



Effect of Demographic Factors on Quality of Life in Children with ADHD under Atomoxetine Treatment: 1-Year Follow-up

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Abstract

Attention-deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in children and adolescents. Symptoms of ADHD and its treatment can impact an individual's quality of life (QoL). The present study aimed to evaluate the effect of atomoxetine treatment, demographic characteristics, and seasonal variation on QoL in children with a recent diagnosis of ADHD and their parents. The present study included a cohort of 200 children diagnosed with ADHD. In addition to the recruited children, one of their parents was included in the study. ADHD symptoms were assessed using Conners' Parent Rating Scale. QoL of the participants was assessed with the PedsQL, while parents' QoL was evaluated using the World Health Organization Quality of Life questionnaire (WHOQOL-Bref). There was significant improvement in pediatric and parental QoL after treatment with atomoxetine. Significant factors related to better QoL in the participants included spring season, above average Conner's score, male sex, and rural residence. However, after using multivariate regression analysis, only patients' sex and Conner's score were significant predictors of pediatric QoL at the end of treatment with atomoxetine. Medical treatment significantly improved QoL in children with ADHD and their parents. Level of improvement was affected by patients' sex and ADHD severity.

Keywords

- ▶ attention deficit hyperactivity disorder
- ▶ quality of life
- ▶ seasonal variation

Introduction

Attention-deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in children and adolescents. It is characterized by behavioral problems such as attention deficit, hyperactivity and impulsivity.¹ Assessment should include careful history taking thorough physical examination and psychological evaluation. Stimulant medications are effective for treatment. However, their side effects and potential of misuse and abuse constitute significant concerns.²

Some demographic characteristics are linked to increased prevalence of ADHD. It is known that ADHD is more common and is characterized by more severe symptoms in males.³ It was also suggested that poor socioeconomic status (SES) increases children's risk of ADHD.⁴

In addition, it was found that genetic and environmental factors play a role in the causation and development of ADHD.⁵ A pattern of increasing prevalence of ADHD has been suggested to be partly linked to exposure to environmental pollutants.⁶ Moreover, it was noted that seasonal and

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circadian rhythm instabilities can significantly influence ADHD symptoms.⁷

Symptoms of ADHD can negatively impact an individual's health and quality of life (QoL) and impair function in multiple settings.⁸ Furthermore, this disorder creates significant difficulties in education, social performance, and personal relationships.⁹ Factors related to QoL in children with ADHD include gender,¹⁰ SES,¹¹ and type of treatment.¹²

The present study aimed to evaluate the effect of demographic characteristics and seasonal variation on QoL in children with ADHD and their parents.

Patients and Methods

The present prospective study included a cohort of 200 newly diagnosed, treatment-naïve children with combined-type ADHD recruited from the outpatient clinic of Ain Shams University Hospitals. The study protocol was approved by the local ethical committee and the legal guardians of all included children gave informed consent to participate in the study. In addition to the recruited children, one of the child's parents were included in the study.

The children included in the study were 6 to 12 years old and their diagnosis of ADHD was based on Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria. Exclusion criteria were associated chronic clinical conditions, such as "diabetes and thyroid abnormalities," or other neurodevelopmental disorders, such as "autism spectrum and seizure disorders," and intake of other medications.

All patients were subjected to careful history taking and thorough clinical examination. SES was assessed using an Egyptian validated scale. The scale comprises various socio-economic parameters including income, education, housing, etc.¹³ Patients received medical treatment in the form of oral atomoxetine capsules (0.5 mg/kg/day as initial dose increased after a minimum of 3 days to 1.2 mg/kg/day with a maximum daily dose of 1.4 mg/kg/day or 100 mg/day). In addition, patients were subjected to cognitive behavioral therapy sessions.

ADHD symptoms were assessed using Conners' Parent Rating Scale short form Arabic version (CPRS-48),¹⁴ which is a 48-item questionnaire. Each item is evaluated using 4-point Likert's scale (from 0 denoting not at all to 3 denoting severely affected). CPRS-48 has seven subscales which are conduct problem (eight items), learning problem (four items), psychosomatic problem (four items), impulsive-hyperactivity (four items), and anxiety (four items), hyperactivity index (10 items), and inattention (eight items). QoL of the studied children was assessed by the Arabic version of PedsQL 4.0 Generic Core Scales (physical, emotional, social, school functioning)¹⁵ while parents' QoL was evaluated using the Arabic version of WHO QoL-BREF instrument.¹⁶ Patients were followed-up for a complete calendar year from September 22, 2018 through September 21, 2019. None of the patients studied were lost to follow-up. Patients' QoL was assessed at baseline (i.e., before treatment) and at the end of every season.

Data obtained from the present study were presented as mean \pm standard deviation (SD), median and interquartile range (IQR) or number and percent. Statistical comparisons were achieved using *t*-test, Mann-Whitney *U*-test, one-way analysis of variance (ANOVA), Kruskal-Wallis test, Fisher's exact test or Chi-square test as appropriate. Regression analysis was used to identify predictors of pediatric QoL. A *p*-value less than 0.05 was considered statistically significant.

Results

The present study included 200 children diagnosed with ADHD. They comprised 123 males (61.5%) and 77 females (38.5%) with a median (IQR) age of 9.0 (7.0–10.0) years. Other baseline data of the studied children are shown in **Table 1**. Parents included in the study included 73 fathers (36.5%) and 127 mothers (63.5%) with a median (IQR) age of 37.0 (33.3–40.0) years. Of note, 14 mothers (7.0%) and 11 fathers (5.5%) had psychopathologies. Most children (79.0%) were delivered by cesarean section and most mothers (96.0%) were exposed to environmental tobacco smoke. Other parental characteristics are shown in **Table 2**.

After 1 year of treatment, the total pediatric QoL score significantly improved in comparison to the pretreatment levels: median (IQR): 65.0 (61.0–69.0) versus 30.0 (27.0–33.0), *p* < 0.001. Significant improvement also applied to all individual scales of pediatric QoL scores. Moreover, the total parental QoL score was significantly improved after

Table 1 Basic data of the studied children (*n* = 200)

Age (y)	
Median (IQR)	9.0 (7.0–10.0)
< Median <i>n</i> (%)	97 (48.5)
≥ Median <i>n</i> (%)	103 (51.5)
Gender <i>n</i> (%)	
Male	123 (61.5)
Female	77 (38.5)
SES <i>n</i> (%)	
Above average	37 (18.5)
Average	147 (73.5)
Below average	16 (8.0)
Conners' Parent Rating Scale score <i>n</i> (%)	
Above average	105 (52.5%)
Average	88 (44.0%)
Below average	7 (3.5%)

Abbreviations: IQR, interquartile range; SES, socioeconomic status. Note: Data presented as median and IQR or number and percent.

Table 2 Basic data of the studied parents ($n = 200$)

Age (y)	
Median (IQR)	37.0 (33.3–40.0)
< Median	102 (51.0)
≥ Median	98 (49.0)
Sex <i>n (%)</i>	
Male	73 (36.5)
Female	127 (63.5)
Work <i>n (%)</i>	
Working	173 (86.5)
Homemaker	27 (13.5)
Residence <i>n (%)</i>	
Urban	126 (63.0)
Rural	74 (37.0)
Education <i>n (%)</i>	
Postgraduate	5 (2.5)
Graduate	181 (90.5)
Elementary	14 (7.0)
Married	175 (87.5)
Divorced	25 (12.5)
Consanguinity <i>n (%)</i>	17 (8.5)
Maternal psychopathology <i>n (%)</i>	14 (7.0)
IVF <i>n (%)</i>	6 (3.0)
Environmental tobacco smoke <i>n (%)</i>	192 (96.0)
Acetaminophen during pregnancy <i>n (%)</i>	174 (87.0)
Alcoholism during pregnancy <i>n (%)</i>	6 (3.0)
Antihypertensives during pregnancy <i>n (%)</i>	8 (4.0)
Diabetes during pregnancy <i>n (%)</i>	13 (6.5)
Labor <i>n (%)</i>	
Cesarean section	158 (79.0)
Vaginal	42 (21.0)
Preterm labor <i>n (%)</i>	15 (7.5)
Preeclampsia <i>n (%)</i>	4 (2.0)

Abbreviations: IQR, interquartile range; IVF, in vitro fertilization.
Note: Data presented as median and IQR or number and percent.

treatment: median (IQR): 87.0 (80.0–92.0) versus 71.0 (65.0–80.0), $p < 0.001$. Likewise, the individual domains were significantly improved (► **Table 3**).

► **Table 4** illustrates the association between pediatric QoL and demographic and clinical data. There was significant association between improved total pediatric QoL scores after treatment and spring season, above average Conners' score of ADHD, male sex of patients, and rural residence. On multivariate regression analysis, significant predictors of QoL included patients sex (odds ratio [OR] = -5.1 , 95% confidence interval [CI]: -6.2 to -4.0 , $p < 0.001$) and Conners' score (OR = -2.1 , 95% CI: -3.0 to -1.1 , $p < 0.001$; ► **Table 5**).

Discussion

The current study revealed significant improvement of pediatric QoL and its individual domains after treatment with atomoxetine. These results are consistent with multiple previous studies. In the study of Haynes et al¹⁷ on approximately 700 children with ADHD, atomoxetine treatment was associated with improved QoL over 2 years. In another study, it was found that atomoxetine withdrawal resulted in significant deterioration of QoL parallel to the changes in ADHD symptoms.¹⁸ In addition, it was found that parents of the studied children experienced significant improvement of their QoL; a finding that accords with the conclusions of Escobar et al¹⁹ who noted that the positive impact of atomoxetine on children QoL was associated with a corresponding positive influence on their parents.

In the present study, it was found that the spring season has the most significant impact on patients' QoL. The improved QoL in spring may be related to improved sun exposure and increased vitamin D levels. This explanation may be supported by findings of other reports. In one recent study, vitamin-D deficiency was associated with ADHD symptoms in children.²⁰ One recent meta-analysis confirmed these conclusions.²¹

Of note, the study of Wynchank et al⁷ found that worsening of ADHD symptoms in autumn and/or winter may be attributed the association between ADHD and seasonal affective disorder (SAD) commonly seen in adult patients with ADHD. However, the prevalence of SAD is much lower in children as compared with adults.²² Moreover, children with SAD were excluded from the present study.

In this study, it was found that the children with below average Conners' score had significantly lower QoL. The association between ADHD symptoms severity and QoL was reported by the study of Mulraney et al²³ on 392 children with ADHD assessed at three time points (0, 6, and 12 months). The study found that parent-reported ADHD symptoms predicted poor QoL at each subsequent time point.

Assessment of the relation between children QoL and various demographic data revealed significantly all-year and seasonal lower QoL in female children after treatment. In harmony with these results, the study of Dallos et al²⁴ on

Table 3 Pediatric and parental quality of life before and after treatment

	Before treatment	After treatment	p-Value
Pediatric QoL			
Total QoL score	30.0 (27.0–33.0)	65.0 (61.0–69.0)	<0.001
Psychosocial scale	31.0 (24.0–42.0)	55.0 (48.0–62.0)	<0.001
Physical functioning scale	38.0 (33.0–40.0)	76.5 (72.0–81.0)	<0.001
Emotional function scale	24.0 (16.0–32.0)	60.0 (50.0–65.0)	<0.001
Social function scale	24.0 (20.0–28.0)	55.0 (45.0–65.0)	<0.001
School function scale	22.0 (20.0–31.0)	55.0 (40.0–65.0)	<0.001
Parental QoL			
Total QoL score	71.0 (65.0–80.0)	87.0 (80.0–92.0)	<0.001
Parental physical health domain	69.0 (63.0–80.0)	86.0 (71.0–91.0)	<0.001
Parental psychological health domain	73.0 (67.0–80.0)	87.0 (80.0–93.0)	<0.001
Parental social relationship domain	73.0 (67.0–80.0)	87.0 (73.0–93.0)	<0.001
Parental environment domain	73.0 (63.0–80.0)	88.0 (83.0–93.0)	<0.001

Abbreviation: QoL, quality of life.

Note: Data presented as median and interquartile range (interquartile range).

Table 4 Relation between pediatric quality of life and demographic and clinical data

	Pediatric QoL	p-Value
Season of assessment		
Spring	64.0 (61.0–67.8)	<0.001
Summer	60.0 (55.0–64.0)	
Autumn	62.0 (59.3–66.0)	
Winter	60.0 (55.0–64.0)	
Conner’s Parent Rating Scale score		
Above average	63.0 (59.0–67.0)	<0.001
Average	60.0 (58.0–64.0)	
Below average	54.0 (53.0–57.0)	
Patients’ age		
< Median	62 (59.0–65.0)	0.12
≥ Median	64.0 (61.0–67.0)	
Patients’ sex		
Male	64.0 (61.0–66.0)	<0.001
Female	58.0 (56.0–60.0)	
Patients’ SES		
Above average	61.0 (57.0–65.5)	0.93
Average	61.0 (59.0–65.0)	
Below average	63.5.0 (57.25–65.0)	
Parental age		
< Median	60.0 (58.0–65.0)	0.15
≥ Median	62.0 (59.0–65.0)	
Parental sex		
Male	64.0 (61.0–65.5)	<0.001

Table 4 (Continued)

	Pediatric QoL	p-Value
Female	60.0)57.0–65.0(
Parental work		
Working	61.5.0 (58.0–65.0)	0.36
Housewife	60.0 (59.0–64.0)	
Residence		
Urban	60.5 (57.75–65.0)	0.028
Rural	63.0 (59.75–65.0)	
Parental education		
Postgraduate	66.0 (64.0–67.5)	0.09
Graduate	61.0 (58.0–65.0)	
Elementary	60.5)58.0–63.0(
Marital status		
Married	61.0 (59.0– 65.0)	0.073
Divorced	60.0 (56.5–64.5)	

Abbreviations: SES, QoL, quality of life; socioeconomic status.

Note: Data presented as median and interquartile range (interquartile range).

178 children with ADHD found that lower self-reported QoL was associated with female gender. This may be related to the less severe form of ADHD symptoms in males probably due to the protective effects of testosterone.²⁵

In addition, the present study found significantly higher QoL after treatment in children living in rural areas. This finding may be surprising in respect to the lower rate of utilization of ADHD medications in rural areas.^{26,27} However, the better QoL in children with ADHD living in rural areas may be related to lower pollution rates.^{28,29}

Table 5 Regression analysis for predictors of pediatric QoL after 1 year

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Age	0.34 (−0.03 to 708.0)	0.074	0.23 (−0.06 to 0.52)	0.13
Sex	−5.6 (−6.8 to −4.5)	<0.001	−5.1 (−6.2 to −4.0)	<0.001
Conners' Parent Rating Scale score	−3.0 (−4.1 to −1.9)	<0.001	−2.1 (−3.0 to −1.1)	<0.001
Residence	1.6 (0.24 to 2.99)	0.021	0.96 (−0.13 to 2.1)	0.084

Abbreviations: CI, confidence interval; OR, odds ratio; QoL, quality of life.

Limitations

Results of the present study are limited by the lack of comparison between children with ADHD under atomoxetine and those under other types of pharmacological and nonpharmacological treatment.

Conclusion

In conclusion, we revealed significant improvement of QoL in children with ADHD and their parents. Improvement is more pronounced in the spring, in male patients, and in patients with less severe ADHD symptoms.

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None.

Conflict of Interest

None declared.

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