Investigating the association between sociodemographic variables, comorbidities and treatment patterns and the risk of falls in children with ASD

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Abstract. Autism spectrum disorder (ASD) is a severe developmental disability, the incidence of which is rapidly increasing. A comorbidity profile and a risk of falls are highly prevalent in children with ASD. The aim of the present study was to map relevant sociodemographic variables, analyze the types of medication that children with ASD receive, and determine the comorbidities that exist among this cohort. In addition, a correlation analysis was conducted to evaluate the risk of falls among the different age groups. A retrospective cohort study was designed using electronic medical record systems. The sample comprised 250 children with ASD, among whom 74.4% were male and 12% were <6 years of age. The demographics of the study participants were analyzed along with the frequency and types of comorbidities. Subsequently, pediatric risk of fall scores [Humpty Dumpty Falls Scale (HDFS)] were obtained and Spearman's correlation analyses and ANOVA were employed to analyze the associations between age and the number of medications taken. Linear regression slopes were then used to determine which variables predicted the risk of falls. The results revealed that the age of the children was positively associated with the total number of medications taken and antipsychotic medications used (P<0.001). There was also a significant association between pediatric risk of falls and age (P<0.001). Binary logistic regression analysis revealed that the risk of falls (HDFS) were predicted by a lower current age and the male sex. Almost 39% of the participants had another health condition, the most prevalent of which was attention deficit hyperactivity disorder (ADHD) (46%), followed by intellectual disability (18.4%) and epilepsy (17.6%). The findings also indicated that functioning improved as children with ASD grew older. In addition, it was revealed that the majority of participants were taking antipsychotics and exhibited clinical features of ADHD. On the whole, the present study provides further evidence regarding the link between the pediatric risk of falls and younger age.

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Introduction

Autism spectrum disorder (ASD) refers to neurodevelopmental disorders marked by significant challenges in socialization, communication and behavior (1). A previous systematic review of 71 studies included sample sizes which were relatively large, ranging from 465 to 50 million participants. Prevalence in these studies ranged from 1.09/10,000 to 436/10,000, with a median majority of 100/10,000 (2). Notably, the reported prevalence of ASD among children has increased over time. This may be attributable to several factors, including a broadening of the diagnostic criteria, heightened public awareness of ASD and its symptoms, and the enhanced availability of early interventions and educational services tailored for children with ASD (3).

Sociodemographic factors, such as socio-economic status, parental education and cultural background significantly affect the development, diagnosis and management of ASD in children. Studies from Australia and Bangladesh have highlighted how parental education, occupation and cultural background influence ASD diagnoses and access to services, emphasizing the need for equitable healthcare policies and intervention programs tailored to diverse needs (4,5). Understanding these factors is essential for ensuring access to support services for all children with ASD, regardless of sociodemographic background.

Medical comorbidities are more common in children with ASD than in the general population. For instance, children with ASD are more likely to develop various neurological disorders, including epilepsy, macrocephaly, migraines/headaches

and congenital abnormalities of the nervous system (6). Additionally, the risk of falls is strongly prevalent in such children. This may be due to cognitive and motor impairments that increase the risk of falls. The high rate of non-fatal falls, the associated healthcare costs and the significant risk of mortality (particularly as a result of head injuries) render it essential to prioritize the prevention of fall-related injuries in child safety efforts worldwide (7).

Numerous risk and protective factors for falls among children have been reported, including sociodemographic characteristics, maternal psychiatric disorders, and child psychological and behavioral issues (8). A previous study employing multivariate logistic regression analyzes identified significant predictors of falls, such as an age <3 years, neurological diagnosis (including epilepsy), dependency in activities of daily living, physical developmental delay and multiple usage of fall-risk-increasing drugs (9). Antipsychotic medications are the agents most critically studied as treatments for reducing symptoms. However, such medications can increase the risk of falls due to syncope, sedation, slowed reflexes, loss of balance and impaired psychomotor function (9). Moreover, the administration of antipsychotic medications requires careful monitoring due to associated safety concerns and the potential for extended utilization (10).

Interventions in general predominantly focus on reducing ASD-specific symptoms, mitigating concurrent issues, and enhancing overall quality of life (11). Notably, early interventions demonstrate considerable efficacy, significantly improving outcomes across domains (12). In Saudi Arabia, children begin treatment at 3.3 years of age, whereas in the USA, treatment is commenced at 2.2 years of age, indicating delayed intervention in Saudi Arabia. Utilizing an online survey methodology with a sample size of ~200 participants, a study conducted >6 years prior highlighted the need for a comprehensive investigation into the prevalence of ASD and related services within the Saudi community (13).

This underscores the necessity of identifying and implementing suitable interventions tailored to children with ASD from different age groups, thus ensuring timely and effective support mechanisms. In Saudi Arabia, to the best of our knowledge, no study has yet evaluated the pediatric risk of falls among children with ASD. To fill this gap in the research literature, the present study examined the ASD profile through an analysis of sociodemographic variables, the type of medications children with ASD receive, and the presence of comorbidities. The present study also conducted a correlational analysis to evaluate the risk of falls among different age groups.

Patients and methods

Study participants. The sample size was determined using G*Power software (http://www.gpower.hhu.de/). A priori power analysis for a two-tailed correlation indicated that the minimum sample size needed to yield a statistical power of 0.95 with an α value of 0.05 and a medium effect size (Cohen's d=0.5) is 134. For an independent samples Student's t-test, a minimal sample size of 210 is required. Furthermore, a minimum of 172 participants are required for a linear regression model with 10 predictor variables, while 66 participants are required for a repeated measures analysis of variance (ANOVA). The sample for the present study comprised 250 autistic children attending the Psychology Clinic at King Khalid University Hospital (KSUM) in Riyadh, Saudi Arabia. This hospital operates under King Saud University. Therefore, the sample size was appropriate. The sample included children diagnosed with ASD from January, 2015 to the end of October, 2023. All the children had received multidisciplinary evaluations, including diagnostic, cognitive and behavioral assessments.

Study design and procedure. A retrospective cohort study was designed using a healthcare digital record system known as electronic medical record (EMR) systems to collect the data from KSUM. Ethical approval for the study was granted by the Institutional Review Board at King Saud University in Riyadh, Saudi Arabia (Ref. E-22-7451 no. 23/0175/IRB), with an issue date of March 2, 2023. The ethics committee granted a waiver of written informed consent.

Measurements and patient demographics. The demographic variables collected from EMR systems included geographical regions of Saudi Arabia (Riyadh and other regions), current age categories in three groups: Early (3-6 years), middle (7-12 years) and late (13-17 years), age at first diagnosis, body mass index (BMI), sex (female or male), education (public school with/without mixed classes, disability/ASD center, others) and parents' knowledge of ASD.

Statistical analysis. The descriptive statistics included frequencies and percentages of survey responses for categorical variables, as well as the mean (M) and standard deviation (SD) values for continuous data. Spearman's (R_S) correlation analyses were performed to examine the correlation between age and the number of medications the participants received. As a sensitivity analysis, a repeated measures analysis of variance (ANOVA) was conducted to examine whether the number of antipsychotic and non-antipsychotic medications taken (repeated measurement) was dependent on the participants' age (early, middle or late childhood). The current medications reported in the study are depicted in Data S1. In addition, supplementary the categorization of diseases reported in children with autism is demonstrated in Table SI and Data S2. The effect size was assessed using partial eta-square (η^2_p), while a Bonferroni post hoc test was performed to evaluate significant differences between particular samples.

The total study sample was divided into two groups in terms of risk of falls, using the cut score of 12 on the Humpty Dumpty Falls Scale (HDFS). The group with a lower risk of falls (HDFS <12) included 176 children with ASD, whereas the group with a higher risk of falls (HDFS ≥12) comprised 74 children with ASD. These two groups were then compared using a Mann-Whitney U test. The following dependent variables (considered as continuous or ordinal data) were examined: Age at first diagnosis, current age, BMI, number of diagnoses, number of comorbidities and number of medications taken per person, including the number of antipsychotics, non-antipsychotics and vitamins. Rank biserial correlation (RBC) was performed to assess the effect size for the Mann-Whitney U test. In addition, the total sample was divided

into three groups according to age stages during childhood: Early (children between 3 and 6 years of age), middle (children between 7 and 12 years of age) and late (adolescents between 13 and 17 years of age). As a sensitivity analysis, Pearson's χ^2 test of independence or Fisher's exact test were then conducted to examine associations between pediatric risk of falls (lower vs. higher) and the categorical variables of age, sex, education status, region of Saudi Arabia, and parent's self-reported knowledge of ASD (answered as either yes or no). The Phi (φ) statistic was used to assess the effect size for bi-categorical variables (i.e., sex, region, and knowledge), while Cramer's V was used to determine the effect size for multi-categorical variables (i.e., age and education status) in the χ^2 test.

Finally, the contribution of demographic variables to the risk of falls among children with ASD was examined using linear regression. The following predictor variables were included in the regression model: Age at first diagnosis, current age, BMI, sex, education status, parents' knowledge about ASD, number of diagnoses, number of comorbidities, number of antipsychotics, non-antipsychotics and vitamins taken. Tolerance was >0.25 (ranging from 0.48 to 0.97) and the variance inflation factor (VIF) was <3 (ranging from 1.03 to 2.19), suggesting that multicollinearity was not an issue in the multiple regression model. All statistical analyses were performed using JASP version 0.18.3.0 software for Windows (https://jasp-stats.org). A value of $P<0.05$ was considered to indicate a statistically significant difference.

Results

Characteristics of the study sample. The demographic characteristics of the study participants are presented in Table I. The mean age of first ASD diagnosis was seven years, whereas the mean current age of participants was twelve years. In terms of sex differences, the majority of the participants were male (74.4%) and the remainder (25.6%) were female. The average BMI was 19. The majority of the patients with ASD were males, had attended some schools or rehabilitation centers and resided in Riyadh. In the majority of the families, both parents took care of the children, and the majority of parents had knowledge about ASD. The majority of the children had been diagnosed with ASD, and were usually diagnosed once. Almost 39% of the children had another health condition, usually took one medication, and often did not take any vitamins. The study sample was divided according to the HDFS. The group with low pediatric risk of falls (HDFS scores <12) prevailed over those who met the criteria for a high risk of falls (HDFS scores ≥12).

Prevalence and type of comorbidity. A diagnosis of ASD was reported in 82% of the participants, among whom childhood ASD was detected in 15.6% and atypical ASD in 2.8%. In the study sample, the majorty of the children with ASD (76.4%) reported a comorbidity (Table I). One additional disease (apart from ASD) was found in 38.8% of the children, two coexisting diseases in 22%, and three in 15.6% of the childrern (Table I). The prevalence of particular types of coexisting diseases is presented in Table II. The most common was ADHD (46% of the total sample), followed by intellectual disabilities (18.4%), epilepsy (17.6%), genetic

Table I. Characteristic of the study participants (n=250).

Variable	Range/code	M/n	SD/%
Age at first diagnosis	0-15	7.27	3.4
Current age	3-22	11.65	3.85
Early (3-6)	0	30	12
Middle (7-12)	1	114	45.6
Late (13-17)	2	106	42.4
Body mass index (BMI)	8.33-42.58	18.56	5.57
Sex	0-1	0.75	0.44
Female	0	64	25.6
Male	1	186	74.4
Education status[a]	0-1	0.57	0.5
Public school with/ without mixed classes	1	71	28.4
Disability and autism center	2	67	26.8
Other	3	4	1.6
Not mentioned	4	108	43.2
Region of Saudi Arabia			
Riyadh	0	181	72.4
Other regions	1	69	27.6
Parents' knowledge about autism	0-1	0.28	0.45
Yes	0	180	72
No	1	70	28
Current diagnosis			
Atypical autism	7	2.8	
Childhood autism	39	15.6	
Autism	204	81.6	
No. of diagnoses	1-3	1.22	0.45
One	1	199	79.6
Two	2	47	18.8
Three	3	4	1.6
No. of comorbidities	0-3	1.29	1
No	0	59	23.6
One	1	97	38.8
Two	2	55	22.0
Three	3	39	15.6
No. of current medications taken per person	0-5	1.96	1.36
No. of antipsychotic drugs	0-4	1.24	0.98
No. of non-antipsychotic drugs	0-5	0.72	1.12
No. of vitamins taken	0-3	0.64	0.88
Humpty Dumpty Falls Scale (HDFS)	2-18	10.66	1.79

Table I. Continued.

Variable	Range/code	M/n	SD/%
Pediatric risk of falls	0-1	0.3	0.46
Low (HDFS <12)	0	176	70.4
High (HDFS ≥12)	1	74	29.6

M/n, mean/number (no. number of participants); SD/%, standard deviation/percentage in column. [a]For education, 0 indicates no school reported and 1 indicates education in a school or support center.

Table II. Frequency of occurrence of various types of comorbidity in the sample (n=250).

Type of comorbidity	No. of participants	%
ADHD	115	46.0
Anxiety disorder	5	2.0
Asthma	16	6.4
Cardiovascular disease	3	1.2
Constipation	3	1.2
Epilepsy	44	17.6
Genetic condition	23	9.2
Global developmental delay	16	6.4
Hematological disease	3	1.2
Infection	1	0.4
Intellectual disability	46	18.4
Metabolic disorder	15	6.0
Obesity	3	1.2
Other neurological diseases	10	4.0
Others	15	6.0
Respiratory disorders	6	2.4

ADHD, attention deficit hyperactivity disorder.

conditions (9.2%), global developmental delay (6.4%), asthma (6.4%) and metabolic disorders (6%). Other types of diseases were less frequent. The categorization of particular diseases is presented in Data S2.

Type of medications taken depending on age. On average, the participants currently took two medications (M=1.96, SD=1.36), the number of which ranged from 0 to 5 per child (Table I). Specifically, the majority of children used one medication (n=102, 40.8%), followed by two medications (n=56, 22.4%), three medications (n=34, 13.6%), four medications (n=20, 8.0%), and five medications (n=19, 7.6%). In total, 19 children (7.6%) reported not using any medication. The frequency with which particular types of medications were currently taken per child is presented in Table III. Participants took more antipsychotic medications (M=1.24, SD=0.98, range 0-4) than non-antipsychotics (M=0.72, SD=1.12, range 0-5) and vitamins (M=0.64, SD=0.88, range 0-3).

The correlation between age and the current number of medications taken was examined using Spearman's correlation analysis (Fig. 1). The results revealed that the age of the children with ASD positively correlated with the total number of medications taken (R_S=0.20, P<0.001) and antipsychotic medications used (R_S=0.16, P<0.05). Non-significant correlations were found between age and non-antipsychotic medication use (R_S=0.10, P=0.10).

A repeated measures ANOVA was then conducted with the type of medication (antipsychotic, non-antipsychotic) as a dependent variable (repeated measures) and the three categories of age during childhood (early, middle, and late) as a factor. A significant difference was found between the mean number of antipsychotic and non-antipsychotic medications taken [F(1,247)=21.15, P< 0.001, η^2_p=0.08)]. A Bonferroni post hoc test revealed that children with ASD used significantly more antipsychotic medications than non-antipsychotic (ΔM=0.56, SE=0.12, t=4.60, P<0.001). A significant effect was also found for childhood stages [F(2,247)=4.98, P=0.008, η^2_p=0.04]. A Bonferroni post hoc test revealed that children in the middle stage took fewer medications on average than adolescents (ΔM=-0.29, SE=0.09, t=-3.15, P=0.005). There was no interaction effect between type of medication and age [F(2,247)=0.71, P=493, η^2_p=0.01)]. Differences in the mean number of antipsychotic and non-antipsychotic medications across ages are presented in Fig. 2.

Differences between children at high and low risk of falls in terms of demographic variable. A Mann-Whitney U test was conducted to assess the differences between children at lower and higher risk of falls for the following continuous or ordinal variables: age of first diagnosis, current age, BMI, number of diagnoses, number of comorbidities and number of medications taken per child, including the number of antipsychotics, non-antipsychotics, and vitamins (Table IV). Significant differences were found between these groups in terms of first diagnosis and current age. In particular, participants at higher risk of falls were diagnosed <6 years of age, whereas those at lower risk were diagnosed at ~8 years of age. Similarly, younger children (mean age, 10 years) had a higher risk of falls than older children (mean age, 12 years). The differences in BMI, number of diagnoses, comorbidity and medications taken per child were not significant.

As regards categorical variables, the analyses identified significant associations between pediatric risk of falls and age (Table V). Among the children who were at a higher risk of falls, those at an early age (60%) were more susceptible than their counterparts in middle childhood (34%) and adolescents (16%). However, the effect size was small (P<0.001, φ=31).

Logistic regression analysis of pediatric risk of falls. Linear regression analysis was performed for pediatric risk of falls, assessed using the HDFS as the dependent variable. The predictors were age at first diagnosis, current age, BMI, sex, education status, parents' knowledge about ASD, number of diagnoses, number of comorbidities, number of antipsychotics and non-antipsychotics taken (Table VI). The regression model explained 23% of the pediatric risk of falls variance [R=0.48, R^2=0.23, F(10,238)=6.92, P<0.001]. However, only

Table III. No. of particular types of medications taken currently per child.

	Antipsychotics		Non-antipsychotics		Vitamins	
No. of medications	No. of participants	%	No. of participants	%	No. of participants	%
0	56	22.4	153	61.2	144	57.4
1	112	44.8	47	18.8	67	26.7
2	54	21.6	26	10.4	26	10.4
3	22	8.8	16	6.4	14	5.6
4	6	2.4	6	2.4		
5			2	0.8		

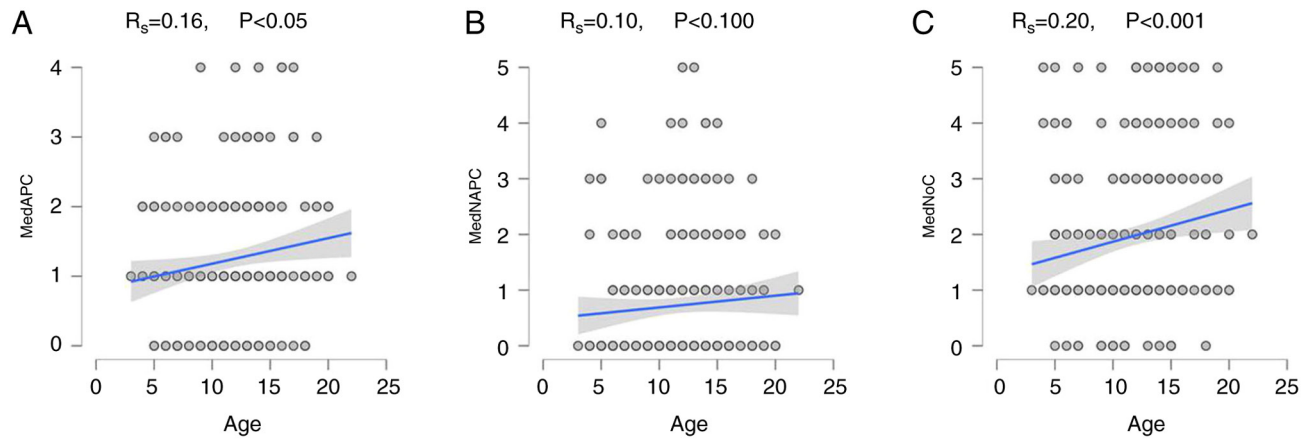

Figure 1. Correlation plots illustrating the correlations between age and (A) antipsychotic medications (MedAPC); (B) non-antipsychotic medications (MedNAPC); and (C) total number of medications (MedNoC) used by children with autism spectrum disorder. The regression line indicates the direction of correlation between two variables.

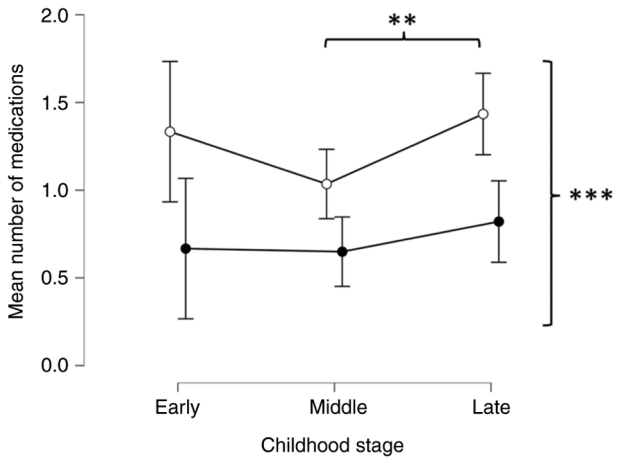

Figure 2. Differences between the mean number of antipsychotic and non-antipsychotic medication used in three samples of children with autism across age (early, middle and late childhood). The error bar represents 95% confidence intervals. White circles represent antipsychotic medications, and black circles represent non-antipsychotic medications. **P<0.01; ***P<0.001.

two variables predicted a high risk of falls in children with ASD: A lower current age of the child (β=-0.34, P<0.001) and being male (β=0.21, P<0.001).

Discussion

The present study identified an association between the age of children and the total number of medications taken and antipsychotic medications used. Furthermore, the findings indicated a significant association between the risk of falls and age. The results of logistic regression analysis suggested that multiple factors, including a lower current age and the male sex, predict the risk of falls. Among the health conditions that were comorbid with ASD, the results revealed that ASD conditions have a high comorbidity burden with a significant co-occurrence of ADHD, followed by intellectual disabilities and epilepsy. Overall, comorbidity profiles were present in almost 80% of ASD cases. This reflects the fact that comorbidity is an emerging health concern in ASD (14). Notably, the high comorbidity profile associated with ASD is a confounding factor in elucidating the pathological mechanisms of ASD and is the foundation of ASD heterogeneity. It has been previously proposed that ASD can be categorized into essential and complex ASD, the latter of which refers to individuals who have a greater number of seizures and lower intellectual capabilities (15).

Presenting with a comorbidity is linked to poorer health outcomes and elevated healthcare needs among children diagnosed with ASD, including, but not restricted, to management by different clinical disciplines, economic burden,

Table IV. Mann-Whitney U test for examining the differences between children at a high and low risk of falls in demographic continuous or ordinal variables.

	Low risk (n=176)		High risk (n=74)				
Variable	M	SD	M	SD	U test	P-value	RBC
Age at first diagnosis	7.84	3.39	5.93	3.02	8632.0	**<0.001**	0.33
Current age	12.43	3.65	9.78	3.67	9082.5	**<0.001**	0.40
Body mass index (BMI)	18.92	5.71	17.69	5.14	7359.5	0.071	0.15
No. of diagnoses	1.24	0.48	1.16	0.37	6923.0	0.261	0.06
Comorbidity	1.33	1.01	1.22	0.97	6917.0	0.418	0.06
No. of medications	1.90	1.32	2.11	1.46	5987.0	0.294	0.00
Antipsychotics	1.26	0.94	1.20	1.07	6818.0	0.535	0.05
Non-antipsychotics	0.65	1.04	0.91	1.27	5865.0	0.156	-0.10
Vitamins	0.62	0.87	0.70	0.92	6228.5	0.542	-0.04

Values in bold font indicate statistically significant differences (P<0.05). M, mean; SD, standard deviation; U test, Mann Whitney U test statistic; RBC, rank biserial correlation as an effect size for the Mann-Whitney U test.

Table V. Analysis of the associations between pediatric risk of falls and categorical demographic variables.

		Low risk (n=176)		High risk (n=74)					
Variable	Categories	No. of participants	%	No. of participants	%	χ^2	df	P	φ/V
Age	Early (3-6 years)	12	40.0	18	60.0	23.82	2	**<0.001**	0.31
	Middle (7-12 years)	75	65.8	39	34.2				
	Late (13-17 years)	89	84.0	17	16.0				
Sex	Female	51	79.7	13	20.3	3.56	1	0.059	0.12
	Male	125	67.2	61	32.8				
Education status	Public school	51	71.8	20	28.2	6.76[a]	3	0.152	0.15
	Disability/autism center	52	77.6	15	22.4				
	Other	4	100.0	0	0.0				
	Not mentioned	69	63.9	39	36.1				
Region	Riyadh	130	71.8	51	28.2	0.64	1	0.425	0.05
	Other regions	46	66.7	23	33.3				
Parents' knowledge	Yes	133	73.9	47	26.1	3.76	1	0.053	0.12
	No	43	61.4	27	38.6				

Values in bold font indicate statistically significant differences (P<0.05). Data were analyzed using Pearson's χ^2 test or [a]Fisher's exact test. df, degree of freedom; φ, phi statistic as an effect size; V, Cramer's V statistic as an effect size.

and coordinating clinical, behavioral and pharmacological management (16). Identifying and characterizing the number of health comorbidities is essential in mapping ASD cases as it aids in treatment and prognosis (17). A comprehensive understanding of comorbidities generally improves health metrics and quality of life (18).

The comorbidity of ADHD and ASD is, however, well recognized. In a previous study, utilizing a cross-sectional study design, the co-occurrence of both conditions was evident in almost 50% of the study sample which comprised more than three thousand children with ASD (19). In a meta-analysis study, it was found that compared to adolescents, children with ASD exhibited a higher prevalence of ADHD and sleep-related issues (20). However, the comorbidity of ASD-ADHD continues to be a subject of debate (21). Furthermore, both ASD and ADHD are described separately in the Diagnostic and Statistical Manual of Mental Disorders version 5 (DSM-5). Nevertheless, both similarities and

Table VI. Linear regression analysis of pediatric risk of falls.

						95% CI		Collinearity	
Independent variables	b	SE	β	t	P-value	LL	UL	Tolerance	VIF
(Intercept)	12.30	0.63		19.61	<0.001	11.06	13.53		
Age at first diagnosis	-0.06	0.04	-0.12	-1.46	0.145	-0.15	0.02	0.48	2.10
Current age	-0.16	0.04	-0.34	-3.96	<0.001	-0.23	-0.08	0.46	2.19
Body mass index (BMI)	-0.01	0.02	-0.04	-0.56	0.578	-0.05	0.03	0.84	1.19
Sex	0.86	0.24	0.21	3.64	<0.001	0.40	1.33	0.97	1.03
Education status	-0.03	0.08	-0.02	-0.31	0.754	-0.19	0.14	0.91	1.11
Parents' knowledge of autism	0.15	0.24	0.04	0.64	0.524	-0.31	0.61	0.93	1.08
No. of diagnoses	0.03	0.12	0.02	0.23	0.818	-0.21	0.26	0.74	1.35
No. of comorbidities	0.02	0.23	0.01	0.10	0.923	-0.44	0.48	0.94	1.07
No. of antipsychotics taken	0.06	0.11	0.03	0.54	0.590	-0.16	0.28	0.88	1.14
No. of non-antipsychotics taken	0.10	0.11	0.06	0.92	0.357	-0.11	0.31	0.71	1.42

b, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; t, t-test statistic; CI, confidence interval; LL, lower level; UL, upper level; VIF, variance inflation factor.

differences between them were included (22), indicating a potential recognition of ASD-ADHD in future versions of DSM. Our findings align with existing literature and highlight the existence of a clinically distinct subgroup of ASD-ADHD (19,21,23). Therefore, moving forward and establishing characteristic diagnostic and management strategies is paramount.

A previous study also indicated that the rate of antipsychotics taken in children with ASD is high (24). According to a previous meta-analysis, the rate is expected to reach 1 adolescent with ASD in every 10 adolescents treated with antipsychotics. This could be driven by the fact that aggression, irritability (25) and other psychiatric conditions are commonplace in ASD (26). Evidence extracted from a systematic review and meta-analysis revealed that antipsychotics engender a significant clinical improvement in children with ASD compared to adults (27). The present study found that the age of the children and the total number of medications taken were positively associated. In support of these findings, previous studies have indicated that increases in age correlate with the number of medicines used (28-30). For instance, a significant association between age and treatment was found in a report utilizing the Simons Simplex Collection (29).

The present study also identified an association between the age at first diagnosis and the risk of falls among children with ASD. Specifically, those at a higher risk of falls were diagnosed with their condition <6 years of age, while those at a lower risk received their diagnosis at ~8 years of age. In general, the risk of falls and fall-related consequences were reported to be higher in younger children than in older ones. Specifically, it was found that there were ~20 fall-related deaths in children <5 years of age and 10 fall-related deaths in children aged between 5 and 9 years (31).

Herein, a significant association was also found between the age at first diagnosis and the risks of falls. This could be driven by the fact that a younger age at first diagnosis is linked to severe behavioral symptoms, including aggression and tantrums (32). In line with this finding, a significant number of toddlers diagnosed with ASD <4 years of age present with more complex medical conditions (33). Alongside this, the time of diagnosis is also clinically relevant (34).

One of the ASD-associated symptoms is motor dysfunction. Hypotonia was documented to have prevailed in 50% of ASD cases in a retrospective study conducted at the New Jersey Medical School autism center. Notably, this functional reduction in muscle tone was found to be improved in older ASD cases (35). Supporting these findings, the risks of falls are reduced as age increases. In support of this, a recent qualitative study demonstrated that children with ASD are prone to accidental injuries. These injuries were associated with risk factors, including comorbidity of other conditions (36). Another report indicated that the most common accidental injury in ASD was a mechanical fall, which was documented in 44% of the study sample (37). According to the World Health Organization, falls account for >600,000 deaths each year, and it is the second leading cause of mortality (38). Yet, the defined characterizations of motor dysfunction consequences, detection, and interventions have not been well investigated in ASD (39).

The prevalence of ASD differs regionally. For example, in some USA states such as Pennsylvania and California, it can reach around 50 cases per 1,000 children. Other states could be estimated to be 15 per 1,000 children (40). On the other hand, ASD is estimated at 9.4 per 1,000 children in Korea (41). Even there are regional differences in the documented ASD cases, the fact that it is comorbid with ADHD and linked to an elevated rate of falls is consistent. The data of the present study enhance existing knowledge regarding the association between the pediatric risk of falls and younger age and the comorbidities of ASD and ADHD. The present study found that in the Saudi population, the comorbidity of ASD-ADHD was consistent with previous findings in Taiwanese (42), English (43) and Korean populations (44). In line with this, the

elevated risk of falls was recognized to be linked to ASD in different populations (8,45).

The associated ASD-ADHD comorbidity and risk of falls are predominant in different cultures, providing insights that enrich global understandings and recognition of ASD-associated conditions and consequences. It underscores the significance of raising parents' awareness of the risks of falls, considering that sometimes falls are not reported to the healthcare system (46). It further highlights the need to establish an early intervention in younger ASD children to reduce the health burden and improve clinical safety in ASD children at the global level.

The present study has several clinical implications. Firstly, it highlights the heterogeneity of ASD and its association with severe consequences such as risk of falls. Thus, it is recommended that healthcare professionals establish policies aimed at raising awareness and educating families about the risk of falls in younger individuals with ASD, particularly those who are taking antipsychotics, and implement these educational workshops to be mandatory appointments/sessions with healthcare professionals, whether under a family care unit or primary healthcare clinic. Secondly, as the association is significant, the findings affirm ASD-ADHD comorbidity, and thus the need to establish characteristic diagnostic and management strategies is paramount.

The present study however, also has certain limitations, which should be mentioned. The present study provides evidence regarding the current status of treatment and comorbidities of children with ASD. The children's comorbidity burden and treatment patterns were characterized. The present study also conducted a correlation analysis to evaluate the risks of falls among different age groups using observational data on 250 patients with ASD from routine clinical practice at KSUMC. However, the present study has a number of limitations that need to be addressed. Firstly, the sample size was relatively small. Although multiple EMR studies have been published with a similar sample size range (47,48), 250 is appropriate if statistically robust conclusions are to be drawn. It is therefore recommended that these findings be replicated using a larger sample size. Furthermore, the present study was a single-center report, thus rendering it necessary to expand these findings using a multicenter study design (49,50). Additionally, the present study focused on the pharmacological treatment approach. Indeed, it is widely acknowledged that a majority of children with ASD take pharmacological treatment (11). However, ASD is also managed using behavioral and pharmacological treatment strategies (51). Furthermore, the findings report the current status of the number of medications taken; however, no history of the number of medications taken was obtained. In addition, although pharmacological treatment was characterized, compliance was not investigated. Moreover, in any follow-up, further adjustment of diverse covariance is required for the multifactorial features of ASD, ASD management, comorbidity and the risk of falls.

In conclusion, ASD is increasingly being recognized as a significant and growing public health concern. It places a substantial socio-economic burden upon families. The findings of the present study confirm existing evidence regarding the link between the pediatric risk of falls and a younger age. Additionally, the present study confirmed the comorbidity of ASD and ADHD, emphasizing the need to identify ASD-ADHD in the future as a clinical subgroup of developmental disorders. These results will also encourage healthcare practitioners to increase parental awareness of the risks of falls in young autistic children.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MAA, TKA and AMR conceptualized the study and were involved in the study methodology. AMR was involved in the formal analysis. HMA and SAA were involved in the investigative aspects of the study. HAA, SAA and AMR were involved in data curation. MAA and TKA confirm the authenticity of all the raw data. HAA, SAA, TKA and AMR were involved in the writing and preparation of the original draft of the manuscript. TKA, MAA and AMR were involved in the writing, reviewing and editing of the manuscript. MAA and TKA supervised the study. MAA was involved in project administration. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

Ethical approval was granted by the Institutional Review Board at King Saud University in Riyadh, Saudi Arabia (Ref. E-22-7451 no. 23/0175/IRB); issue date, March 2, 2023. A waiver of written informed consent was granted by the ethics committee.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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