The Psychopathology, Depression, and Anxiety Levels of Children and Adolescents With Vasovagal Syncope

A Case-Control Study

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Abstract: Vasovagal syncope constitutes 61% to 80% of syncope cases in the pediatric age group. Syncope is frequently associated with psychopathologies such as depressive disorders, anxiety disorders, somatization disorders, etc. Our study aims to evaluate vasovagal syncope cases in terms of additional psychopathologies, depression, and anxiety levels with a control group. A total of 97 people were included in the study (47 cases and 50 controls). After conducting a cardiological examination, the participants were evaluated for psychopathologies using Kiddie-Sads-Present and Lifetime Version, Child Depression Inventory, and Screen for Child Anxiety Related Emotional Disorders. The case group had a higher rate of psychopathology compared with the control group. Depression, social anxiety disorder, generalized anxiety disorder, separation anxiety, and conversion disorder were significantly higher in the case group than in the control group. Syncope in children can be an underlying psychopathology or the clinical manifestation of a psychosomatic condition. Psychological assessment, which could offer beneficial contributions to the diagnosis and treatment of syncope, was considered necessary for a holistic evaluation of patients.

Key Words: Vasovagal syncope, psychopathology, depression, anxiety

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Syncope is defined as a sudden, self-limited loss of consciousness and postural tone followed by spontaneous and complete recovery without any neurological sequelae (Singhi and Saini, 2018). It can occur at different rates across all age groups with varying etiological factors. Common causes of syncope can be listed as hypovolemia, hypoxemia, hypoglycemia, hypotension, vasodilation, and insufficient cardiac systole (Feit, 1996; Friedman et al., 2012). Its incidence in the children and adolescent age group is 15% (Johnsrude, 2000). It has a female predominance, and this difference becomes even more conspicuous during the adolescence stage (Bo et al., 2009; Wong and So, 2002). Syncope can be classified into three main groups in the pediatric age group. These include neurally mediated, cardiogenic, and noncardiogenic syncope (Kaçar Bayram et al., 2016). Neurocardiogenic syncope, also known as vasovagal syncope, accounts for 61% to 80% of the cases in the pediatric age group (Massin et al., 2004). Vasovagal syncope occurs as a result of vasodilation and bradycardia resulting from the suppression of the sympathetic nervous system by factors that include prolonged standing, standing up quickly, intense emotional stimuli, etc. (Kaçar Bayram et al., 2016; Wieling et al., 2004). A patient's history offers the best diagnostic element for vasovagal syncope. Head-up tilt test (HUTT) can be performed if the diagnosis is not clear and there is increased likelihood of vasovagal syncope after undertaking anamnesis, physical examination, laboratory, and imaging methods (Calkins et al., 1995; Natale et al., 1995). Different HUTT protocols are beneficial in the diagnosis of vasovagal syncope. However, it is not fully standardized, and its specificity and reproducibility are controversial (Moya et al., 2001). Although vasovagal syncope is often a benign condition, it can be alarming for patients, families, and teachers due to the risk of injury that can be involved (Anderson et al., 2012). Less commonly encountered cardiac-originating syncope indicates a serious health concern (Massin et al., 2007; Yeh, 2015).

Alhuzaimi et al. (2018) compared patients with syncope in the adult age group with a control group and found no difference between the groups in terms of depression, anxiety, and phobia. However, a statistically significant difference for somatization disorder was found between the groups. In the same study, a subanalysis of the case group showed that patients with six or more syncopal episodes had higher rates of depression, anxiety, and somatization disorder compared with those with lesser syncopal attacks (Alhuzaimi et al., 2018). In another study, Giada et al. (2005) reported that they found psychopathology in 71% of patients with vasovagal syncope, with a prevalence of somatization disorders (29%), anxiety disorders (28%), and mood disorders (18%). In a 2-year follow-up study conducted in children, Hyphantis et al. (2012) reported that depressive symptoms were more in patients with neurocardiogenic syncope than the control group and that a positive correlation between the number of syncopal episodes and depressive symptoms existed. In a study of children with syncope in which depression and anxiety symptoms were investigated, Ding et al. (2010) found higher depression and anxiety levels in the case group than in the control group.

Although the association of vasovagal syncope and psychopathology has been frequently investigated in the adult age group, the number of such investigations for the childhood period is limited. Although the above-mentioned studies investigated the symptoms of depression and anxiety in children and adolescents, there is no study in which all psychopathologies were screened, and psychopathologies identified on the outcome of structured psychiatric interviews. This study aims to determine the psychopathology of children and adolescent patients with vasovagal syncope using a structured psychiatric interview to identify their depression and anxiety levels with self-report scales and to reveal the differences by comparing them with a control group.

METHODS

This prospective case-control study was conducted between February 1 and June 30, 2020 after obtaining ethics committee's approval (date: October 25, 2019; issue number: 2019/0014). Participants were informed about the study according to the Declaration of Helsinki, and their written consents were obtained.

A total of 97 children and adolescents (ages between 8 and 18) including 47 in the case group and 50 in the control group were included in the study. Patients in the case group consisted of syncope cases in which neurological pathologies were ruled out. The control group was composed of individuals who presented for routine cardiological examination. Individuals with a known chronic disease or psychopathology as

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well as those using medication(s) were excluded from the study. The case and control groups were evaluated by a pediatric cardiologist, and detailed physical examinations were performed. Blood pressure was measured for each patient, electrocardiography, echocardiography (ECHO), and blood tests (blood glucose, thyroid function test, hemogram, vitamin B12, folic acid levels, etc) were evaluated. During the cardiological evaluations, pathological ECHO findings in two patients and anemia in one patient resulted in their exclusion from the study.

Psychiatric Evaluation

All participants were examined by a child and adolescent psychiatrist who was blinded to group distribution. The Kiddie-Sads-Present and Lifetime Version (K-SADS-PL) semistructured diagnostic interview was used for psychopathology screening. K-SADS-PL is a semistructured diagnostic interview that determines past and present psychopathologies in children and adolescents according to the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (*DSM-IV*) diagnostic criteria (Kaufman et al., 1997). The interview screens for many psychiatric diagnoses such as depressive disorders, anxiety disorders, psychotic disorders, eating disorders, attention deficit hyperactivity disorder, and tic disorders. The validity and reliability study of the interview in our language has been done previously (Gökler et al., 2004). Participants and their parents were asked to fill out the Child Depression Inventory (CDI) and the Screen for Child Anxiety Related Emotional Disorders (SCARED) forms to determine the levels of depression and anxiety. CDI provides information on the psychological state over the past 2 weeks in children and adolescents. The scale consists of 27 items, with scores ranging from 0 to 2. The cutoff score was set at 19. High scores indicate an increase in the severity of depression (Kovacs, 1981). The validity and reliability study of the scale was conducted by Öy (1991). SCARED is a self-report scale with a total of 41 items used for anxiety screening in children and adolescents. The scale provides the opportunity to compare five different anxiety domains (Birmaher et al., 1997). The scale's validity and reliability study was carried out by Çakmakçı (2004).

Statistical Analysis

SPSS 22.0 package program was used for statistical analysis. Variables were evaluated for normal distribution using the Kolmogorov-Smirnov and visual methods (histograms and probability plots). Average and standard deviation were used for normally distributed variables for descriptive statistics. Student's *t*-test was used to evaluate the differences in parametric data. Mann-Whitney *U*-test was used to evaluate nonparametric data. Chi-square test was used to evaluate categorical data. Univariate analysis was performed to assess the syncope predictability of scales. In the analysis, parameters with a value of $p < 0.05$ among those found to be significant in the association with syncope were taken into a multivariate analysis. Backward stepwise method was used in the logistic regression analysis (model; $\chi^2[3] = 25.884$, $p < 0.001$, Nagelkerke $R^2 = 0.312$). A p value of less than 0.05 was considered statistically significant.

RESULTS

There were 47 (28 girls/19 boys) children and adolescents in the case group and 50 (25 girls/25 boys) in the control group. The mean age of the case group was found to be 13.30 ± 2.58, and that of the control group was 12.48 ± 2.08. There was no statistically significant difference between the groups in terms of sex and age ($p = 0.344$ and $p = 0.063$, respectively). The clinical features of the case group obtained from the outcome of cardiological evaluation are provided in Table 1.

Major depressive disorder (MDD) was detected in 10 (21.3%) participants of the case group and 1 (2%) of the control group. There was a statistically significant difference between the groups ($p = 0.003$). In the case group, separation anxiety disorder was detected in eight (17%) patients; social anxiety disorder (SAD), generalized anxiety disorder

TABLE 1. Characteristics of Vasovagal Syncope

	n	%			*n*	%
Position			Sudden cardiac death in the family			
Standing	45	95.7	Present		5	10.6
Sitting	2	4.3	Absent		42	89.4
Duration of pain			Heart disease in the family			
Short	46	97.9	Present		13	27.7
Long (more than 15 min)	1	2.1	Absent		34	72.3
Exercise association			Associated symptom			
Present	4	8.5	Dizziness	Absent	6	12.8
				Present	41	87.2
Absent	43	91.5	Light-headedness	Absent	8	17
				Present	39	83
Spasm			Palesness	Absent	37	78.7
				Present	10	21.3
Present	2	4.3	Chest pain	Absent	43	91.5
				Present	4	8.5
Absent	45	95.7	Palpitations	Absent	38	80.9
				Present	9	19.1
Incontinence			Headache	Absent	37	78.7
				Present	10	21.3
Present	2	4.3	Nausea	Absent	33	70.2
				Present	14	29.8
Absent	45	95.7	Sweating	Absent	37	78.7
				Present	10	21.3

TABLE 2. Comparison of the K-SADS-PL–Based Diagnoses Between Groups

	Case, *n* (%)	Control, *n* (%)	*p*
MDD	10 (21.3)	1 (2)	0.003*
Adjustment disorder	0 (0)	1 (2)	0.330
SAD	9 (19.1)	0 (0)	0.001*
GAD	9 (19.1)	1 (2)	0.006*
PD	2 (4.3)	0 (0)	0.141
Posttraumatic stress disorder	1 (2.1)	0 (0)	0.300
Obsessive compulsive disorder	3 (6.4)	1 (2)	0.278
Separation anxiety disorder	8 (17)	0 (0)	0.002*
Specific phobia	14 (29.8)	10 (20)	0.264
Enuresis	9 (19.1)	8 (16)	0.684
Encopresis	2 (4.3)	0 (0)	0.141
Attention deficit/hyperactivity disorder	8 (17)	4 (8)	0.177
Oppositional defiant disorder	3 (6.4)	1 (2)	0.278
Conduct disorder	2 (4.3)	0 (0)	0.141
Tic disorder	0 (0)	1 (2)	0.330
Conversion disorder	9 (19.1)	0 (0)	0.001*
Anorexia nervosa	2 (4.3)	0 (0)	0.141

*Statistically significant.

(GAD), and conversion disorders were detected in nine (19.1%) patients each. There was a statistically significant difference between the groups ($p = 0.002$, $p = 0.001$, $p = 0.006$, and $p = 0.001$, respectively). The comparison of the case and control groups based on the psychiatric diagnoses they received based on of K-SADS-PL outcome is given in Table 2.

A statistically significant difference was found between the case and control groups in terms of the total scores of CDI and SCARED filled out by children and adolescents ($p = 0.001$ and $p = 0.002$, respectively). In the parent versions of the CDI and SCARED, a statistically significant difference was found in the comparison of CDI total scores ($p = 0.004$); however, no statistical significance was identified ($p = 0.052$) for SCARED despite higher SCARED total scores in the case group. The comparison in terms of CDI and SCARED scores filled out by the participants and parents in the case and control groups is shown in Table 3.

After comparing the case and control groups in terms of CDI and SCARED scores, the statistically significant values that could be used as predictive factors for syncope were investigated. It was determined that total scores of the CDI and SCARED child forms and panic disorder (PD) subscale scores of SCARED child form predicted vasovagal syncope. The results are shown in Table 4.

DISCUSSION

In this prospective case-control study, groups were compared in terms of cardiac symptoms and accompanying psychopathologies. According to the study, statistically significant high levels of depression and anxiety were determined in the case group. In addition, statistically significant high rates of MDD, SAD, GAD, separation anxiety disorder, and conversion disorder diagnoses were found in the case group.

TABLE 3. Comparison of the Survey Scores

	Case (Mean ± SD)	Control (Mean ± SD)	*p*
CDI-total score of child form	12.49 ± 7.17	7.58 ± 3.87	0.001*
CDI-total score of parent form	10.28 ± 6.59	6.74 ± 4.88	0.004*
SCARED-total score (child form)	28.34 ± 15.48	19.72 ± 10.71	0.002*
PD	8.11 ± 5.97	3.90 ± 3.58	0.001*
GAD	6.32 ± 4.94	3.78 ± 3.33	0.004*
Separation anxiety disorder	5.81 ± 3.70	5.12 ± 2.73	0.303
SAD	5.91 ± 3.01	5.38 ± 2.59	0.350
School phobia	2.19 ± 1.55	1.34 ± 1.36	0.005
SCARED-total score (parent form)	20.74 ± 13.74	15.50 ± 12.53	0.052
PD	5.34 ± 4.41	3.44 ± 4.13	0.031*
GAD	4.96 ± 3.93	3.28 ± 3.40	0.027*
Separation anxiety disorder	3.85 ± 3.46	3.18 ± 2.93	0.305
SAD	4.55 ± 3.67	5.32 ± 2.69	0.247
School phobia	2.04 ± 1.69	1.34 ± 1.57	0.037*

*Statistical significant.

TABLE 4. Predictive Values of Scales for Syncope

	Univariate Analyses			Multivariate Analyses		
	OR	**% 95 CI**	***p***	**OR**	**% 95 CI**	***p***
CDI-total score						
Child form	1.196	1.083–1.321	<0.001	1.192	1.040–1.367	0.012*
Parent form	1.120	1.032–1.216	0.070			
SCARED-total score						
Child form	1.053	1.017–1.090	0.004	0.914	0.836–0.999	0.047*
Parent form	1.032	0.999–1.065	0.058			
SCARED-child form						
PD	1.212	1.09–1.347	<0.001	1.350	1.075–1.695	0.010*
GAD	1.162	1.043–1.296	0.007			
School phobia	1.514	1.114–2.059	0.008			
SCARED-parent form						
PD	1.114	1.007–1.232	0.037			
GAD	1.137	1.011–1.279	0.032			
School phobia	1.318	1.007–1.723	0.044			

CI indicates confidence interval; OR, odds ratio.

Besides peripheral autonomic dysfunctions, disturbances in serotonergic systems in the central nervous system play a role in vasovagal syncope. The involvement of serotonin in the vasovagal syncope mechanism supports the relationship between neurocardiogenic syncope and psychopathologies (Hainsworth, 2004). In addition, it has been stated that the quality of life deteriorating with recurrent syncope attacks contributes to the formation of psychopathology (Anderson et al., 2012).

The relationship between syncope and psychological factors is often shown in studies. Psychopathology is detected in up to 81% of patients with syncope (Giada et al., 2005; Kouakam et al. 2002; Ventura et al., 2001). Especially depression, anxiety disorders, and somatic disorders have been detected at high rates in patients with syncope (D'Antono et al., 2009; Giada et al., 2005; Hyphantis et al., 2012; Ng et al., 2019). In a study in which children with neurocardiogenic syncope were followed up for 2 years, it was stated that the case group had depressive symptoms that is 2.6 times more than that of the control group and that children whose depressive symptoms improved during follow-up did not experience syncopal relapse (Hyphantis et al., 2012). In another study investigating psychopathologies in children with vasovagal syncope, it was determined that the case group received low marks in statements carrying positive content and high marks in sentences with negative content in the depression scale. Considering the total scores, the depression scores of the case group were found to be higher (Ding et al., 2010). In contrast to these studies, there was no difference between the groups in a study categorizing children with syncope into a positive and negative tilt according to HUTT outcome and comparing them in terms of depression (Blount et al., 2004). However, this study received criticisms for reasons including lack of appropriate controls, low sensitivity of the HUTT, and failure of negative test results to exclude the diagnosis (Hyphantis et al., 2012). Our study found higher rate of depression diagnosis and CDI scores in the case group, a finding that is similar to other studies documenting high depression rates in patients with syncope. Our study has more advantages than other studies in the sense that diagnosis of depression was established on the outcome of a semistructured diagnostic interview, referral to family's information was implemented, and this was supported with CDI scale scores. If children and adolecents score higher on the scale, they are at high risk for depression.

Patients with syncope in adult studies were often divided into subgroups and were compared in pairs. As a result, higher rates of anxiety were found in the vasovagal syncope groups (Atici et al., 2020; D'Antono et al., 2009). In studies where patients with syncope were compared with a control group, anxiety rates were high among the psychopathologies (Giada et al. 2005; Ng et al., 2019). In the study of Rafanelli et al. (2013), adult patients with syncope ere assessed according to *DSM* diagnostic criteria. The psychopathologies in patients with syncope were listed according to their detection rates as specific phobia, SAD, GAD, depression, PD, somatization disorder, etc. (Rafanelli et al., 2013). In line with previous data, our study found high rates of both depression and anxiety disorders according to K-SADS-PL in the case group. In addition, the total scores of the SCARED scale filled out by children and parents were higher in the case group. A total score of 25 or more from the SCARED suggests anxiety disorders. These data are also consistent with a study conducted in children with vasovagal syncope (Ding et al., 2010). However, Ding et al. evaluated cases in their study using scales only. Our study stands out due to the implementation of K-SADS-PL for psychopathological screening. However, SCARED subscales and K-SADS-PL did not yield similar results in terms of PD, SAD, and separation anxiety disorder. It was thought that the difference between the two data stems from the fact that the scales are self-report scales.

Somatization disorders are also one of the psychopathologies that may be associated with and should be considered in the differential diagnosis of syncope. Conversion disorders are among the causes of childhood syncope and are more common especially in young girls. In conversion disorders, the person avoids an unpleasant emotional state in an abnormal manner (Moodley, 2013). Conversion disorders can be easily differentiated from other causes of syncope based on clinical presentation and medical history. However, patients may receive unnecessary treatments in cases where syncope and conversion disorder coexist (Kaçar Bayram et al., 2016). In adult studies, rates of somatization disorder up to 28% in case groups are reported (Giada et al. 2005; Linzer et al., 1991; Rafanelli et al., 2013). Similarly, in our study, this rate was found to be 19.1%. Analyzing syncope and somatization disorders in children and adolescents concurrently in our study is important for raising awareness as a result of high detection rates in these children.

Limitations

Our study stands out by using K-SADS-PL for psychopathological screening and by the additional use of CDI and SCARED for the

severity of common diseases such as depression and anxiety disorder in children and adolescents with syncope. Despite this, failure to use HUTT even though it has low sensitivity and the fact that the case and control groups were not evaluated for quality of life are possible limitations to our study.

CONCLUSIONS

Despite neurocardiogenic syncope being a benign condition, affected children are noted to have problems related to depression, anxiety, somatization, and dissociation disorders when evaluated from a psychological point of view. Syncope in children may present as an underlying psychosomatic illness or a manifestation of psychopathological predisposition. Our study found a high rate of psychopathologies associated with vasovagal syncope in children and adolescents. In addition, it was revealed that self-report questionnaires filled out by children and adolescents could predict syncope. With the scale usage put in place in outpatient settings, the cases at risk can be identified within a short period and referred for psychiatric examination. As a result, unnecessary treatment, frequent hospital admissions, and further examination costs can be minimized. There is a need for studies examining the association of vasovagal syncope and psychopathology, the effect of syncope on quality of life, and the coping skills of children and adolescents.

DISCLOSURE

The authors declare no conflict of interest.

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