

Intellectual Profile of Children with Autism Spectrum Disorder

Identification of verbal and nonverbal subscales predicting intelligence quotient

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ABSTRACT: Objectives: This study aimed to explore the intelligence quotient (IQ) profile among children with autism spectrum disorder (ASD) and identify the most important subscales that predict the IQ. The analysis of an intellectual profile with age and gender differentials and the identification of a battery of subscales of intelligence are important for clinical management of ASD among children and for facilitating placement for remedial and educational services. **Methods:** Data were collected through an exploratory study of 100 children aged between three and 13 years, who were referred to the department of child health and development in Sultan Qaboos University Hospital, a tertiary hospital, in Oman between June 2016 and June 2019. **Results:** Among the 100 participants of this study, 79% were male, resulting in a male–female ratio of 4:1. The mean of full-scale IQ was found to be 68.6 ± 18.1 . Furthermore, the mean of nonverbal IQ (73.5 ± 17.5) was significantly higher than that of verbal IQ (65.5 ± 17.6). Finally, more than half (61%) of the children were observed to have had mild to moderate impairment in their IQ levels. **Conclusions:** Age and gender showed no significant association with IQ level. The regression analysis identified nonverbal fluid reasoning, nonverbal visual-spatial processing, nonverbal working memory and verbal knowledge as the significant predictors of total IQ. The crucial dimensions of verbal and nonverbal IQ identified in this study can be used to evaluate complicated cases.

Keywords: Autism; Intelligence; Oman.

ADVANCES IN KNOWLEDGE

- The intellectual profile of Omani autistic children is described on the Stanford–Binet Intelligence Scales (fifth edition; SB-5).
- A prediction concerning the total intelligence quotient (IQ) of Omani autistic children is offered concerning the most important verbal and nonverbal subscales.

APPLICATIONS TO PATIENT CARE

- The prediction of the total IQ scores of autistic children from specified subscales can facilitate a better understanding of cognitive abilities in difficult cases where performing a full IQ test is challenging.
- The significant dimensions of verbal and nonverbal IQ identified in this study can be used to evaluate difficult cases.

AUTISM SPECTRUM DISORDER (ASD) IS characterised by deficits in social communication and social interaction along with restricted and repetitive patterns of behaviour, interests or activities.¹ Enhancing understanding, awareness and recognition of ASD is crucial given its globally increasing prevalence. Review articles point to median global estimates released in 2012 that suggested ASD's prevalence worldwide to be about 62 per 10,000 persons.² The recalculated analysis of the Center for Disease Control and Prevention (CDC) in the US estimated a prevalence of 240 per 10,000 in 2018.³ The recognition of children with ASD is also increasing in developing countries, but the prevalence rate in these countries has generally been noted to be lower than that observed in the industrialised countries.⁴ This has been attributed to cross-cultural variations in the presentation of ASD as well as a lack of registry

and services for children with ASD.⁵ A recent study suggests that the prevalence of ASD among Omani children (0–14) who fulfilled the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria jumped to 20.4 per 10,000 in 2018, whereas it was 1.4 per 10,000 in 2011.⁶

Intelligence has been perceived as a stable measure among the general population.⁷ However, the picture is not sufficiently clear after the introduction of the autism phenotype and given that the concept of the stability of intelligence quotient (IQ) is still under discussion. For instance, on the one hand, some authors postulated that intellectual abilities in children with autism are stable over time, mirroring the general population studies.^{8,9} On the other hand, others documented improvement in the IQ of autistic children and linked that to improvement in autism symptoms.^{10,11} The above discrepancy can be

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partially explained by the idea that subtests and index scores of IQ in autistic children are driven by those measures which represent characteristic strengths and weaknesses in autism phenotypic features.^{12,13}

On the other hand, intellectual abilities showed variability concerning autism symptomatology across different IQ assessment tools. This was further demonstrated by the better performance of autistic patients on the Raven Progressive Matrices, a well-established tool assessing complex reasoning, compared to that on the Wechsler Intelligence Scales (WISC).¹⁴ Furthermore, autistic patients showed better performance on the Leiter International Performance Scale when compared to that on the Stanford–Binet Intelligence Scales (fifth edition; SB-5).¹⁵ Drawing on these findings, the characterisation of subscales in intellectual function has been indicated to overcome the existing constraints and to add to the body of knowledge. Moreover, quantification of intellectual functioning has the potential to define the direction for intervention, both remedial and rehabilitative, in addition to the administrative decision and professional communication.¹⁶

There are a plethora of studies that examine the most suitable instrument in assessing the intellectual capacity in ASD.¹³ Presently, it appears that WISC and the SB-5 have garnered the highest empirical support.¹⁷ However, there is a dearth of documentation on how children with ASD in societies in transition, such as those in Oman, fare on such intellectual measures.

While the importance of quantifying intellectual functioning among children with ASD has been increasingly gaining ground,¹⁸ to the best of our knowledge, there are no studies, barring a few exceptions, that focus on populations in the Arab-Islamic countries that have reported the profile of intellectual functioning in children with ASD.¹⁹ To fill the gap in the literature, this study deciphers the profile of children with ASD in Oman using the SB-5. To lay the ground for their remedial and educational intervention, it is essential to ascertain the performance of such a paediatric population on indices of intellectual functioning using this scale.²⁰ A related aim of this study is to explore the profile of autistic children on the SB-5 and predict the total IQ regarding the most important subscales which carry the highest variability. This can facilitate a better understanding of cognitive abilities in those difficult cases where performing a full IQ test is challenging.

Methods

Oman's national healthcare service is free for its citizens. Tertiary care in this country is largely compartmentalised and centralised. The first point of

contact for most children with special needs and talent is a primary healthcare centre or an educational setting. These children are thereafter referred to relevant services in tertiary hospitals. The present cohort was retrospectively extracted from Sultan Qaboos University Hospital's (SQUH) Department of Child Health's Developmental Paediatric Clinic. Participants in the present study consisted of consecutive patients who were either being followed-up or were referred for such services. The inclusion criteria consisted of subjects whose diagnostic and clinical observations indicated the presence of ASD as detailed below.

Clinical and demographic information were collected from patients' hospital medical records. The exclusion criteria included participants who were blind, deaf or otherwise seriously impaired by sensory or motor disorders that would render them inaccessible for protracted evaluation of intellectual functioning. Omani children with ASD who were aged between three and 13 years were identified as eligible participants for this study from the hospital registry at the Developmental Clinic, SQUH. The study period was between June 2016 and June 2019. During this period, there were 334 cases diagnosed as ASD in the Developmental Paediatric Clinic at SQUH by utilising gold standard methods. A convenient sampling method was employed to select cases that fulfilled the inclusion criteria. A total of 100 children (79 males and 21 females) were identified to participate in this study. The adequacy of the sample (of 100 children) for evaluating the IQ profile of children with ASD was examined by statistical power analysis. Generally, 'power' refers to the number of observations required to avoid a Type II error in testing a hypothesis. The power analysis of the sample of 100 children indicated that it would provide a power of 0.91 for estimating the IQ of children with ASD within five units of the population value with a 95% confidence level.

ASD was diagnosed based on the DSM-5 criteria which were applied to the clinical history provided by the parents of the study subjects, direct clinical observations of the children and a review of prior evaluations and records of early interventions if any were available. The assessment of ASD was conducted by a multidisciplinary team consisting of a psychologist, an occupational therapist, a speech therapist, paediatricians and a social worker, and it was headed by an experienced developmental paediatrician who was well versed in diagnosing ASD by applying the DSM-5 criteria.¹

The SB-5 was used to measure the participants' intellectual ability. The SB-5 taps into five weighted factors through verbal and nonverbal subtests. The five

factors tested were knowledge, quantitative reasoning, nonverbal visual-spatial processing (NVVSP), nonverbal working memory (NVWM) and nonverbal fluid reasoning (NVFR). This study considered five cognitive profile groups: 'average and above level of IQ' (IQ = 90–129), 'low average level of IQ' (IQ = 80–89), 'borderline impaired level of IQ' (IQ = 70–79), 'mildly impaired level of IQ' (IQ = 55–69) and 'moderately impaired level of IQ' (IQ = 40–54). The superior (IQ = 120–129) and higher average (IQ = 110–119) categories were combined into one category of average and above because, in the sample, a very small number of children had superior and higher average IQ levels, giving the categories very low statistical power for analysis.

This study was ethically approved by the Medical Research and Ethics Committee at Sultan Qaboos University. This study adhered to the principles laid out in the World Medical Association's Declaration of Helsinki (1964–2008) concerning ethical human research vis-à-vis participant confidentiality, privacy and management of data.

The study considered IQ levels (measured in full scale) as the outcome variable and the demographic characteristics (such as age and gender) and subscales of both verbal and nonverbal IQ as the explanatory or predictor variables. Both descriptive and inferential statistical techniques were used for data analysis. Frequency distribution was used to describe the demographics and IQ profiles of the selected sample of children with ASD. One-way analysis of variance (ANOVA) and correlation analysis were conducted to examine the statistically significant relationship between full-scale IQ and background characteristics. A *P* value of <0.05 was considered statistically significant.

Multivariate statistical analyses using the generalised linear model approach were carried out to ascertain the significant predictors of the intellectual ability of the children with ASD being studied. It is worth mentioning here that our response variable (full-scale IQ score) is a count variable with over-dispersion (variance = 326.51 > mean = 68.6) and a skewed distribution (skewness = 0.745), which is the usual characteristic of count variables. Verbal and nonverbal IQ and all the IQ subscales are also count variables measured in an interval scale.

As such, the count variable violates the basic assumptions of continuity, normality and homoscedasticity of the ordinary least square regression technique and the standard test statistics, such as the *t*-test, for testing a hypothesis.²¹ For modelling count data, Poisson regression is a natural choice. However, the most serious limitation of Poisson regression is that

it assumes that the variance of the distribution of the count response variable is equal to its mean which is usually termed as the *equidispersion* property. However, the response variable in this study is over-dispersed. For the over-dispersed count variable, negative binomial (NB) regression is one of the alternative models to be used.^{22,23} Thus, this study employed an NB regression model with a log link function for estimating the regression coefficients (β).

For the convenience of interpreting the estimated coefficients, the incidence rate ratio (IRR) was calculated by exponentiating the beta coefficient, i.e. $IRR = \exp(\beta)$, for each category of the predictors. The 95% confidence interval (CI) of the IRR was also provided. The Statistical Package for the Social Sciences (SPSS), Version 25, (IBM Corp., Armonk, New York, USA) was used for all statistical analyses. To test the internal consistency and reliability of the IQ measurement scales, the Cronbach index was used.²⁴ A high value of alpha = 0.91 indicates an adequate level of reliability of the measurements. Given that the observed total IQ scores and the verbal and nonverbal subscales' scores were obtained through a counting process, the Poisson rate test was employed for testing the hypothesis regarding the mean or difference between two means instead of the standard *t*-test.²⁵ In fact, the Poisson rate is nothing but the mean of the distribution. The statistical package MINITAB has the tool used for running the Poisson rate test on the data.

Results

Table 1 presents the distribution of the children with ASD participating in this study according to their gender, age and IQ classification profiles. Of the 100 participating children, 79 (79%) were males and 21 (21%) were females. The age of the children at the time of the study ranged between three and 13 with a mean age of 7.1 ± 2.5 years. Two-thirds (75%) of the participating children were aged 6–13 years. Both male and female children had a similar age distribution.

In terms of the performance of full-scale IQ measures, the mean IQ level among children with ASD was 68.6 ± 18.1 , ranging between 40 and 129. According to the five cognitive profile groups considered in this study, more than half (61%) of the children were found to have mild to moderate impairment in IQ level (IQ score <70), while 16% were found to have average and above level of IQ (IQ = 90–129) and 14% had a borderline impaired or delayed level of IQ (IQ = 70–79). The distribution of IQ, as previously mentioned, was found to be positively skewed with skewness of 0.745. This value of skewness indicates that the full-scale IQ measure was moderately skewed. The mean of

Table 1: Mean and standard deviation of full-scale intelligence quotient, nonverbal intelligence quotient and verbal intelligence quotient by age and gender, Oman, 2020

	Full-scale IQ		Nonverbal IQ		Verbal IQ	
	Mean ± SD (95% CI)	F, P value	Mean ± SD (95% CI)	F, P value	Mean ± SD (95% CI)	F, P value
Age		1.40, 0.251		1.77, 0.175		3.62, 0.031
3–5	73.3 ± 19.9 (65.1–81.5)		79.2 ± 17.3 (72.4–85.9)		72.3 ± 19.3 (64.7–79.9)	
6–8	65.9 ± 15.9 (61.4–70.5)		71.5 ± 16.5 (65.0–77.9)		61.2 ± 15.1 (56.3–68.1)	
9–13	69.2 ± 19.9 (60.9–77.4)		72.0 ± 19.2 (64.4–79.5)		67.0 ± 18.8 (59.6–74.4)	
Gender		0.11, 0.748		0.01, 0.932		0.47, 0.494
Male	68.3 ± 18.1 (61.2–75.4)		73.6 ± 17.6 (66.7–80.5)		64.8 ± 17.6 (57.9–71.7)	
Female	69.7 ± 18.5 (62.4–76.9)		73.2 ± 17.9 (66.1–80.2)		67.8 ± 17.8 (60.8–74.8)	
Total	68.6 ± 18.1 (65.0–72.2)		73.5 ± 17.5 (70.1–77.0)		65.5 ± 17.6 (62.0–68.9)	

IQ = intelligence quotient; SD = standard deviation; CI = confidence interval.

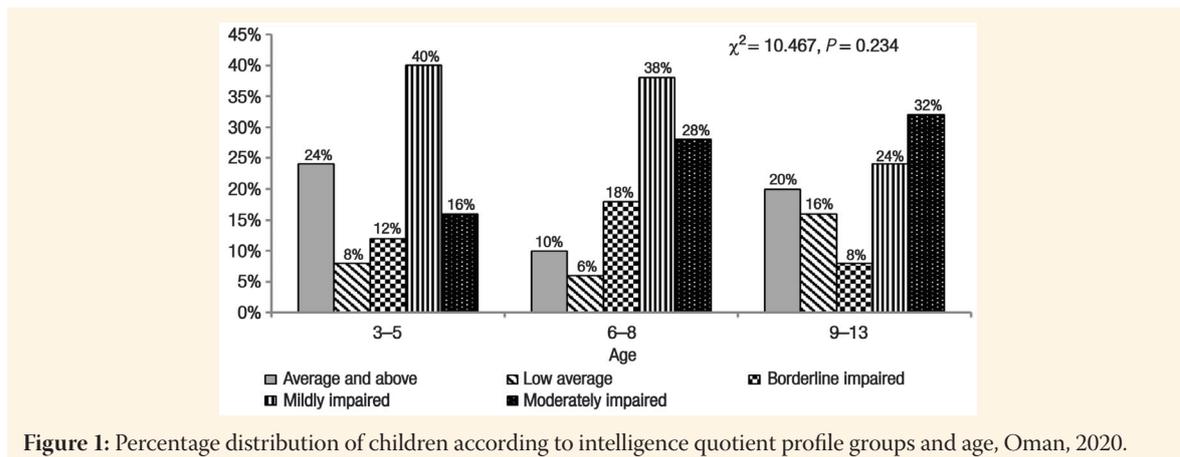


Figure 1: Percentage distribution of children according to intelligence quotient profile groups and age, Oman, 2020.

nonverbal IQ was found to be 73.5 ± 17.5 , while that of verbal IQ was 65.5 ± 17.6 [Table 1].

The level of full-scale IQ varied with age, but the differences were not statistically significant. The IQ level showed a U-shaped pattern with age. Younger children below six years of age tended to have a higher average IQ score than their older counterparts. The nonverbal and verbal IQ also showed a similar pattern of distribution with age. However, the relation was found to be statistically significant in the case of verbal IQ [Table 1].

Female children with ASD were found to have a slightly higher average IQ level (69.7 ± 18.5) than their male counterparts (68.3 ± 18.1). This is also true for verbal and nonverbal IQ level. However, the male-female differences in IQ levels were found to be statistically insignificant [Table 1].

To further examine the association between age and gender with IQ profile groups, chi-square analysis was performed. The results presented in Figure 1 showed no significant association between age and cognitive groups ($\chi^2 = 10.467, P = 0.234$) [Figure 1]. However, it was found that there were more younger children (age groups 3–5 and 6–8 years) in the mildly impaired as well as in the borderline impaired groups, while there were more older children (age group 9–13 years) in the moderately impaired and low average groups. Younger children were more likely to have an average and above level of IQ than their older counterparts. The gender of the children also showed no significant association with cognitive groups ($\chi^2 = 4.639, P = 0.326$) [Figure 2]. However, male children were found to be more likely to be mildly impaired or borderline impaired than the female children, while

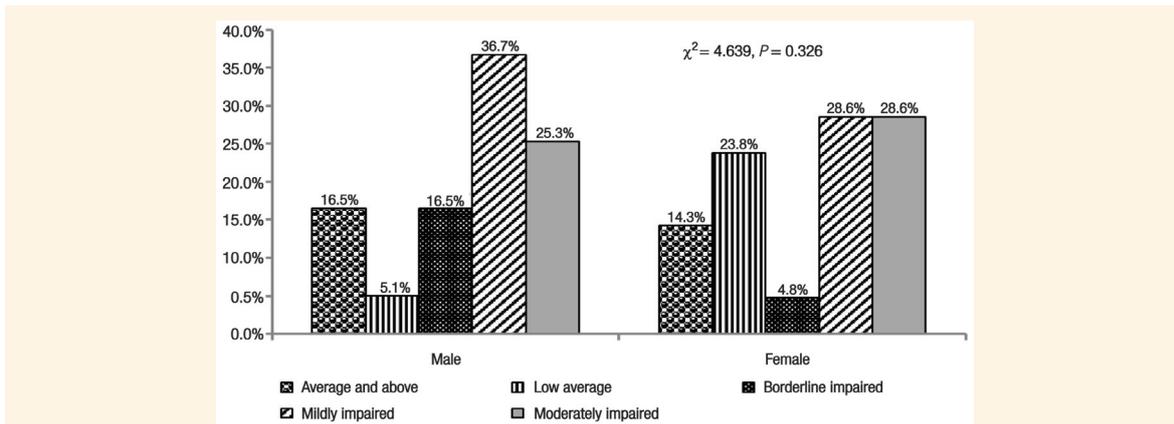


Figure 2: Percentage distribution of children according to intelligence quotient profile groups and gender, Oman, 2020.

Table 2: Mean and standard deviation of verbal and nonverbal intelligence quotient subscales and statistical significance test of the difference between means of verbal and nonverbal subscales, Oman, 2020

IQ subscales	Mean \pm SD		Z*	P value	95% CI for difference of mean
	Verbal	Nonverbal			
Fluid reasoning	3.87 \pm 3.39	5.93 \pm 3.66	6.58	< 0.001	(1.45, 2.67)
Knowledge	5.34 \pm 3.46	5.16 \pm 3.24	0.56	0.579	(-0.81, 0.45)
Quantitative reasoning	4.79 \pm 3.55	4.66 \pm 3.46	0.42	0.672	(-0.73, 0.47)
Visual-spatial processing	3.91 \pm 3.59	7.36 \pm 3.62	10.28	< 0.001	(2.79, 4.11)
Working memory	3.99 \pm 2.82	5.29 \pm 3.42	4.27	< 0.001	(0.70, 1.89)
Total IQ	65.46 \pm 17.60	73.53 \pm 17.54	6.85	< 0.001	(5.76, 10.38)

CI = confidence interval, IQ: intelligence quotient, SD: standard deviation.

*Z: Poisson rate test for count data.

Table 3: Zero-order correlations between total intelligence quotient and intelligence quotient subscales, Oman, 2020

	IQ	NVER	NVK	NVQR	NVVSP	NVWM	VFR	VK	VQR	VVSP	VWM
IQ	1	0.819*	0.824*	0.853*	0.709*	0.768*	0.823*	0.796*	0.805*	0.835*	0.778*

IQ = intelligence quotient; NVER = nonverbal fluid reasoning; NVK = nonverbal knowledge; NVQR = nonverbal quantitative reasoning; NVVSP = nonverbal visual-spatial processing; NVWM = nonverbal working memory; VFR = verbal fluid reasoning; VK = verbal knowledge; VQR = verbal quantitative reasoning; VVSP = verbal visual-spatial processing; VWM = verbal working memory.

*indicates P value < 0.001.

female children were often in a low average cognitive group compared to their male counterparts (23.8% versus 5.1%).

Overall, the mean IQ for nonverbal scales was found to be significantly higher than that of verbal IQ ($Z = 6.85, P < 0.001$) [Table 2]. However, not all components or subscales of nonverbal IQ were higher than the corresponding components or subscales of verbal IQ. Among the five subscales of both verbal and nonverbal IQ, the means of 'verbal knowledge' (VK) and 'verbal quantitative reasoning' were found to be higher than those of nonverbal subscales, but the differences were not statistically significant. On the other hand, NVER, NVVSP and NVWM were found to be significantly higher than those of verbal subscales.

To evaluate the predictive validity of verbal and nonverbal subscales' scores in explaining the IQ performance of children with ASD, correlation analysis followed by regression analyses were performed. Table 3 presents the zero-order correlation coefficients between full-scale IQ scores and the 10 verbal and nonverbal subscale' scores along with the intercorrelation among the latter. The significance tests of the estimated correlation coefficients were also conducted. The results indicate that all the correlation coefficients were found to be positive and significant at the $P < 0.001$ level. Full-scale IQ scores have a strong correlation with the 10 subscales' scores, ranging from $r = 0.709$ to $r = 0.853$. The amount of total variation (measured by R^2) in IQ level explained by the subscales ranged from 50% to 73%. This indicates that

Table 4: Negative binomial regression analysis of the intelligence quotient among children with autism spectrum disorders, Oman, 2020

Parameter	IRR	95% CI of IRR		P value	Collinearity statistics: VIF
		Lower	Upper		
Intercept	39.145	34.139	44.885	< 0.001	
Gender (female)	1.013	0.953	1.077	0.682	1.803
Age	1.008	0.995	1.021	0.223	1.096
Nonverbal fluid reasoning	1.013	1.002	1.023	0.020	2.870
Nonverbal knowledge	1.008	0.995	1.022	0.207	3.255
Nonverbal quantitative reasoning	1.011	0.999	1.024	0.083	3.706
Nonverbal visual-spatial processing	1.015	1.003	1.025	0.012	2.143
Nonverbal working memory	1.011	1.001	1.022	0.038	2.304
Verbal fluid reasoning	0.996	0.984	1.008	0.517	3.434
Verbal knowledge	1.012	1.009	1.028	0.047	3.266
Verbal quantitative reasoning	1.010	0.999	1.021	0.088	2.764
Verbal visual-spatial processing	1.005	0.994	1.017	0.371	3.502
Verbal working memory	1.008	0.995	1.022	0.208	2.592

CI = confidence interval; IRR = incidence rate ratio; VIF = variance inflation factor.

both verbal and nonverbal subscales are important in predicting overall IQ level and there is a significant linear relationship between IQ level and the subscales' levels.

To identify the verbal and nonverbal subclasses that have significant predictive power in explaining the overall IQ level, the regression technique was employed. After checking the assumptions of linearity, multicollinearity and homoscedasticity of the predictor variables, a generalised linear regression model with NB log link was fitted with IQ level as the outcome variable and the verbal and nonverbal subscales as well as age and gender of the children with ASD as the predictors. The results of the standardised residual analysis indicated that the assumption of linearity and homoscedasticity has been met. Although there was a moderate to strong correlation between the predictors, the low (<5) variance inflation factors (VIFs) indicate that multicollinearity was not an issue. The resulting model could describe 92% of the variability in total IQ by the predictors considered in the model, as the adjusted R² was observed to be 0.92. The likelihood-ratio chi-square value of 356.5 with 12 degrees of freedom and the P value < 0.001 indicated that the model significantly improved the prediction of total IQ. Table 4 presents the results of the regression analysis. The results indicate that NVFR, NVVSP and NVWM and VK are the significant predictors of total IQ.

The level of IQ is likely to be increased by 1.3% with a one-unit increase in NVFR (IRR = 1.013, 95% CI: 1.002, 1.023, P = 0.020). Similarly, a one-unit increase in the nonverbal VSP increased the IQ level by 1.5% (IRR = 1.015, 95% CI: 1.003, 1.025, P = 0.012). Among the five verbal subscales, only VK appeared as a significant predictor of IQ level. However, nonverbal quantitative reasoning and verbal quantitative reasoning appeared as marginally significant (0.05 < P < 0.10) predictors of IQ level. Gender and age of the children with ASD did not show any significant effect on IQ level.

Discussion

This is a cross-sectional study on children with ASD to explore their intellectual profile with age and gender differentials and to identify a short battery of the verbal and nonverbal subscales that predict their full-scale IQ. Among the 100 participants of this study, 79% were male, resulting in a male-female ratio of 4:1, which is in line with the global scenario of the gender distribution of more males with ASD than females.² Half of the cases of this study were between the ages of six and eight years. The mean IQ of the autistic children in the study sample was observed to be 68.6 ± 18.1. This is comparable to the total IQ which was found to be 70.4 in a study for the validity of the SB-5.²⁰ Moreover, another study found the mean IQ of the samples from a special needs and autism project in

the UK to be 69.4 ± 24.1 .²⁶ The mean of nonverbal and verbal IQ was found to be 73.5 ± 17.5 and 65.5 ± 17.6 , respectively.²⁶ This indicates that the nonverbal subscales outnumbered their verbal counterparts, which the other studies also indicate.^{27,28}

The findings of this study revealed that more than half (61%) of the participating children with ASD fall in the category of 'mild to moderate' impairment. This finding differs from that found in the UK dataset or the CDC surveillance dataset in which more than a quarter of the participants with ASD were found to have had average or above-average IQs.^{26,29} This could be attributed to the severity of cases at the detection point. In Oman's settings of underdiagnosis, the more severe cases tend to be diagnosed more than the mild ones and the mild cases tend to go undetected in mainstream schools and/or misclassified as intellectual disability or other learning disabilities.^{6,30}

Male profiles were not significantly different from female ones, either in our cohort or in a study of Canadian children with ASD.³¹ This can be attributed to the proximity of age groups as the mean age of the Canadian children was 7.07 ± 2.50 years which was similar among males and females. After controlling the effect of age and gender, the regression analysis identified a shorter number of verbal and nonverbal subscales as significant predictors of full-scale IQ. Interestingly, among the 10 subscales, NVFR, NVVSP, NVWM and VK were noted, in this study, to be significant predictors of total IQ. Children with ASD scored the highest on the NVVSP subscale, with a mean score of 7.36 ± 3.625 , while the lowest scores were on the verbal fluid reasoning (VFR) scale with a mean score of 3.87 ± 3.395 . In line with this finding, one study found that VFR scores were low and NVVSP scores were comparable to our cohort with a mean score of $7.27 \pm SD 4.28$.³² In general, intellectual profiles were found to be constant between high and low IQ groups across many studies, essentially reflecting the influence of autism on psychometric assessment.^{33,34} The predictability of NVFR, NVVSP, NVWM and VK of the total IQ went up to 92%, thereby indicating their helpfulness in assessing difficult cases of autism in children.

This study found high calculated power and predictability of certain subscales of IQ in autistic children. However, the fact that this is a single-centre study is considered a limitation. Undoubtedly, the findings of this study can pave the road for future research and further testing of variables predicting IQ in autistic children.

Conclusion

To the best of our knowledge, this is the first study that examines intellectual profile and their verbal and nonverbal predictors among children diagnosed with ASD in Oman. The present study suggests no difference in IQ between male and female children. It finds non-verbal IQ to be significantly higher than verbal IQ across both genders. The most important determinants of total IQ achievement among variable subscales are NVFR, NVVSP, NVWM and VK. These variables can indeed assist as reliable dimensions in evaluating IQ, thus, defining the direction for intervention and professional communication going forward.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

FUNDING

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AUTHORS' CONTRIBUTION

WM and AI conceptualized the idea and drafted the manuscript. SJ, WM, AG, AM and AI did the clinical assessment. The data collection was done by MJ, AG and AM. SJ revised the initial manuscript versions. The data management and data analysis was done by RA, AI and MI. MA and SA revised the final manuscript. All authors approved the final version of the manuscript.

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