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Antipsychotic Medication Adverse Effect on Autistic Patients among Saudi Papulation

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ABSTRACT:
Background: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by persistent impairments in social communication and restricted, repetitive patterns of behavior. Pharmacological treatments for the core symptoms of ASD are currently lacking, with existing medications primarily targeting associated symptoms and comorbidities such as irritability and psychiatric conditions. Early implementation of behavioral therapies has shown promise in alleviating core ASD symptoms and improving functional outcomes. Combining behavioral therapies with psychopharmacological monitoring is considered a beneficial approach.
Methodology: This cross-sectional study aimed to assess the level of knowledge regarding autism spectrum disorders among general care physicians and psychiatric physicians in a specific region. A self-reported questionnaire, comprising demographic information, understanding of autism, experience with patients with autism, and knowledge-based questions, was administered. The collected data were analyzed using Statistical Package for Social Science (SPSS) software.
Results: The study included 286 participants, with 59.1% acknowledging inadequate knowledge of autism spectrum disorders. However, 40.2% reported experience in diagnosing and collaborating with individuals with ASDs. Among the participants, 80.8% were aware of the challenges faced by children with ASDs in social interaction, communication, and behavior, while 61.9% correctly recognized the higher prevalence of ASDs in boys. The study also revealed potential adverse consequences of antipsychotic medication use in individuals with ASDs, including weight increase (67.8%), hyperprolactinemia (29.4%), extrapyramidal symptoms (32.2%), drowsiness (56.1%), and cognitive adverse effects (18.3%).
Conclusion: This study highlights a lack of knowledge among healthcare providers regarding Autism Spectrum Disorders (ASDs). This has implications for accurate diagnosis and effective treatment. The study also emphasizes the potential adverse consequences of using antipsychotic medications in individuals with ASDs. Additional education and training are needed to address these knowledge gaps and improve care for individuals with ASDs.

KEYWORDS: Autism, Antipsychotic Medication, Autism Spectrum Disorder

INTRODUCTION

Autism spectrum disorder (ASD) is one of the neurodevelopmental disorders that is considered a complex dynamic condition that appears early in childhood and is characterized by persistent impairments in mutual social communication and social interactions with others as well as the presence of restricted, repetitive patterns of interests, activities, and behaviors [1]. In previous studies conducted to assess the prevalence of ASD in children with an age range between 7-9 years old, the reported prevalence in Italy was 1.14 % and 1.3 % [2], worldwide with 1 and 4.36 % [3] with male to female ration of 4 :1 and high prevalence of total children who have an intellectual disability [4,5]. In Saudi Arabia, data about the confirmed cases of ASD are not available, and subjective data showed that many children with ASD have not been diagnosed yet where only one recent study reported that the prevalence of ASD was 2.5 % depending on the hospital-based sample [6].
Until now, there is no pharmacological medication that could show to be effective in the management of the core symptoms of ASD where most of the pharmacological treatments with psychological interventions are mainly used for the treatment of the associated symptoms including irritability or coexisting psychiatric conditions as attention deficit disorders, schizophrenia spectrum disorder or oppositional disorders which are frequent in ASD patients [7]. Antipsychotic medications are used in ASD patients for the management of associated comorbidities including schizophrenia spectrum disorders (SSD) and behavior disorders [8]. There is a

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significant relation between ASD and SSD where the prevalence rate of SSD symptoms among patients with ASD was 9.6 % [9] and patients with SSD have a significantly higher Tate of autistic symptoms than healthy controls [10].

Evidence suggests that the early implementation of behavioral therapies could be associated with the alleviation of the core ASD symptoms and improve the impact of ASD on functional outcomes [8]. Moreover, evidence indicates that a combination of behavioral therapies with psychopharmacological monitoring is considered the most beneficial approach [8,11]. Two atypical antidepressants, risperidone, and aripiprazole have been approved by the Food and Drug Administration (FDA) in the United States for the treatment of irritability in youth with ASD. In addition, preliminary evidence supports the use of other antipsychotic medications to treat psychiatric symptoms associated with autism [8]. Emerging data suggest a relatively high dose of at least two antidepressants used concurrently to treat behavioral symptoms in some ASD patients [12]. Although this advantage is often associated with clinical manifestations of autism spectrum disorder in patients with ASD, there is limited information about tolerance, safety, and clinical benefits, especially for long-term use [13]. The rate of prescribing psychotropic drugs specifically in youth with ASD is increasing where recent studies showed that about 57.4 % of patients with ASD receive at least one psychotropic medication with antipsychotics is the most common prescribed drug class [14].

However, the use of antipsychotic medications is associated with different side effects. Weight gain is one of the most disruptive adverse effects of atypical antipsychotics while used in children and adolescents [15]. It is particularly concerning for the reason that obesity can set the stage for the improvement of severe medical problems including diabetes, hyperlipidemia, and cardiovascular disease. Other side effects included hyperprolactinemia, EPS, sedation, and adverse cognitive effects [16].

This study aims to assess the prevalence of adverse effects of antipsychotic medication on autistic patients in Saudi Arabia according to family medicine physicians and psychiatric physicians. In addition, it was aimed to determine the knowledge of family medicine physicians and psychiatric physicians.to adverse effects of antipsychotic medication on autistic patients. The results of this study will fill the gap in the limited information about the management of autistic patients in Saudi Arabia and help in improving patients' compliance with their medications.

METHODOLOGY

The study was intended as a cross-sectional study that utilized a pre-made online questionnaire. The inclusion criteria were all family medicine and psychiatric physicians practicing in the region of interest. The sample size was determined using the Roasoft web tool with a confidence level of 95% and an error margin of 5%. The estimated sample size was 350 participants, with 81% of responses collected and analyzed.

The questionnaire used in the study was self-reported and based on a review of the relevant literature and previous research [17]. The questionnaire was adapted by the investigators and was piloted on 25 participants to evaluate its applicability, It contained participant characteristics such as age, gender, highest degree, occupation, and years of experience. In addition, participants were asked about their awareness of autism, autistic patients, and autistic patients who are taking antipsychotic medication. Other concerns concerned the frequency and nature of adverse effects linked with antipsychotic drugs. Based on earlier research, eight knowledge-based questions with agree, disagree and unsure answers were also included.

Ethical considerations were taken into account, and the Institutional Review Board (IRB) of King Saud Medical City in Riyadh authorized the study. The participants were informed that The purpose of this research study is to investigate and understand the incidence rate of adverse effects caused by antipsychotic medication in patients with autism spectrum disorder (ASD) in Saudi Arabia. Additionally, the names and affiliations of the researchers were provided to all participants. They were also informed that their participation was optional and that their data would be stored securely and handled during the analysis by KSMC policies and regulations, ensuring anonymity. All participants provided informed consent.

Version 26 of the Statistical Package for Social Science (SPSS) software was utilized for data management. As applicable, descriptive statistics were applied in the form of tables and graphs. For regularly distributed quantitative variables, the student t-test was utilized, whereas the Mann-Whitney U test was utilized for non-normally distributed data. Chi-square tests were applied to qualitative variables. The significance level was chosen at p=0.05.

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RESULTS

Table 1 displays the demographic characteristics of the 286 study participants. 38.5 % of the participants were male, and 61.5 % were female. The majority of participants (77.6 %) were aged 25 to 35, while only 3.1% were 45 or older. The largest group of individuals (40.9 %) had 4-5 years of clinical experience, whereas 8.4 percent had more than 10 years of expertise. The majority of participants (78%) were general medicine doctors, whereas 16.4% were psychiatrists and 5.6% were psychologists. The majority of participants had a bachelor's degree (66.4%), while 33.6% had an advanced degree (MSc and Ph.D.). The bulk of participants (77.6 %) were employed in Riyadh, while 22.4% were employed elsewhere.

Table 1: Demographic factors of the participants (N=286)

		Count	Column N %
Gender	Male	110	38.5%
	Female	176	61.5%
Age	21-24	21	7.3%
	25-35	222	77.6%
	35-44	34	11.9%
	45 or older	9	3.1%
Years of clinical experience	1-3	113	39.5%
	4-5	117	40.9%
	5-10	32	11.2%
	> 10	24	8.4%
Your specialty	Psychiatrist	47	16.4%
	Family medicine physician	223	78.0%
	Psychologist	16	5.6%
Highest Degree Attained	Bachelor's Degree (BSc)	190	66.4%
	Advanced Degree (MSc and Ph.D.)	96	33.6%
Your work region	Riyadh	222	77.6%
	Outside Riyadh	64	22.4%

Table 2 illustrates the diagnostic and prescribing practices of participants for individuals with autism spectrum disorders (ASDs). 40.2% of the volunteers had treated patients diagnosed with ASDs, whereas 59.8% had not. 63.6 % of participants reported prescribing antipsychotic medication to ASD patients, whereas 36.4% reported not doing so. When asked how often they prescribed antipsychotic drugs to individual patients, the majority of participants (60.8%) said they had never done so before. 25.5% of individuals who had been administered medication had been prescribed a single medication, while 8.7% had been prescribed two medications. Fewer participants had been prescribed three or more drugs (1.7 %).

Table 2: Practice of the participants toward diagnosis and antipsychotic medication prescription

		Count	Column N %
Have you treated patients diagnosed with autism spectrum disorders (ASDs)?	No	171	59.8%
	Yes	115	40.2%
Have you prescribed antipsychotic medication to patients diagnosed with autism spectrum disorders?	No	104	36.4%
	Yes	182	63.6%

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In your clinical experience, how frequently do you prescribe antipsychotic medications to individual patients?	Never prescribed medication before	174	60.8%
	One medication	73	25.5%
	Two medications	25	8.7%
	Three medications	9	3.1%
	More than 3	5	1.7%

Participants reported the prevalence of side effects linked with the use of antipsychotic medication in Figure 1. 7.2% of the subjects reported no adverse effects. Weight gain was the most often reported adverse impact, with 67.8 percent of patients reporting this side effect. Hyperprolactinemia was reported by 29.4% of participants, while 32.2% of participants had extrapyramidal symptoms. 56.1 % of subjects felt sedation, whereas 18.3 percent reported negative cognitive side effects.

FIGURE 1: THE PREVALENCE OF ADVERSE EFFECTS OF USING ANTIPSYCHOTIC MEDICATION

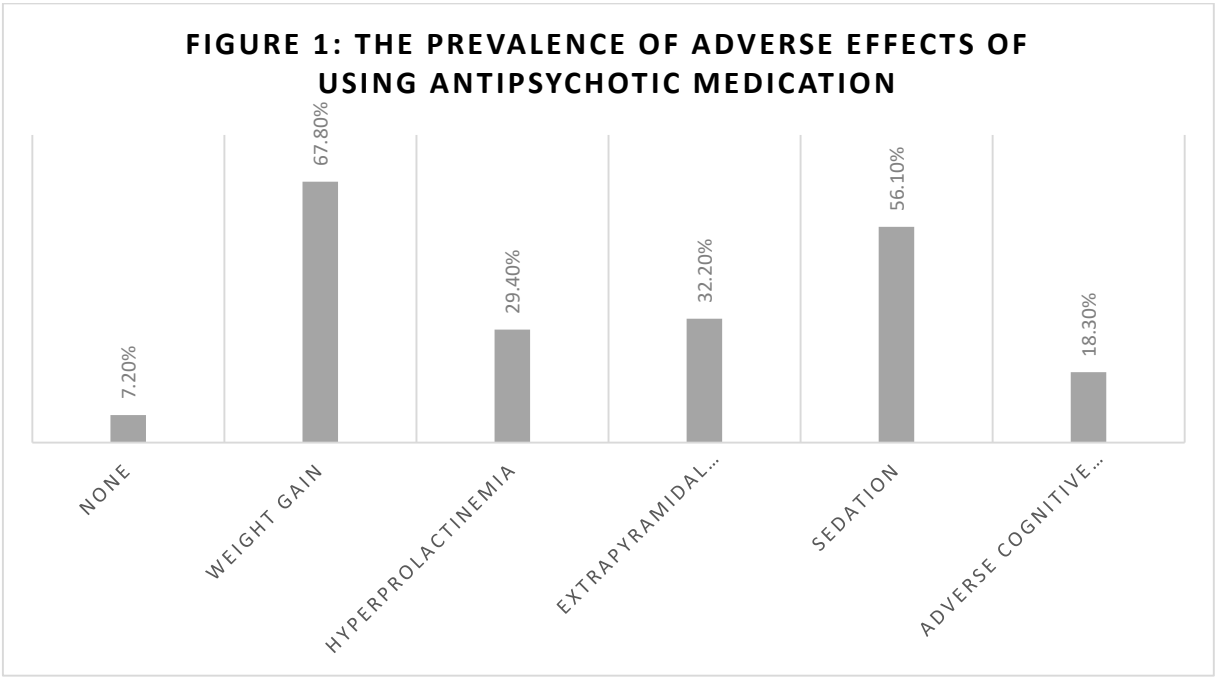

Table 3 illustrates the participants' knowledge of autism spectrum diseases (ASDs). The majority of responders (80.8%) concurred that children with ASDs typically demonstrate deficits in social interaction, communication or language, and behavioral development. Likewise, a majority (61.9%) concurred that ASDs are more prevalent in males than in girls. Regarding the prevalence of ASDs in comparison to other conditions, opinions were split. 36.7 % disputed that the prevalence of ASDs is higher than that of juvenile diabetes, while 37.1% agreed and 26.2% were undecided. Similarly, 39.2% of respondents disagreed that ASDs are more prevalent than Down syndrome, while 37.1% agreed and 23.8% were unclear. The majority of individuals (64%) disputed that ASDs are regarded treatable, while 24.8% agreed and 11.2% were uncertain. The majority of respondents (59.1 %) agreed that the FDA had approved risperidone and aripiprazole to treat irritability associated with ASDs, while 13.3 % disagreed and 27.6 percent were unclear. The majority of participants (77.6 %) disagreed that vaccines cause ASDs, while 14.3 percent agreed and 8.0% were unclear. Similarly, most participants (61.5%) disagreed that emotionally distant or rejecting parents are the primary cause of ASDs, while 26.2% agreed and 12.2% were unsure. 67.1 % of participants believed that genetic factors significantly contribute to the etiology of ASDs, whereas 20.3% disagreed and 12.6% were uncertain. In conclusion, 66.8 % of individuals disagreed that ASDs are rare illnesses, whereas 19.6 % agreed and 13.6 % were undecided.

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Table 3: The knowledge of the participants about Autism

	Disagree		Agree		Unsure	
	Count	Row N %	Count	Row N %	Count	Row N %
Children with ASDs commonly exhibit impairments in social interaction, communication or language, and behavioral development.	43	15.0%	231	80.8%	12	4.2%
ASDs are more prevalent in males than females.	54	18.9%	177	61.9%	55	19.2%
ASDs have a higher prevalence compared to juvenile diabetes.	105	36.7%	75	26.2%	106	37.1%
ASDs have a higher prevalence compared to Down syndrome.	112	39.2%	106	37.1%	68	23.8%
ASDs are considered curable.	183	64.0%	71	24.8%	32	11.2%
Risperidone and aripiprazole have obtained FDA approval for treating irritability associated with ASDs.	38	13.3%	169	59.1%	79	27.6%
Vaccines are causally linked to the development of ASDs.	222	77.6%	41	14.3%	23	8.0%
Emotionally distant or rejecting parents are the primary cause of ASDs.	176	61.5%	75	26.2%	35	12.2%
Genetic factors significantly contribute to the etiology of ASDs.	58	20.3%	192	67.1%	36	12.6%
ASDs considered rare disorders	191	66.8%	56	19.6%	39	13.6%

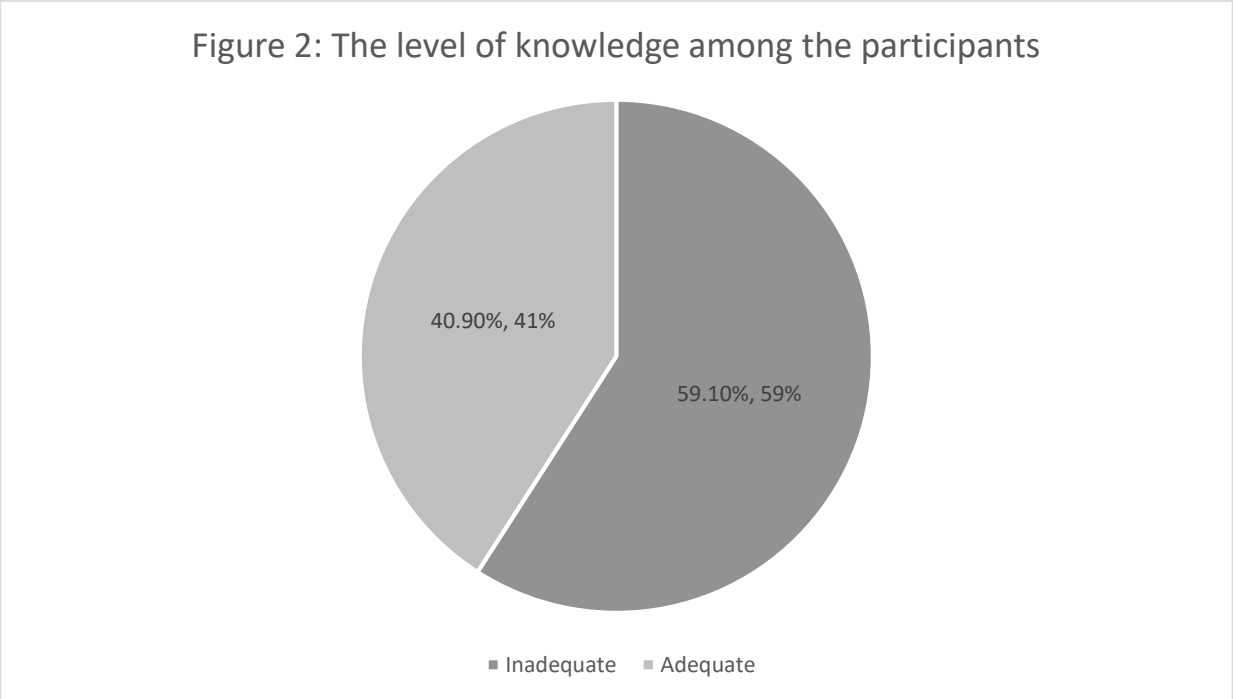

Figure 2 depicts the participants' level of knowledge of autism spectrum diseases (ASDs). 59.1 % of the 286 participants rated their knowledge as inadequate, while 40.9% rated their knowledge as adequate.

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Table 4 displays the correlation between the participants' degree of knowledge and their demographic characteristics. The level of knowledge was either deemed insufficient or adequate. The results reveal that there were no significant differences between male and female participants' levels of knowledge (p = 0.458). Age was shown to be substantially linked with knowledge level (p = 0.010), with participants aged 45 or older more likely to have appropriate knowledge than those aged 21-24. There was no correlation between knowledge level and years of clinical experience (p = 0.126), or highest degree earned (p = 0.945). However, there was a strong correlation between the amount of knowledge and the specialty of the participants (p = 0.000), with psychiatrists more likely than family medicine physicians or psychologists to have enough understanding. The employment region of the participants was not significantly connected with their degree of expertise (p =.600).

Table 4: The relation between knowledge and demographic factors

		Knowledge				
		Inadequate		Adequate		P-value
		Count	Row N %	Count	Row N %	
Gender	Male	68	61.8%	42	38.2%	0.458
	Female	101	57.4%	75	42.6%	
Age	21-24	17	81.0%	4	19.0%	0.010*
	25-35	134	60.4%	88	39.6%	
	35-44	16	47.1%	18	52.9%	
	45 or older	2	22.2%	7	77.8%	
Years of clinical experience	1-3	63	55.8%	50	44.2%	0.126
	4-5	77	65.8%	40	34.2%	
	5-10	19	59.4%	13	40.6%	
	> 10	10	41.7%	14	58.3%	
Your specialty	Psychiatrist	15	31.9%	32	68.1%	0.000*
	Family medicine physician	144	64.6%	79	35.4%	
	Psychologist	10	62.5%	6	37.5%	
Highest Degree Attained	Bachelor's Degree (BSc)	112	58.9%	78	41.1%	0.945
	Advanced Degree (MSc and Ph.D.)	57	59.4%	39	40.6%	
Your work region	Riyadh	133	59.9%	89	40.1%	0.600
	Outside Riyadh	36	56.3%	28	43.8%	

DISCUSSION

ASD is a complex, varied, and lifelong neurodevelopmental disease characterized by stereotyped and repetitive behaviors and impaired social and communication abilities [18,19]. The purpose of this study was to assess the knowledge and prescribing practices of healthcare providers regarding the diagnosis and administration of antipsychotic drugs to individuals with autism spectrum disorders (ASDs). The purpose of the study was also to investigate the participants' understanding of ASDs and the variables that may influence their knowledge and practice.

The study's findings indicate that a sizeable proportion of healthcare workers lack adequate knowledge of ASDs. In reality, 59.1 % of participants regarded their understanding as inadequate. This finding is consistent with earlier studies done by *Chiarotti F, and Venerosi A. that* have found a paucity of ASD knowledge among healthcare workers [20]. And this is reinforcing the result of a study done in Africa, numerous investigations have demonstrated that physician knowledge and understanding of ASD are minimal [23,24]. Moreover, in our study, 40.2% of the participants reported diagnosing and treating patients with autism, which is higher in comparison to a previous study, done by *Altay M*, which was conducted among family medicine physicians and reported that 70.8% of the participants had seen autism cases [25]. Per studies that medical students and different medical staff [26,27], approximately 80.8%

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of participants in the current study were aware that children with ASDs had deficits in social interaction, communication or language, and behavioral development. However, a concerning finding was that only approximately 61.9% of participants correctly recognized the higher susceptibility of males to Autism Spectrum Disorders (ASDs), aligning with a study conducted in Palestine by Shawahna et al. [28]. With the increasing prevalence of ASDs, healthcare professionals have a crucial role in their diagnosis and treatment.

In addition, the results of the study indicate a significant prevalence of antipsychotic medication prescriptions for patients with ASDs. 63.6% of respondents reported giving antipsychotic medications to ASD patients. This result is consistent with prior reports of the use of antipsychotic drugs to address the irritability associated with ASDs [29,30]. In a systematic review of 10 trials, *Loy J et al.* found an upward trend in the dispensing of psychotropic medications from 2009 to 2012, with Risperidone being the most commonly prescribed medication, given in 61.5% of cases to patients with ADHD and 35.5% of cases to patients with conduct disorders [31]. In another study, *Hong M et al.* found that among 17,606 cases of autism, 5,348 patients were taking psychotropics, with atypical antipsychotics and antidepressants being the most common [32]. In addition, *Spencer et al.* showed that 63.6% of participants with ASD younger than 20 were prescribed psychotropics [33]. In a previous study done by *Aishworiya R et al*, the authors reported a drug use rate as low as 35% for children with autism, which was attributed to a low participation rate (20%) in the medical aid group [34]. In addition, a previous study by *Schein J, Childress A, Adams J, et al.* showed that 92% of both children and adolescents initiated a stimulant and 11% initiated combination therapy [35] while the incidence of multiple prescriptions was 13.7% in our study.

It is noteworthy that a significant number of participants in this study reported experiencing undesirable side effects from long-term use of antipsychotic medications, including weight gain, hyperprolactinemia, extrapyramidal symptoms, sedation, and adverse cognitive effects. Specifically, weight increase was reported by 68% of subjects, aligning with previous research by Pillinger T, McCutcheon RA, Vano L, et al., as well as other studies, highlighting the prevalence of this adverse effect in patients with ASDs receiving antipsychotic drug treatment [16,36,37]. Weight increase can result in a variety of health issues, such as obesity, diabetes, and cardiovascular disease, which can have severe effects on ASD sufferers [38,39]. A high percentage of subjects also reported that hyperprolactinemia is a significant and common side effect (29.4 %). This is consistent with prior research by *Lu Z, Sun Y, Zhang Y, et al.* that identified hyperprolactinemia as a side effect of antipsychotic drug treatment [40]. Hyperprolactinemia can lead to a range of symptoms that have a negative impact on the well-being of individuals with ASDs, including disruptions in menstrual cycles, the occurrence of galactorrhea, and sexual dysfunction. These effects can significantly diminish the overall quality of life experienced by individuals with ASDs. [42]. In addition, 32,2 % of patients had extrapyramidal symptoms including akathisia, dystonia, and parkinsonism. These symptoms can be incapacitating and have a substantial influence on the quality of life of those with ASDs [43]. A considerable majority of participants (56.1%) also reported sedation, which might impair cognitive performance and lead to daytime drowsiness.

In addition, the study's findings imply that demographic factors may influence the understanding and practice of healthcare providers about ASDs. Age was found to be substantially linked with knowledge level, with older participants being more likely to possess appropriate information. Similarly, there was a strong association between the specialty of the participants and their degree of expertise, with psychiatrists more likely to have enough understanding than family medicine physicians or psychologists. These results show that healthcare practitioners, particularly those who are younger or who are not psychiatrists, may require additional education and training to improve their understanding and practice.

In conclusion, this study underscores a noteworthy knowledge gap among healthcare providers concerning Autism Spectrum Disorders (ASDs). Despite a substantial number of participants claiming experience in diagnosing and managing individuals with autism, more than half of them acknowledged a perceived insufficiency in their understanding. This lack of comprehension among healthcare professionals holds significant consequences for the precise diagnosis and optimal treatment of individuals with ASDs, particularly in light of the increasing prevalence of these disorders.

Furthermore, the study reveals the potential adverse consequences associated with the use of antipsychotic medications in individuals with ASDs. Healthcare practitioners should consider these findings when making treatment decisions, ensuring that the potential risks and benefits are thoroughly evaluated.

Additionally, the study identifies demographic factors such as age and specialty that are associated with the knowledge level of healthcare workers. This suggests the necessity for additional education and training to enhance knowledge and improve practices

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related to ASDs. Addressing these gaps through professional development opportunities can lead to better outcomes for individuals with ASDs and ultimately improve the overall quality of care provided by healthcare practitioners.

RECOMMENDATION

We recommend thoroughly focused programs and Continue medical education so that all healthcare providers of ASD patients should familiarize themselves with evidence-based guidelines and recommendations for the diagnosis and treatment of ASDs.

It is crucial for family medicine residents to work collaboratively with other healthcare professionals, such as psychologists, psychiatrists, and developmental specialists, who possess expertise in ASDs. By establishing a multidisciplinary approach, all healthcare providers can benefit from the insights and guidance of these specialists, ultimately leading to improved care for individuals with ASDs.

We recommend that the Ministry of Health in Saudi Arabia promotes regional periodic courses conducted by experts for all healthcare providers involved in the care of autism patients and their families. These courses would aim to enhance the knowledge and skills of healthcare professionals in effectively managing autism spectrum disorders.

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