of Blood Disorders-Related Death	8 (80%)	7 (75%)	1
Pain Episodes			
1-4	6 (60%)	5 (41.7%)	0318
5-9	3 (30%)	5 (33.3%)	
≥10	1 (10%)	3(25.0%)	
BDI Scores			
<16	6 (60.0%)	7 (58.3%)	1
≥17	4 (40.0%)	5 (41.7%)	
Anxiety			
None or Mild	9 (90.0%)	8 (66.7%)	0.323
Moderate to Severe	1 (10.0%)	4 (31.3%)	

Table 2: Some clinical parameters according to gender in SCD patients.

	Male Median (min-max)	Female Median (min-max)	p
Physical functioning	62.5 (40-90)	65.0 (35.-95)	0.667
Role-physical	50.0 (0-100)	25.0 (0-100)	0.247
Bodily pain	31.5 (12-100)	37.0 (22-100)	0.712
General health	37.5 (10-72)	35 (20-67)	0.643
Vitality	55.0 (15-75)	45.0 (30-80)	0.814
Social functioning	75.0 (37.5-100)	62.5 (0-100)	0.422
Role-emotional	33.3 (0-100)	16.6 (0-100)	0.889
Mental health	58.0 (36-68)	64.0 (20-76)	0.163
Physical health component summary (PHCS)	51.5 (32.4-68.8)	44.3 (31.4-69)	0.509
Mental health component summary (MHCS)	53.2 (37-74.3)	54.6 (15.3-83.6)	0.742

Table 3: Scores of Health-Related Quality of Life of the Adolescents with SCD, according Gender.
**Mann Whitney U Test.*

Patients with frequent pain episodes (>10 annually) were found to have tendency to depression and anxiety, and their mental and physical components of HRQOL were lower than patients with infrequent pain episodes (<5 annually). Relationship between depression, anxiety, health-related quality of life and pain crisis frequency was shown in table 4.

	Group 1 (n=11) Median (min-max)	Group 2 (n=7) Median (min-max)	Group 3 (n=4) Median (min-max)	p*	p 1 vs 2	p 1 vs 3	p 2 vs 3
BDI Scores	9 (2-26)	11 (6-17)	22 (17-38)	0.033	0.615	0.018	0.020
BAI Scores	11 (2-15)	12 (8-20)	20.5 (10-40)	0.049	0.158	0.036	0.088
PHCS	53.2 (32.4-68.8)	51.2 (37.4-69)	34.6 (31.4-37.4)	0.030	0.892	0.019	0.013
MHCS	60.2 (51.8-83.6)	37 (29.6-78.2)	37.5 (15.3-57.5)	0.037	0.063	0.026	0.450

Table 4: Relationship between Depression, Anxiety, Health-Related Quality of Life and Pain Episode Frequency.
**Kruskal-Wallis and Mann Whitney U Tests were used.*

Discussion

The results of the present study have great value for showing the significant relationship between pain episode frequencies, HRQOL and mental health. To our knowledge it is the first study in Turkish adolescents with SCD.

Median of BDI scores in the group was relatively high and this might be an important indicator of depression. Although the patients were not examined or psychiatrically evaluated according to DSM-IV criteria, there appears to be a positive correlation between the frequency of pain episodes and depressive symptoms. It was similar in both sexes. Also no significant relationship could be found between physical and mental health components of HRQOL of the patients and depression.

Pain episode frequency might be the main determinant of higher depression. Previously published studies established that adolescents with chronic diseases might be at risk for psychosocial problems and they have higher risk of depression[16-18].

Although the risk factors of depression in SCD are not completely known, there is evidence that disease related factors may have an influence. Coping with complications of a chronic disease with pain episodes may influence psychosocial and cultural aspects of health. Disease duration and intensity inhibits coping skills leading to social isolation school absence and a decrease in daily activities. Screening and assessing depression and anxiety in SCD especially with frequent pain attacks, is an effective management strategy.

Anxiety was also found common in adolescents with SCD. No difference was found in comparison according to sex. Physical and mental health components of HRQOL were not affected by anxiety presence. Pain episode frequency is the main determinant of anxiety rate. Pain episodes and following hospitalizations may cause fear and worry. Also during adolescence social relationships with peer groups are affected because of body image, delayed puberty or introversion in adolescents with SCD. These changes appear to contribute the increased risk of anxiety[6,19]. Furthermore the frequency of vaso-oclussive attacks is also related with an increased risk of anxiety symptom[17].

Physical and Mental components of HRQOL in adolescents with SCD was found relatively low. No difference was found in comparisons according to sex. Physical and Mental Health of the patients was not affected from depression and anxiety presence. Pain episode frequency might be the main determinant decreasing HRQOL component scores. HRQOL also have been studied previously in adolescents with SCD. Those studies have reported a lower HRQOL when compared to the normal controls[9, 20]. Adolescents with SCD were frequently hospitalized for acute complications such as splenic sequestration, infection and stroke. Also management of chronic problems including gallstones, failure to thrive, pulmonary or adrenal disease may affect school absence and daily life. All these factors might have negative impact on HRQOL[1,21].

The findings must be considered in light of several limitations. First, the participants were selected during outpatient's visits and in any case suffering from complications of SCD. Symptoms of the disease and other problems might have affected patient's responses to questionnaires. Second, patients were evaluated only at study entry. Therefore, changes over the year in relationship to pain episodes could not be evaluated. Third, the sample size was small to define relationships that were eligible to generalize. Similar studies with larger sample size are needed. Fourth, self-assessment tools were used for depression; any specialists have made no objective diagnosis of depression.

Conclusion

Depression and anxiety in adolescents with SCD was found relatively high, while physical and mental components of HRQOL were relatively low. However, Physical and Mental Health of the patients was not affected from depression and anxiety presence. Pain episode frequency seemed to be the main determinant of higher depression and anxiety and lower HRQOL component scores.

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