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Chapter

Prevalence and Treatment of Anxiety Disorders Comorbidities in a Clinical Romanian Sample of Children and Adolescents with Psychiatric Disorders

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Abstract

The prevalence of anxiety disorders is known to be increasing among children and adolescents and often co-exist with another psychiatric disorder. There is some evidence that anxiety disorders in nonwestern countries have the same comorbidity patterns as in other world regions and may have similar predictors including age and gender. However, more evidence from different countries is needed. The major goal of the study was to evaluate the prevalence of anxiety disorders in a clinical setting and to describe the comorbidity patterns and predictors. We conducted a retrospective study on the admitted patients in the Clinic of Pediatric Psychiatry from Cluj-Napoca, Romania, between January 2017 and December 2017. A clinical sample of 2471 patients aged between 3 and 18 years with psychiatric disorders, assessed and/or treated in the clinic, was included into the study. About 9.88% patients (N = 244) of the clinical sample were diagnosed with an anxiety disorder as a primary diagnosis. About 79.5% of the selected sample had a comorbid disorder and 34.4% had an anxiety or mood comorbidity. Preference in treatment was nonpharmacological and, according to the degree of severity, SSRI medication. Our results underline the significant prevalence of anxiety disorders and the high rate of comorbidities.

Keywords: anxiety disorders, prevalence, comorbidities, children and adolescents, pharmacological treatment

1. Introduction

1.1 Diagnostic systems

Anxiety disorders (ADs) are one of the most important conditions in child and adolescent psychiatry with a heterogeneous spectrum of clinical manifestations and variable levels of severity. ADs are commonly found at all levels of mental health services and involve the use of large resources for the appropriate assessment and therapeutic approach.

Anxiety disorders (ADs) are classified in *DSM-5* (APA) [1] or *ICD-10* (WHO) [2] diagnostic systems. Although developmental pathway features or a variety of other factors can significantly influence clinical presentation, both classification systems describe common clinical features for AD [3] and use roughly the same diagnosis criteria for children and adolescents as compared to adults. *ICD-10*, in contrast to *DSM-5*, uses several separate diagnostic codes for children. The new proposed disorder categories in *ICD-11* are largely the same as those in the equivalent section of *DSM-5* and recognize that the same disorders occur across the life span with developmentally distinct presentations [4]. Therefore, diagnoses in *ICD* are made based on essential features, with the expectation that the clinicians will use their clinical judgment on exact symptom counts and duration in a manner that is consistent with the diagnostic guidance provided [5]. Although this descriptive diagnosis criteria facilitated the development of diagnostic instruments for AD assessment [6–10], clinicians should be aware of their limitations, particularly related to developmental issues in obtaining self-reports from children and adolescents [11]. Due to these considerations, the core diagnostic criteria might present differently in the young, requiring special assessment strategies.

1.2 Prevalence

Mental disorders affect a significant number of children and adolescents worldwide [12]. Among the children and adolescent psychiatric disorders, ADs are a representative category. Prevalence rates reported in studies are varying considerably sometimes, depending on the sample, assessment methods, the assessed period, or study design, between 6.5 [12] and 8.3% [13] and up to 27% [14]. In a meta-analysis of multiple data sets, Costello et al. have found the prevalence of 10.2% for any AD, 5.4% for specific phobia (SPEC), 3.6% for social phobia (SOC), 2.6% for separation anxiety disorder (SAD), 1.7% for generalized anxiety disorder (GAD), and 0.8% for panic disorder (PD) [15]. In the National Comorbidity Survey Replication and Adolescent Supplement, Kessler et al. reported a lifetime prevalence of any anxiety disorders of 32.4%, for the ages of 3–17 [16]. Spence et al.'s results are slightly different, with reported prevalence rates of 2.3% for social phobia (SOC), 4.3% for separation anxiety (SAD), and 2.2% for generalized anxiety disorder (GAD) [17]. Previous studies reported similar prevalence rates in diverse cultures [18–20].

In terms of onset age, Merikangas et al. found a prevalence of 31.4% for the age group of 13–14 years, 32.1% for the age group of 15–16 years, and 32.3% for the age group of 17–18 years, with particularly high rates of specific phobia (SPEC) [13]. Generalized anxiety disorder and social anxiety disorder are among the most common AD in youth [21]. Panic disorder is rare and occurs in adolescents rather than in young children [15, 21]. Findings from different studies have demonstrated that, in the general population, anxiety symptoms first decrease during early adolescence and subsequently increase from middle to late adolescence [22]. Separation anxiety disorder and specific phobias tend to emerge and predominate during childhood, whereas the initial onset of generalized anxiety disorder, panic disorder, and social anxiety disorder most often occurs during adolescence [16, 23].

The literature describes the theory on distinct latent developmental trajectories for different anxiety disorder symptoms, emphasizing the importance of examining separate anxiety dimensions rather than considering anxiety as a general construct. For example, girls were significantly more likely than boys to be in numerous latent generalized anxiety disorder symptom trajectory classes, including those distinguished by very high initial symptoms that decrease rapidly, high initial symptoms that decrease less markedly over time, and moderate initial symptoms that decrease slightly over time [24]. The results from Crocetti et al.'s study regarding latent

growth trajectory classes found that adolescent population was best typified by a low-anxiety class, characterized by a low initial anxiety level that decreased over time and a high-anxiety class characterized by a higher initial anxiety level that increased over time [25]. In a 5-year study of Dutch, youth aged between 10 and 12 years at baseline, generalized anxiety disorder, panic disorder, and social anxiety disorder symptoms slightly decreased and then leveled off from early to middle adolescence, followed by a slight increase in generalized anxiety disorder and social anxiety disorder symptoms during middle adolescence and in panic disorder symptoms during late adolescence [22, 26]. Similar results have been reported by recent studies [24, 27].

There are mixed data regarding the differential gender prevalence rates of anxiety. Similar to gender ratio for adults, girls tend to have more of all subtypes of anxiety disorders, but there is no significant difference between boys and girls in the mean age at onset of anxiety [28]. Some studies showed that girls have a higher risk to develop AD [13, 16], are more affected [13, 24], and report higher cross-sectional anxiety symptom levels [29–31], and these differences remain stable during adolescence [20].

1.3 Comorbidities

Generally, in child and adolescent psychiatry, the comorbidities are the rule, and anxiety disorders fit into this pattern. In the clinical practice, AD comorbidities in internalization symptom area are commonly identified and closely monitored compared with the externalization symptoms. However, there are very few papers focused on the comorbidity between specific anxiety disorders and other psychiatric diagnoses.

Comorbidity occurs frequently, both within the anxiety disorders and also with other psychiatric disorders. At least one third of the children and adolescents diagnosed with anxiety disorders meet the criteria for two or more anxiety disorders [32]. Children with a primary anxiety disorder were significantly more likely to be diagnosed with separation anxiety disorder than adolescents. Adolescents with a primary anxiety disorder received more frequently a primary diagnosis of social anxiety disorder, mood disorders, and irregular school attendance [33]. Anxiety disorders are associated with all the other major classes of disorders, including mood disorders, disruptive behaviors, ADHD, eating disorders, and substance use disorders [19, 28, 34–36]. Merikangas et al. reported in their national survey among adolescents aged 13–18 years that the anxiety disorders were the most common condition (31.9%), with approximately 40% of those with one class of disorder also meeting criteria for another class of lifetime disorder [13]. Costello et al. found that comorbidity with other psychiatric disorders was common, ranging from 53% of the generalized anxiety disorder cases to 100% of specific phobia cases. The most common type of comorbidity with non-anxiety disorders was with depression [15, 20, 37, 38]. Adolescents with high levels of depressive symptoms experienced less significant decline over time in symptoms of physical, social, and separation anxiety [30]. The Oregon Adolescent Depression Study, looking at lifetime diagnoses, revealed that depression was significantly associated with each of the anxiety disorders except obsessive-compulsive disorder. Other lifetime associations found were ADHD with specific phobia and bipolar disorder with separation anxiety in males [39]. In preschool children, Sterba et al. used confirmatory factor analysis to show that the best-fitting model for the emotional disorders had three factors (social phobia, separation anxiety, and a factor that combined GAD and depression) with significant correlations between these three factors and conduct disorder, oppositional disorder, and

ADHD [40–42]. Social, separation, and generalized anxiety disorders in young people are relatively common and with a high level of comorbidity. All three ADs have a relatively high level of comorbidity with depression and a moderate degree of comorbidity with ADHD [17].

The major goal of the present study was to assess the prevalence of anxiety disorders among children and adolescents in a clinical setting and to describe the comorbidity and pharmacological treatment patterns.

2. Method

2.1 Participant selection

We conducted a retrospective study on the admitted patients in the Clinic of Pediatric Psychiatry from Cluj-Napoca, Romania, between January and December 2017. A clinical sample of 2471 patients aged between 3 and 18 years, with different psychiatric disorders, assessed and/or treated in the clinic, was included in the study. 9.88% (N = 244) of the clinical sample were children and adolescents diagnosed with an anxiety disorder via the 10th revision of the *International Statistical Classification of Diseases and Related Health Problems (ICD 10)*-based clinical interviews. Participants were grouped according to the “primary” diagnosis, the primary diagnosis referring to the severity of current diagnoses and not the order of onset (the reason for admission). In accordance with the removal of OCD and PTSD from the broad anxiety disorders category in *DSM-5* (American Psychiatric Association, 2013), the patients with a primary diagnosis of OCD and PTSD were excluded from this study.

We included in the study: boys or girls aged 3–18 with a diagnosis of anxiety disorders (agoraphobia; social phobias; specific phobias; other/unspecified phobic anxiety disorders; panic disorder; generalized anxiety disorder; mixed anxiety and depressive disorder; other mixed, specified, or unspecified anxiety disorders; separation anxiety disorder of childhood; social anxiety disorder of childhood), according to *ICD-10* international diagnosis criteria, admitted for assessment or treatment; agreement (children/adolescent and caregiver) to participate after the purpose and protocol of the study was explained. We excluded from the study: children and adolescents admitted with other diagnosis than anxiety disorders and the patients receiving services in outpatient settings.

Data were collected from the patients’ medical records (sociodemographic, clinical evaluations, and treatment recommendations). From the total of the 2471 patients selected, 244 children and adolescents were diagnosed with a type of anxiety disorder as a primary diagnosis. The patients come from all the countries and are diverse in terms of socioeconomic status. The mean age of participants was 12.75 (SD = 3.90), their age ranging from 3 to 18 years. All the participants were Caucasian. Data were used ensuring the privacy and subject’s identity protection.

2.2 Statistical analysis

The Statistical Program for Social Sciences (SPSS) v. 17 was used for data analysis. To describe and assess the selected population, we used univariate statistical analysis (mean, standard deviation, frequencies). Pearson chi-square test was used to verify the association among categorical variables, and t-test was used to compare the mean age. The level of significance was set at 5%, and a confidence interval (CI) of 95% was used in all tests.

2.3 Results

Two hundred forty-four patients with a primary diagnosis of anxiety disorder were included in the study of which 130 (53.3%) were males and 114 (46.7%) were females. The boy-girl ratio was 1.14:1. The mean age of boys and girls differs significantly (mean (SD) boys = 12.02 (4.08), girls = 13.60 (3.52), $t = -3.24$, $p = 0.001$).

2.3.1 Primary disorder prevalence

We analyzed the prevalence data for all anxiety disorder diagnosis of the patients included in the study, with current ICD 10 principal diagnosis are presented. As seen in **Table 1**, the most commonly occurring diagnosis were generalized anxiety disorder (GAD) 35.7% of the sample, social phobias (SOC) 12.3%, mixed anxiety and depressive (MAD) disorder 11.5%, other specified anxiety disorders (OSA) 9%, and separation anxiety disorder (SAD) of childhood 8.6%. The other anxiety disorders were less represented in our sample: specific phobias (SPEC) 6.1%, other phobic anxiety disorders (NOS) 4.9%, anxiety disorder, unspecified (ADU) 3.7%, panic disorder (PD) 3.3%, other mixed anxiety disorders (OMAD) 1.6%, phobic anxiety disorder, unspecified (UNS) 0.8%, and social anxiety disorder of childhood (SADC) 0.8%. About 20.5% of the sample ($N = 50$) had only 1 diagnosis at admission, 46.7% ($N = 114$) had 2 diagnoses, and 32.8% ($N = 80$) had 3 or more clinical diagnoses. Comorbidity is defined as having two or more co-occurring current diagnoses. **Table 1** presents the prevalence of the additional diagnosis for the participants grouped by the principal diagnosis. 34.4% of the participants had a diagnosis of anxiety or depressive disorder in addition to their principal anxiety disorder diagnosis. The other frequent comorbidities were attention deficit hyperactivity disorder (ADHD) (28.7%) and autism spectrum disorder (ASD) (8.6%).

2.3.2 Age and gender

The participants were divided into two groups by age: children ($N = 88$; 3–11 years of age) and adolescents ($N = 156$; 12–18 years of age). Among participants who met diagnostic criteria for the targeted anxiety disorders ($N = 244$), adolescents were significantly more likely to receive a principal diagnosis of GAD than children (39.7 vs. 28.4%, chi-square = 13.11, $p < 0.001$) or MAD (13.5 vs. 8%, chi-square = 9.33, $p = 0.02$). The prevalences of generalized anxiety disorder (GAD) and mixed anxiety and depressive (MAD) disorder were found higher in adolescents than in children (**Table 1**), but with a higher prevalence in adolescent girls, the proportion of boys diagnosed with GAD and MAD being relatively stable with age. Children were more likely to receive a principal diagnosis of SPEC than adolescents (11.4 vs. 3.2%, chi-square = 3.75, $p = 0.05$). For specific phobias (SPEC), the prevalence was higher in children than in adolescents, but while the proportion of boys remained relatively stable, the diagnosis wasn't present in adolescent girls.

No significant differences by age were found for the other anxiety disorders. The odds for boys to have a primary diagnosis of anxiety disorder was 2.63 (95% CI 1.52, 4.55), with a risk of 1.87 in children (95% CI 1.29, 2.72) and 0.71 in adolescents (95% CI 0.59, 0.86).

Among the participants that met the diagnosis criteria for at least one comorbidity ($N = 194$), adolescents were more likely than children to meet criteria for other anxiety disorder (14.7 vs. 13.6%, chi-square = 5.41; $p = 0.02$) or MDD (25.6 vs. 10.2%, chi-square = 5.49; $p = 0.019$). When looking at the age and gender trends for these comorbidities, we can observe some differences. While for the comorbidity with other anxiety disorder, the prevalence in adolescent boys is decreasing; in

		Children			Adolescents			Statistic
		Male (N = 60)	Female (N = 28)	All (N = 88)	Male (N = 70)	Female (N = 86)	All (N = 156)	(Children vs. adolescents)
Anxiety disorders	F40.0—(AG)	1 (1.7%)	1 (3.6%)	2	2 (2.9%)	0	2	$\chi^2(1) = 1.33, p = .24$
	F40.1—(SOC)	7 (11.7%)	3 (10.7%)	10	13 (18.6%)	7 (8.1%)	20	$\chi^2(1) = 0.75, p = .78$
	F40.2—(SPEC)	5 (8.3%)	5 (17.9%)	10	5 (7.1%)	0	5	$\chi^2(1) = 3.75, p = .05$
	F40.8—(NOS)	3 (5%)	4 (14.3%)	7	2 (2.9%)	3 (3.5%)	5	$\chi^2(1) = 0.01, p = .92$
	F40.9—(UNS)	0	1 (3.6%)	1	0	1 (1.2%)	1	—
	F41.0—(PD)	1 (1.7%)	0	1	3 (4.3%)	4 (4.7%)	7	$\chi^2(1) = 1.14, p = .28$
	F41.1—(GAD)	20 (33.3%)	5 (17.9%)	25	23 (32.9%)	39 (45.3%)	62	$\chi^2(1) = 13.11, p = .000$
	F41.2—(MAD)	7 (11.7%)	0	7	7 (10%)	14 (16.3%)	21	$\chi^2(1) = 9.33, p = .002$
	F41.3—(OMAD)	0	1 (3.6%)	1	0	3 (3.5%)	3	—
	F41.8—(OSA)	3 (5%)	0	3	8 (11.4%)	11 (12.8%)	19	$\chi^2(1) = 3.47, p = .06$
	F41.9—(ADU)	2 (3.3%)	0	2	5 (7.1%)	2 (2.3%)	7	$\chi^2(1) = 0.73, p = .39$
	F93.0—(SAD)	11 (18.3%)	8	19	1 (1.4%)	1 (1.7%)	2	$\chi^2(1) = 0.046, p = .83$
	F93.2—(SADC)	0	0	0	1 (1.4%)	1 (1.7%)	2	—
Comorbid anxiety disorders		8 (13.3%)	4 (14.3%)	12	6 (8.6%)	17 (19.8%)	23	$\chi^2(1) = 5.41, p = .02$

		Children			Adolescents			Statistic
		Male (N = 60)	Female (N = 28)	All (N = 88)	Male (N = 70)	Female (N = 86)	All (N = 156)	(Children vs. adolescents)
Mood disorder	MDD	7 (11.7%)	2 (7.1%)	9	14 (20%)	26 (30.2%)	40	$\chi^2(1) = 5.49, p = .019$
Other	ADHD	31 (51.7%)	13 (46.4%)	44	18 (25.7%)	8 (9.3%)	26	$\chi^2(1) = 0.012, p = .91$
	ASD	6 (10%)	4 (14.3%)	10	10 (14.3%)	1 (1.2%)	11	$\chi^2(1) = 2.75, p = .097$
	MR	3 (5%)	1 (3.6%)	4	4 (5.7%)	1 (1.2%)	5	—
	OCD	0	1 (3.6%)	1	1 (1.4%)	2 (2.3%)	3	—
	Conduct disorder	0	0	0	1 (1.4%)	1 (1.2%)	2	—
	ODD	1 (1.7%)	0	1	0	1 (1.2%)	1	—
	ATP	0	0	0	0	1 (1.2%)	1	—
No disorder		4 (6.7%)	3 (10.7%)	7	15 (21.4%)	28 (32.6%)	43	$\chi^2(1) = 1.26, p = .261$

Note: AG = agoraphobia; SOC = social phobias; SPEC = specific phobias; NOS = other phobic anxiety disorders; UNS = phobic anxiety disorder, unspecified; PD = panic disorder; GAD = generalized anxiety disorder; MAD = mixed anxiety and depressive disorder; OMAD = other mixed anxiety disorders; OSA = other specified anxiety disorders; ADU = anxiety disorder, unspecified; SAD = separation anxiety disorder of childhood; SADC = social anxiety disorder of childhood; OAD = other anxiety disorders; MDD = major depressive disorder; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ASD = autism spectrum disorder; MR = mental retardation; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder; ATP = acute and transient psychotic disorders.

Table 1.
Child/adolescent primary anxiety disorder and comorbidities.

Anxiety disorders	OAD (N = 35)	MDD (N = 49)	ADHD (N = 70)	ASD (N = 21)	MD (N = 10)	ODD/CD (N = 5)	No disorder (N = 50)
F40.0—(AG)	1 (25%)	0	2 (50%)	0	0	0	1 (25%)
F40.1—(SOC)	4 (13.3%)	9 (30%)	10 (33.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	4 (13.3%)
F40.2—(SPEC)	1 (6.7%)	1 (6.7%)	7 (46.7%)	3 (20%)	2 (13.3%)	0	1 (6.7%)
F40.8—(NOS)	2 (16.7%)	0	7 (58.3%)	0	0	0	2 (16.7%)
F40.9—(UNS)	0	0	1 (50%)	1 (50%)	0	0	0
F41.0—(PD)	1 (12.5%)	3 (37.5%)	0	0	1 (12.5%)	0	3 (37.5%)
F41.1—(GAD)	21 (24.1%)	22 (25.3%)	18 (20.7%)	9 (10.3%)	0	2 (2.2%)	14 (16.1%)
F41.2—(MAD)	3 (10.7%)	2 (7.1%)	8 (28.6%)	1 (3.6%)	0	1 (3.6%)	13 (45.4%)
F41.3—(OMAD)	1 (25%)	1 (25%)	1 (25%)	0	0	0	1 (25%)
F41.8—(OSA)	0	7 (31.8%)	3 (13.6%)	1 (4.5%)	3 (13.6%)	0	7 (31.8%)
F41.9—(ADU)	0	4 (44.4%)	1 (11.1%)	3 (33.3%)	0	0	1 (11.1%)
F93.0—(SAD)	1 (4.8%)	0	12 (57.1%)	2 (9.5%)	3 (14.3%)	1 (4.8%)	1 (4.8%)
F93.2—(SADC)	0	0	0	0	0	0	2 (100%)

Note: AG = agoraphobia; SOC = social phobias; SPEC = specific phobias; NOS = other phobic anxiety disorders; UNS = phobic anxiety disorder, unspecified; PD = panic disorder; GAD = generalized anxiety disorder; MAD = mixed anxiety and depressive disorder; OMAD = other mixed anxiety disorders; OSA = other specified anxiety disorders; ADU = anxiety disorder, unspecified; SAD = separation anxiety disorder of childhood; SADC = social anxiety disorder of childhood; OAD = other anxiety disorders; MDD = major depressive disorder; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ASD = autism spectrum disorder; MR = mental retardation; ODD = oppositional defiant disorder.

Table 2.
Comorbidity patterns by principal diagnosis [percentage].

Anxiety disorders	Fluoxetine (N = 23)	Sertraline (N = 65)	Risperidone (N = 25)	Benzodiazepine (N = 38)	Other antipsychotics (N = 22)	Mood stabilizers (N = 18)	No pharmacological treatment (N = 116)
F40.0—(AG)	2 (50%)	1 (25%)	0	1 (25%)	0	0	1 (25%)
F40.1—(SOC)	2 (6.7%)	5 (16.7)	2 (6.7%)	2 (6.7%)	1 (3.3%)	0	21 (70%)
F40.2—(SPEC)	0	1 (6.7%)	3 (20%)	2 (13.3%)	1 (6.7%)	1 (6.7%)	10 (66.7%)
F40.8—(NOS)	0	4 (33.3%)	2 (16.7%)	1 (8.3%)	2 (16.6%)	5 (41.7%)	4 (33.3%)
F40.9—(UNS)	0	1 (50%)	0	0	0	0	1 (50%)
F41.0—(PD)	3 (37.5%)	4 (50%)	1 (12.5%)	4 (50%)	1 (12.5%)	0	0
F41.1—(GAD)	12 (13.8%)	30 (34.5%)	7 (8%)	19 (21.8%)	13 (14.9%)	6 (6.9%)	32 (36.8%)
F41.2—(MAD)	2 (7.1%)	7 (25%)	3 (10.7%)	1 (3.6%)	1 (3.6%)	4 (14.2%)	13 (46.4%)
F41.3—(OMAD)	0	0	0	1 (25%)	0	0	3 (75%)
F41.8—(OSA)	0	8 (36.4%)	3 (13.6%)	5 (22.7%)	2 (9%)	0	10 (45.5%)
F41.9—(ADU)	1 (11.1)	2 (22.2%)	2 (22.2%)	0	1 (11.1%)	0	4 (44.4%)
F93.0—(SAD)	1 (4.8%)	1 (4.8%)	2 (9.5%)	1 (4.8%)	0	0	17 (81%)
F93.2—(SADC)	0	1 (50%)	0	1 (50%)	0	2 (100%)	0

Note: AG = agoraphobia; SOC = social phobias; SPEC = specific phobias; NOS = other phobic anxiety disorders; UNS = phobic anxiety disorder, unspecified; PD = panic disorder; GAD = generalized anxiety disorder; MAD = mixed anxiety and depressive disorder; OMAD = other mixed anxiety disorders; OSA = other specified anxiety disorders; ADU = anxiety disorder, unspecified; SAD = separation anxiety disorder of childhood; SADC = social anxiety disorder of childhood.

Table 3.
Pharmacological treatment patterns by principal diagnosis (percentage).

adolescent girls it rises, being accountable for the significant difference between children and adolescents. For the comorbidity with MDD, the prevalence trends regarding age and sex are different than those for anxiety disorders. The comorbidity with MDD is rising with age, disregarding the gender, mentioning that the prevalence of MDD is higher in boys and the increase with age is milder than in girls.

There were no statistically significant relationships between the primary anxiety disorder diagnosis and gender. Regarding the comorbid diagnosis, the girls were more likely to receive an additional diagnosis of other anxiety disorder (18.4 vs. 10.8%), MDD (24.6 vs. 16.2%), while the boys were more likely to receive an additional diagnosis of ADHD (37.7 vs. 18.4%), ASD (12.3 vs. 4.4%), or MR (6.2 vs. 1.8%).

A chi-square analysis demonstrated that there was a significant difference in the presence of comorbidities between the principal diagnosis categories (chi-square = 132.46; $p = .08$). The principal anxiety disorders diagnosis with a higher number of comorbidities were GAD, SOC, MAD, OSA, and SAD, as seen in **Table 2**. Comorbidities associated with anxiety disorders are very common, especially among them. Patients with anxiety disorders had also high rates of depression and ADHD.

About 92% of the children and 72.4% of the adolescents with a primary diagnosis of anxiety disorder had at least one comorbidity, underlining that in our sample, the children had more comorbidities than the adolescents. The pattern of comorbidities was different for the most frequent anxiety disorders in our sample. For GAD, the most common comorbidities were other anxiety disorders and MDD, counting for almost half of the patients. Another 20.7% of them had comorbid ADHD. For MAD, the most frequent association was with ADHD, 28.6%, but the diagnosis includes specific symptoms of anxiety and depression, with neither type of symptom severe enough to justify a diagnosis if considered separately, so symptoms of depression are necessary for diagnosis. For SOC, the most frequent comorbidities were ADHD and MDD (~30%), followed by other anxiety disorders. SAD, which is a diagnosis specific for children, had comorbid ADHD in 57.1% of the cases.

From the 70 patients with ADHD comorbid diagnosis, 20 (28.6%) were treated with atomoxetine and 10 (14.3%) with methylphenidate. One hundred twenty-one (49.6%) patients in our sample didn't receive pharmacological treatment, 49 (55.7%) children and 72 (46.2%) adolescents, 65 (50%) boys and 56 (49.1%) girls (see **Table 3**). Seventy-five (30.7%) patients received only one medication, of which 30 (34.1%) children and 45 (28.8%) adolescents, 41 (31.5%) boys and 34 (29.8%) girls. Forty-eight patients received more than one pharmacological treatment, of which 9 (10.2%) were children and 39 (25%) were adolescents, 24 (18.5%) boys and 24 (21.1%) girls. There were no statistically significant relationships between the recommended treatment and gender, but there were significant differences regarding the age group (children vs. adolescents). A chi-square analysis demonstrated that there was a significant difference in mono and without versus more pharmacological treatments between children and adolescent categories (chi-square = 7.77; $p = .02$), the adolescents being more likely to receive more medication.

3. Discussion and conclusions

Anxiety disorders are considered to be the most common psychiatric disorder in children and adolescents. In our study out of 2471 patients assessed and/or treated in the Clinic of Pediatric Psychiatry from Cluj-Napoca, Romania, between January and December 2017, only 244 (9.88%) patients received a primary diagnosis of different anxiety disorders, meaning that the anxiety disorders were the reason for admission. This low frequency of anxiety disorders in a clinical sample of children and adolescents can be explained by the selection criteria but also by the fact that

children internalization problems are less recognized by parents and referred for treatment. Merikangas et al. reported an overall prevalence of anxiety disorders with severe impairment and/or distress of 8.3%, which is close to the prevalence reported in our study [13]. In a meta-analysis of multiple data sets, Costello and Egger have found the prevalence of 10.2% for any AD, 5.4% for specific phobia (SPEC), 3.6% for social phobia (SOC), 2.6% for separation anxiety disorder (SAD), 1.7% for generalized anxiety disorder (GAD), and 0.8% for panic disorder (PD) [15]. In our sample, the prevalences for these disorders were 35.6% for GAD, 12.3% for SOC, 8.6% for SAD, 6.1% for SPEC, and 3.3% for PD.

The study results showed that 79.5% of the selected sample had a comorbid disorder, and 34.4% had an anxiety or mood comorbidity which is similar to the findings from other studies on comorbidity rates of anxiety disorders in children. Previous studies found constantly elevated comorbidity rates in people with anxiety disorders [43], associated with increased symptom severity and greater functional impairment and worse outcome [15, 44]. The Child/Adolescent Anxiety Multimodal Study (CAMS) identified children and adolescents with social phobia, GAD, or SAD. They found that 78.6% of the sample had two or more of those disorders, and 35.9% met criteria for all three diagnoses simultaneously [36]. Kendall et al. find a comorbidity rate of 55.3% in a sample of youth with anxiety disorders [45]. Costello et al. found that comorbidity of AD with other psychiatric disorders was common, varying from 53% for GAD to 100% for SPEC. The most common type of comorbidity with non-anxiety disorders was with depression [15]. Also, the association between GAD and depression was found by Moffitt et al. in the Dunedin, New Zealand, longitudinal study with GAD predicting depression and depression predicting GAD across the life course [46]. In our study, 83.9% of the patients diagnosed with GAD had comorbidities, and 50% of them were diagnosed also with other anxiety disorder or depression.

Comorbidity patterns varied by *ICD-10* diagnosis. The principal diagnoses associated with significantly elevated risk for a comorbid diagnosis were GAD, MAD, SOC, OSA, and SAD. The association between GAD and other anxiety/depressive disorders raised many questions regarding the need for more accurate description in order to increase the reliability and validity of this disorder [47]. For SOC, the highest rate of comorbidities was with depression and ADHD. OSA had the highest comorbidity rate with depression, MAD with other anxiety disorders and ADHD and SAD with ADHD.

In our study, the prevalence of anxiety disorders primary diagnosis was 9.88%, with slightly different rates in females (46.7%) and males (53.3%). Although there were a greater number of boys than girls included in the study, the situation was different on age groups, more boys than girls in children group and more girls than boys in adolescent group; gender was not significantly associated with any of the anxiety diagnosis or comorbidity. The most common disorders in both males and females were GAD, SOC, MAD, other specified anxiety disorders (OSA), and separation anxiety disorder of childhood (SAD). Adolescents were more likely to receive a principal diagnosis of GAD or MAD than children. The prevalences of generalized anxiety disorder (GAD) and mixed anxiety and depressive (MAD) disorder were found higher in adolescents than in children (see **Table 1**), but with a higher prevalence in adolescent girls, the proportion of boys diagnosed with GAD and MAD being relatively stable with age. Children were more likely to receive a principal diagnosis of SPEC than adolescents. For specific phobias (SPEC), the prevalence was higher in children than in adolescents, but while the proportion of boys remained relatively stable, the diagnosis wasn't present in adolescent girls. No significant differences by age were found for the other anxiety disorders.

Different anxiety disorders have different age and gender distributions during childhood and adolescence. Separation anxiety disorder (SAD) and specific phobias (SPEC) are more common in children, while panic disorder and social phobia are more common in adolescents. Recent studies showed that, in the general population, anxiety symptoms first decrease during early adolescence and subsequently increase from middle to late adolescence [22]. SAD and SPEC tend to emerge and predominate during childhood, whereas the initial onset of generalized anxiety disorder (GAD), panic disorder (PD), and social anxiety disorder (SAD) most often occurs during adolescence [24, 46].

According to the findings of our study, gender and age contributed to the presence of comorbidity. Adolescents were more likely than children to meet criteria for other anxiety disorder or MDD. The age and gender trends for these comorbidities were different. While for the comorbidity with other anxiety disorder, the prevalence in adolescent boys is decreasing; in adolescent girls, it rises, being accountable for the significant difference between children and adolescents. For the comorbidity with MDD, the prevalence trends regarding age and sex are different. The comorbidity with MDD is rising with age, disregarding the gender, mentioning that the prevalence of MDD is higher in boys and the increase with age is milder than in girls. The girls were more likely to receive an additional diagnosis of other anxiety disorder and MDD, while the boys were more likely to receive an additional diagnosis of ADHD, ASD, or MR. This pattern is consistent with other studies which have found either no difference between the sexes or greater rates of comorbidity in males [48]. When examined separately, no difference was found in the presence of comorbidity by sex, for the principal diagnoses, but there were significant differences by age. The fact that adolescents experience higher levels of comorbid depressive disorders is consistent with findings from a clinical population [49].

Regarding the treatment patterns, in our study, the most frequently recommended pharmacological treatment was SSRIs, 36% of the patients receiving fluoxetine or sertraline. Other recommended treatments were benzodiazepines recommended to 15.6% of the patients, antipsychotics recommended to 19.3%, and mood stabilizers recommended to 7.4% of them. About 49.6% of the patients in our sample did not receive pharmacological treatment, 30.7% patients received only one medication, and 19.7% received more than one pharmacological treatment. There were no statistically significant relationships between the recommended treatment and gender, but there were significant differences regarding the age group (children vs. adolescents), the adolescents being more likely to receive more medication. These results should be interpreted keeping in mind that the sample had a high rate of comorbidities (79.5%) and that the pharmacological treatment may target those disorders. There is some evidence that medication can be effective in treating anxiety in children and adolescents, at least on the short term. A recent meta-analysis showed anxiolytic medication to be associated with a significantly greater clinical response than placebo (58.1 vs. 31.5%). Selective serotonin reuptake inhibitors (SSRIs) are regarded as the pharmacological treatment of choice for anxiety disorders in children and adolescents because of their effectiveness and safety profile. It is important to note that benzodiazepines have not been systematically assessed in children and adolescents, and, in view of concerns about dependency and side effects, their use is not recommended. It is unclear if there is an age below which medication would be contraindicated and what the duration of treatment should be [36]. Understanding the common patterns of anxiety disorders comorbidities and its treatments has important implications for child anxiety disorders treatment planning. Whether comorbid conditions might increase the need for treatment or cause patients to respond more poorly to psychological or psychiatric interventions is an important research area. Future treatments might need to be

adapted to better meet the needs of patients with commonly occurring comorbid conditions. This will help facilitate a better choice of existing treatments and may improve treatment outcomes.

It is important to consider the methodological limitations of the study which may impact the conclusions drawn based on this data. The age was considered within two categories, based on childhood and adolescence that can be seen as distinct developmental periods, and future studies should look at narrower age bands. Additionally, the sample included only admitted patients and excluded those receiving services in outpatient settings.

Conflict of interest

The authors declare that they have no conflict of interest.

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