

Autism spectrum disorders: a review of the literature from Arab countries

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Background

In the developing countries and specifically in the Arab world, the field of child psychiatry is relatively new. Autism became a subject of interest in the region only during the late 1990s. Tremendous effort is needed to raise the awareness of policy makers toward the need for implementation of services and research plans aiming to bridge the gap between the needs of and services provided for autism.

Aim

The aims of the study were to: (a) focus on the magnitude of the problem of autism in the Arab world; (b) highlight research conducted in this field; and (c) shed light on services provided for autistic patients and their families in the Arab world with special focus on cultural and economic characteristics of the region and its impact on autism.

Methods

All internationally published English language articles and their reference lists were reviewed using MEDLINE (1992–2012) and studies on autism spectrum disorder conducted in all Arab countries were selected.

Results

Data from studies conducted by different Arab countries on various fields of autism research – genetic, autoimmune, oxidation stress, nutritional deficiencies, environmental toxins, errors of metabolism, mitochondrial dysfunction, clinical studies, imaging, treatment outcome, and available services for autistic patients – were collected and reviewed. Between 1992 and 2012 a total of 75 articles were published from Arab countries, most of which ($n=55$, 73.3%) were published in the last 4 years. Most of the articles discussed possible etiologies of the disorder ($n=42$, 56.6%). Autoimmune theory was the most commonly investigated in the Arab region ($n=12$, 16%). Review articles constituted 16% ($n=12$) of the published articles. The least addressed topic was treatment outcome ($n=4$, 5.3%). Most of the research came from Saudi Arabia ($n=23$, 30.6%) and Egypt ($n=16$, 21.3%). Lebanon came third ($n=11$, 14.7%) and had mostly review articles ($n=6$). Internationally published studies on the prevalence of autism in Arab countries showed inconsistent frequency.

Conclusion

There is growing interest in autistic disorders in the Arab world, particularly in Egypt and Saudi Arabia, as evidenced by the increase in research in this field in the last few years. Research on autism in Arab countries is still in its infancy and needs organizational efforts to be fruitful. Further research is needed within Arab countries to determine the most effective and efficient means of improving diagnosis and service delivery in the context of the particular country, culture, and governmental structure.

Keywords:

Arab countries, autism, autistic disorder, research, services

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Introduction

Research is an important means of finding effective ways to lessen the burden of disease. Most research into autism spectrum disorder (ASD) has been conducted in affluent English-speaking countries, which have extensive professional support services [1]. Initial research on autism diagnosis and service delivery in developing countries has suggested that diagnosis can be a cumbersome and frustrating process. Access to effective therapeutic services is often limited or nonexistent, and the

greater part of the burden of care rests on family members [2–4]. Publications on child psychiatry in the Arab region, particularly in the field of autism, were found to be under-represented [5]. This shortage of information has raised the unwarranted assumption that autism is rare in non-western cultures [6].

The authors have previously published an overview of the condition in the Arab world in which a holistic approach to autism was observed. Nevertheless, the authors by the end of their work found out that, in addition to being

scanty and unorganized, there were no data available for the state of autism in the Arab region collectively. In most cases data are presented for each country separately, which poses a major obstacle to proper administration of service to this group of patients in the region [7]. We believe that research-policy makers should consider autism research as a priority in the Arab region if they intend to improve the recognition of and services offered to autistic individuals in their countries. Accordingly, we decided to bring forth a detailed article on the research condition in the field of autism in the Arab world with respect to its prevalence, clinical profile, etiology, services provided, and outcome.

The authors thus aimed to gather all available articles published on autism in the Arab countries and analyze them in order to help highlight which areas of research need to be adopted in the near future.

The aims of this work were to: (a) focus on the magnitude of the problem; (b) highlight research conducted in this field; and (c) shed light on the services provided for autistic patients and their families in the Arab world with special focus on cultural and economic characteristics of the region and its impact on autism.

Methods

A review of the published work according to the PRISMA statement [8] was conducted. Relevant studies were identified by searching Medline via Pubmed (from 1992 to May 2012). The following keywords were used in the search: 'autism', 'autistic disorder', 'asperger', 'Egypt', 'Libya', 'Tunisia', 'Algeria', 'Morocco', 'Mauritania', 'Sudan', 'Somalia', 'Djibouti', 'Lebanon', 'Jordan', 'Gaza', 'Syria', 'Iraq', 'Saudi Arabia', 'Kuwait', 'Qatar', 'Bahrain', 'United Arab Emirates', 'Oman', 'Yemen'. The reference lists of these papers were searched for additional articles. All identified articles were reviewed for eligibility by both authors. Publications with a comprehensive abstract or full text were included. Publications in local journals and periodicals were excluded because of difficulty in accessing all national periodicals and the full-text articles published in them.

Both authors independently extracted data from selected articles using a specially designed data extraction form that included the name of the study, the date of publication, country of research, scope of research, number of patients included, and main results. Data were then entered in SPSS, version 17 (IBM Corporation, New York, USA) for further analysis.

Results

A total of 79 articles were published from all Arab countries from 1992 to 2012, most of which ($n = 58$, 73.4%) were published in the last 4 years. Most of the research came from Saudi Arabia ($n = 25$, 31.6%) and Egypt ($n = 16$, 20.25%). Lebanon came third ($n = 11$, 13.9%) (Table 1). Most of the articles discussed possible etiologies of the disorder ($n = 42$, 56.6%). Autoimmune

Table 1 Frequency of studies on autism published from different Arab countries

Country	N (%)	Comments
Egypt	16 (20.25)	–
Libya	1 (1.2)	–
Tunisia	6 (7.2)	–
Algeria	0	–
Morocco	1 (1.2)	–
Mauritania	0	–
Sudan	0	–
Somalia	4 (5)	Subjects were people of Somali origin living outside Somalia (were not included)
Djibouti	0	–
Gaza	0	–
Lebanon	11 (13.9)	6 review articles and 2 conducted in Lebanon
Jordan	2 (2.5)	–
Syria	0	–
Iraq	0	–
Kuwait	4 (5)	–
Bahrain	0	–
Qatar	2 (2.5)	–
UAE	2 (2.5)	–
Sultanate Oman	4 (5)	–
Saudi Arabia	25 (31.6)	–
Yemen	0	–

Adapted from Hussein and Taha [7].

theory was the most commonly investigated in the Arab region ($n = 12$, 15.1%). Review articles constituted 17.7% ($n = 14$), many of which were from Lebanon ($n = 6$, 7.5%). The least addressed topic was treatment outcome ($n = 4$, 5%) (Tables 2 and 3).

Research on prevalence

The contribution of different Arab countries to international prevalence studies of ASD is scarce. One report from Saudi Arabia estimated that there were 42 500 confirmed cases of autism in 2002 and that many more remained undiagnosed [9]. This translates to about 18/10 000 cases of autism [5]. Another field study conducted in Saudi Arabia for 3 years, using the Arabic version of CARS, reported that there were 57 110 children younger than 16 years of age with ASD. Most cases were found outside Riyadh, giving a prevalence of 0.6% with a ratio of ~1:2 for girls to boys [10]. In the Sultanate of Oman, prevalence was 1.4 cases per 10 000 children [11], whereas in the United Arab Emirates (UAE), from a representative random sample of 3-year-old UAE national children, 29 per 10 000 children had autism [12].

Other studies tried to determine the frequency of autism in clinical samples. In Jordan, 5.2% ($n = 12$) of a clinical sample of children with Global Developmental Delay ($N = 229$) were found to be autistic [13]. In Libya, a total of 38 508 children were seen in the pediatric clinic of KH, Tripoli, of which 128 children were autistic. This gives a frequency rate of one in 300 [14]. The prevalence of ASD among children with developmental disorders in Egypt and Tunisia was documented as 33.6 and 11.5%, respectively [15]. According to the CAPMS-ARE, roughly two million Egyptians are disabled or have special needs,

Table 2 Distribution of articles with respect to etiology across Arab countries

Field of research	Country	N (%)
Genetics	Egypt	1 (10)
	Tunisia	3 (30)
	Morocco	1 (10)
	Lebanon	2 (20)
	Qatar	1 (10)
	Saudi Arabia	2 (20)
	Total	10 (12.6)
Autoimmune	Egypt	6 (42.8)
	Saudi Arabia	8 (57.2)
	Total	14 (17.7)
Hormonal	Egypt	1 (100)
	Total	1 (1.2)
Imaging	Egypt	1 (50)
	Lebanon	1 (50)
	Total	2 (2.5)
Nutritional deficiency	Egypt	1 (25)
	Somalia	1 (25)
	Oman	1 (25)
	Saudi Arabia	1 (25)
	Total	4 (5)
Environmental toxins	Kuwait	1 (50)
	Saudi Arabia	1 (50)
	Total	2 (2.5)
Oxidative stress	Egypt	2 (33.3)
	Oman	1 (16.7)
	Saudi Arabia	3 (50.0)
	Total	6 (7.5)
Error of metabolism	Tunisia	1 (25)
	Somalia	1 (25)
	Saudi Arabia	1 (25)
	Sultanate Oman	1 (25)
	Total	4 (5)
Mitochondrial dysfunction	Lebanon	1 (50)
	Saudi Arabia	1 (50)
	Total	2 (2.5)
Grand total		43 (54.4)

Table 3 Distribution of articles other than etiology across Arab countries

Field of research	Country	N (%)
Prevalence	Libya	1 (12.5)
	Jordan	1 (12.5)
	UAE	1 (12.5)
	Oman	1 (12.5)
	Saudi Arabia	3 (37.5)
	Tunis and Egypt	1 (12.5)
	Total	8 (10.6)
Diagnostic tools	Egypt	1 (33.3)
	Saudi Arabia	2 (66.7)
	Total	3 (3.7)
Caregivers	Qatar	1 (100)
	Total	1 (1.2)
Treatment outcome	Egypt	2 (50)
	Lebanon	1 (25)
	Kuwait	1 (25)
	Total	4 (5)
Clinical picture	Tunisia	1 (12.37)
	Jordan	1 (12.37)
	Saudi Arabia	1 (12.37)
	Egypt	1 (12.37)
	Across countries	5 (50.5)
	Total	9 (11.3)
Review articles	Total	14 (17.7)
Grand total		36 (45)

of which 1 515 100 are mentally handicapped [16]. A simple calculation, as used by Seif Eldin *et al.* [15], reveals that in Egypt as many as 509 073 children might be affected by autism.

Research on etiology

As mentioned before, most of the research coming from the Arab world was concerned with the possible etiologies of autism.

Genetics etiology research

Ten articles were published on genetics in the region. However, the sample size was generally too small, and in many cases published articles were case reports (Table 4).

Autoimmune etiology

Twelve articles were published on this topic in the Arab world, with Egypt and Saudi Arabia publishing an equal number of articles, mostly within the past 3 years (Table 5).

Hormonal disturbances research

Only one study was reported internationally from Egypt. It was carried out on 50 patients with autism. It revealed that 16% of autistic patients had high adrenocorticotrophic hormone (ACTH) levels, 10% had low basal cortisol levels, and 10% did not show adequate cortisol response to ACTH stimulation. Autistic patients had lower basal ($P = 0.032$) and stimulated cortisol ($P = 0.04$) levels and higher ACTH ($P = 0.01$) levels compared with controls. CARS scores correlated positively with ACTH level and negatively with basal and stimulated cortisol levels. The hormonal profile did not differ in relation to electroencephalogram abnormalities, IQ, and self-aggressive symptoms [37].

Nutritional deficiencies and errors of metabolism

The majority of the internationally published research was from Egypt and Saudi Arabia. Egyptian children with autism showed significantly lower 25(OH)D and 1,25(OH)(2)D levels as well as lower calcium serum values compared with controls. A significant positive correlation was obtained between 25(OH)D and calcium levels in children with autism. The researchers concluded that serum values of 25(OH)D in children with autism in this study could classify them as being 'vitamin D inadequate,' which lends support to the hypothesis that autism is a vitamin D deficiency disorder [38]. Another study from Saudi Arabia showed remarkable alteration in polyunsaturated fatty acids (PUFA) and omega-3/omega-6 and significantly lower levels of phospholipids among autistic children [39]. Another Omani study found that mean serum Hcy levels were significantly ($P < 0.05$) higher in autistic children ($20.1 \pm 3.3 \mu\text{mol/l}$) as compared with controls ($9.64 \pm 2.1 \mu\text{mol/l}$). Significantly ($P < 0.05$) lower serum folate ($1.8 \pm 0.4 \mu\text{g/l}$) and vitamin B₁₂ ($191.1 \pm 0.9 \text{ pg/ml}$) levels were observed in autistic children as compared with controls ($6.1 \pm 0.6 \mu\text{g/l}$ and $288.9 \pm 1.3 \text{ pg/ml}$, respectively). A high serum homocysteine (Hcy) level is regarded as an indicator of impairment of the folate-dependent methionine cycle and is associated with oxidative stress, as reported in an Omani study. The levels of homocysteine in autistic children were also much higher as compared with normal reference values (5–15 $\mu\text{mol/l}$). The results suggest that high fasting serum homocysteine and low folate and

vitamin B₁₂ levels could be used as clinical biomarkers for early diagnosis and management of ASD [40].

Environmental toxins research

Three studies from Saudi Arabia and one from Kuwait investigating the effect of environmental toxins on autistic patients were published internationally. Studies from other Arab countries in this issue are lacking (Table 6).

Mitochondrial dysfunction and oxidative stress

Seven studies from Egypt, Saudi Arabia, and the Sultanate of Oman were internationally published in this issue (Table 6).

Research on clinical status

There were only a few studies published internationally in this field, and they were mainly from Saudi Arabia, Egypt, UAE, and Jordan. In a clinical study from Saudi Arabia investigating 49 patients with autism (37 male and 12 female patients), female patients were older than male patients at the time of referral; 11 patients had a history of seizure disorder, and one patient had a chromosome abnormality. Twenty-five patients were taking psychotropic medications and 14 patients were the product of consanguineous marriages. Communication deficits were the most common cause for referral of Saudi autistic children. Hyperactivity and aggression were reported in 44.8% of Saudi patients; epilepsy was found in 22.4% and almost half of them were referred for co-occurring behavioral problems, particularly hyperactivity and

Table 4 Genetic studies from different Arab countries

Country	References	Results
Egypt	Gebril and Meguid [17]	The relation with hemochromatosis gene polymorphism was not supported
Saudi Arabia	Kaya <i>et al.</i> [18]	An autism-predisposing chromosomal aberration (Xq12-q13.3 duplication) was detected
	Abu-Amero <i>et al.</i> [19]	They described autism in partial 9 p duplication syndrome
Tunisia	Bayou <i>et al.</i> [20]	They found a boy with autism carrying a de-novo translocation t (7;16) (p22.1; p11.2) responsible for the expression of the creatine transporter paralogous in the testis and brain
	Bayou <i>et al.</i> [21]	This study described a Tunisian boy with autism with 7p22.1, which was identified as a positional candidate region for autism on chromosome 7
Morocco	Ouldin <i>et al.</i> [22]	A case report of a boy with infantile autism and cytogenetic abnormalities on chromosomal region 15q11-q13
Qatar	Omar <i>et al.</i> [23]	A case report of Trisomy 13 in a 7-year-old girl with cerebellar tumor, eye abnormalities, and autistic features
Kuwait	Bastaki <i>et al.</i> [24]	45% of children with fragile X syndrome were autistic

Table 5 Autoimmune etiology of autism in the Arab countries

Country	References	Results
Egypt	Mostafa and Shehab [25] Mostafa <i>et al.</i> [26]	C4B-null allele was significantly higher in autistic patients CD4 (+) CD25 (high) regulatory T cells, which play an important role in the establishment of immunological self-tolerance, are deficient in many children with autism
	Mostafa and Kitchener [27]	Higher percentage of seropositivity of antinuclear antibodies and antimyelin-associated antibodies as compared with controls
	Mostafa <i>et al.</i> [28] Kawashti <i>et al.</i> [29]	Higher antimyelin-associated glycoprotein positivity as compared with controls A high seropositivity for autoantibodies to casein and gluten: 83.3 and 50%, respectively, in autistic children as compared with 10 and 6.7% in the control group
Egypt and Saudi Arabia	Mostafa and Al-Ayadhi [30]	Positivity for antineuronal antibodies in Egypt and Saudi Arabia
Saudi Arabia	Mostafa and Al-Ayadhi [31] Al-Ayadhi and Mostafa [32]	Serum neurokinin A levels were elevated in some autistic children Autistic children had significantly lower plasma progranulin levels, which may result in many years of reduced neurotrophic support, together with cumulative damage in association with dysregulated inflammation, which may have a role in autism
	Al-Ayadhi and Mostafa [33]	Serum osteopontin levels (proinflammatory cytokine that has been shown to play an important role in various autoimmune neuroinflammatory diseases) were increased in many autistic children
	Mostafa and Al-Ayadhi [34] Mostafa and Al-Ayadhi [35]	Serum levels of antiganglioside M1 antibodies were increased in many autistic children Increased serum levels of serotonin and anti-MBP autoantibodies in 92 and 80% respectively, of autistic patients. However, serum serotonin levels had no significant correlations with serum levels of anti-MBP autoantibodies
	Mostafa and Al-Ayadhi [30]	Autistic children had a significantly higher percentage of positivity for serum antineuronal antibodies (62.5%) compared with healthy controls (5%) ($P < 0.001$). The frequency of positivity for serum antineuronal antibodies was significantly higher in children with severe autism (87.5%) than in children with mild to moderate autism (25%) ($P < 0.001$). Similarly, the frequency of the positivity of these antibodies was significantly higher in female children with autism (90%) than in male autistic children (53.3%) ($P = 0.001$)
	Zakareia <i>et al.</i> [36]	The levels of vascular endothelial growth factor (VEGF) showed a nonsignificant change in autistic children compared with control children ($P = 0.065$). The levels of platelet-derived growth factor (PDGF) were significantly higher in autistic children compared with controls ($P = 0.01$). Further, this increase was significantly more pronounced in children with severe autism as compared with children with mild autism ($P = 0.001$), and it was not correlated to the severity of the disorder

Table 6 Summary of studies investigating environmental toxins among different Arab countries

Country	References	Results
Environmental toxins		
Saudi Arabia	Al-Yafee <i>et al.</i> [41]	Sulfur-dependent detoxification mechanisms in the plasma of Saudi autistic children were deficient, as evidenced by significantly reduced glutathione, total glutathione, GSH/GSSG and activity levels of GST, whereas GR showed nonsignificant differences; Trx, TrxR, and both Prx I and III recorded remarkably higher values in autistic patients compared with controls
	El-Ansary <i>et al.</i> [42]	Saudi autistic patients had remarkable higher levels of lead and significantly elevated levels of GABA, 5HT, and DA compared with healthy individuals, which suggests that postnatal lead toxicity in autistic patients could represent a causative factor in the pathogenesis of autism
Kuwait	Fido and Al-Saad [43]	The in-hair concentration levels of antimony, uranium, arsenic, beryllium, mercury, cadmium, lead, and aluminum from 40 boys with autism and from 40 healthy boys were determined by Perkin-Elmer mass spectrometry. The children with autism had significantly higher in-hair concentration levels of lead, mercury, and uranium. There was no significant difference between the two groups with respect to the other five toxic elements
Mitochondrial dysfunction and oxidative stress		
Lebanon	Fillano <i>et al.</i> [44]	Reduced levels of specific respiratory activities were found solely in enzymes with subunits encoded by mitochondrial DNA, as well as increased levels of large-scale mitochondrial DNA deletions. Mitochondrial structural abnormalities were detected in a group of 12 children clinically presenting with hypotonia, intractable epilepsy, autism, and developmental delay who did not fall into previously described categories of mitochondrial encephalomyopathy
Egypt	Meguid <i>et al.</i> [45]	A pilot study found that in children younger than 6 years of age, levels of SOD and GSH-Px were significantly lower in autistic children compared with their controls, whereas MDA was significantly higher among patients than among controls. In children older than 6 years, there was no significant difference in any of these values between cases and controls. The researchers concluded that children with autism are more vulnerable to oxidative stress in the form of increased lipid peroxidation and deficient antioxidant defense mechanism, especially at younger children
	Mostafa <i>et al.</i> [46]	Oxidative stress, resulting from elevated plasma F2-isoprostane and/or reduced glutathione peroxidase, was found in 88.64% of autistic children. Significant risk for antineuronal positivity was found in 54.5% of autistic children
Saudi Arabia	Al-Gadani <i>et al.</i> [47]	Saudi autistic children were found to be under hydrogen peroxide stress due to GSH depletion, overexpression of superoxide dismutase, and unchanged levels of catalase enzyme. This could be helpful in the early diagnosis of young autistic patients and suggests the possibility of antioxidant supplementation for the early intervention of autistic children
	El-Ansary <i>et al.</i> [48]	Saudi autistic patients have a remarkably lower plasma caspase3, IL6, TNF α , and calcium levels and significantly higher potassium compared with age and gender-matched controls. In contrast, both magnesium and sodium were nonsignificantly altered in autistic patients
	Al-Ayadhi [49]	Serum levels of Sonic hedgehog (SHH) protein and brain-derived neurotrophic factor might be linked to oxidative stress in autism spectrum disorder
Sultanate Oman	Essa <i>et al.</i> [50]	A significant elevation was observed in the levels of NO, MDA, and protein carbonyl, and lactate to pyruvate ratio, in the plasma of Omani autistic children as compared with their age-matched controls. These oxidative stress markers are strongly associated with major cellular injury and manifest severe mitochondrial dysfunction in autistic pathology

aggression. The researchers argued that the higher incidence of epilepsy in the Saudi group may be attributed to higher genetic loading and more developmental and perinatal problems [2], whereas in the UAE the presence of autistic features was associated with male gender, presence of behavioral problems, and a family history of developmental delay. Also, the rate of pervasive developmental disorders observed in the UAE is comparable to that reported from western countries [12]. From Jordan, a study reported that motor and tactile-perceptual skills (grip strength, motor speed, and coordination) were impaired in individuals with high-functioning autism when compared with matched normally developing individuals [51]. In Egypt, a study was conducted to determine the possible risk factors of autism in 100 Egyptian autistic patients recruited from a pediatric hospital at Ain Shams University; 46% of patients presented at the age of 1.5 years and 32% at the age of 2 years. Moreover, 55% of patients had mild to severe retardation. High maternal age at birth was found in 23% of autistic children. Also, advanced paternal age at birth was found in 91% of cases. Positive family history was found to be significantly associated with the risk of autism (16% of cases vs. 1% of controls). Postnatal factors such as history of hypoxia, resuscitation, and history of jaundice were considered significant risk factors for autism [52].

In contrast, there were only five studies comparing clinical status across two or more Arab countries simultaneously. With the apparent increase in the prevalence of ASD in Arab countries, the development of an Arabic tool for early diagnosis and intervention became essential to better understand the prevalence of this disorder. Accordingly, a study was conducted in nine Arabic speaking countries aiming to validate M-CHAT as an Arabic tool for the screening of autism. The final analysis included 228 children (122 of whom screened positive for ASD). The new translated tool showed acceptable reliability and validity. Maternal health problems during pregnancy and labor were more significant for ASD mothers than for controls. Pediatric health problems were significantly more evident among ASD patients than among controls [15]. Another recent study investigated 37 boys and 23 girls from three Arab countries (Egypt, Saudi Arabia, and Jordan). The results showed that boys had poor emotional responsiveness and girls had more cognitive problems. Boys exhibited significantly more delinquent behavior [53]. The third study investigated and compared patients with autism in Egypt ($n = 20$) and Saudi Arabia ($n = 28$) with respect to both demographic and clinical characteristics. Patients in both groups had typical autism rather than atypical autism, with regression reported in 30% of Egyptian

patients and 21.4% of Saudi patients. Fifty percent of Egyptian patients showed hyperactivity as compared with 60.7% of Saudi patients. Five percent of Egyptian patients suffered from epilepsy in comparison with 25% of Saudi patients. Psychiatric comorbidities were reported in 71.4% of Egyptians and 67.5% of Saudi patients. Egyptian autistic patients were characterized by delayed language development, earlier age at start of treatment intervention, high preference for behavioral and phonetic therapies, higher paternal and maternal education, higher employment among parents, and higher family concern. In contrast, Saudi patients were characterized by delay in all developmental milestones, severe and profound communication defects, more stereotypes and developmental deficits, younger age at detection of abnormality and older age at start of treatment intervention, with marked difference between the two (being around 2 years), higher percentage of missing examinations, older birth order, and significantly higher preference for drug treatment. The study attributed the reported differences between Egyptian and Saudi autistic patients to cultural factors and differences in awareness of autism [54].

Only one preliminary study tried to determine the general outcome of Egyptian and Saudi autistic children after 2 years of follow-up. It revealed a nonstatistically significant tendency toward better outcome in Egyptian autistic patients compared with Saudi patients. This tendency is revealed in the form of improvement in the Gilliam severity of autism in Egyptian children and worsening of Vineland scores in Saudi children. Good outcome was generally associated with higher age at detection of abnormality, high IQ, mild severity of autism, high Vineland scores, low stereotype scores, atypical autism, absence of seizures and regression, and high parental concern [54,55]. An interesting study that was published recently investigated a possible association between psychiatric comorbidities and autism in Egypt, Saudi Arabia, and Jordan. It was found that 63% of children were diagnosed with at least one comorbid disorder. The most commonly reported comorbid disorders were anxiety disorders (58.3%), ADHD (31.6%), conduct disorders (23.3%), and major depressive disorder (13.3%). Out of the total sample, obsessive compulsive disorder was the most prevalent anxiety disorder (55%). Elimination disorders were also diagnosed in 40% of patients of patients [56].

Research on imaging

Imaging studies are scarce in the Arab region. Thus far, only one Egyptian study has been published internationally. It shows significant decrease in the medial prefrontal cortex bilaterally and in the left anterior cingulate cortex in autistic children. Regression analysis revealed a positive correlation between the medial prefrontal cortical thickness and social IQ [57].

Research on treatment outcome

Three studies on this issue were published internationally from Egypt, Kuwait, and Lebanon. The Egyptian study was conducted on 30 autistic children (18 boys and

12 girls) aged 3–11 years; 30 healthy children comprised the control group. This study reported that, before taking Efalex, autistic patients showed a significant reduction in linolenic acid levels (71%), followed by docosahexaenoic acid (65%) and arachidonic acid (45%) levels, whereas linoleic acid was the least affected PUFA (32%). After taking Efalex, 66% of autistic children showed clinical and biochemical improvement. Linolenic acid and docosahexaenoic acid showed the highest levels after Efalex supplementation. The results imply that PUFA supplementation may play an important role in ameliorating autistic behavior [58]. The Kuwaiti study was carried on 40 autistic patients over a period of 13 weeks. It showed that olanzapine treatment can be beneficial in alleviating some behavioral symptoms (irritability, hyperactivity/noncompliance, and lethargy/withdrawal) associated with autism. The short period of this trial limits inferences about adverse effects such as body weight increase and tardive dyskinesia [59]. The Lebanese study was carried out on Lebanese autistic children in the USA. It showed statistically significant improvements in correct responses following exercise in open air. No significant differences were found for on-task behavior or stereotypic behaviors [60].

Only one study was carried out on caregivers in the Arab world: this study was conducted in Qatar. It compared the caregivers of autistic children between 3 and 17 years of age with caregivers of normally developing children. There was no significant difference in the quality-of-life domains between the two groups of caregivers, but caregivers of autistic children rated their health as poor and likely to get worse. This study provided some evidence for the impact of caring for a child with autism on the life of the caregiver. The findings should help health-policy makers in Qatar to provide better and more focused support to children with autism and to their caregivers [61].

Research on services available and support for autism spectrum disorder families

Research in this field is available only from Saudi Arabia and Egypt. In Saudi Arabia, access to early intervention services is limited to the major cities of Riyadh, Jeddah, and Al-Dammam. Almassoud [62] in his study stated that services are provided mainly by the private sector, which is unable to meet the increased demand on services. Local and public services are not available to support the parents of autistic children and provide the required knowledge and help in Saudi Arabia. Al-Othman [63] reported the recent establishment of an autism research and treatment institute related to King Fahd University, and across the Kingdom of Saudi Arabia there are three centers specializing in autism – the Academy of Special Education, Jeddah Centre for Autism, and Prince Faisal bin Fahd mother's Centre. All of these centers adopt Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) as a comprehensive educational program for all children of school age. One of the problems of using TEACCH in all of these centers is that it is not suitable for all autistic

children, especially for children with high-functioning autism [62,63].

In Egypt, services are usually clustered in large cities such as Cairo and Alexandria. They provide speech therapy, cognitive training, and skill-oriented behavioral modification. A few might provide psychomotor training. It is worth mentioning that those services are available at a governmental or nongovernmental level. The Egyptian state plays a restricted role in healthcare provision, particularly with respect to developmental/learning disabilities. According to Mendoza [4], few families used ASD interventions or institutionalized autism-related services, citing lack of knowledge about ASD and effective interventions, limited state or community resources, limited financial resources, and lack of faith in the services. He reported that the more urbanized communities tend to have greater access to, and hence utilize, health and welfare resources. In contrast, in rural areas, virtually every individual with ASD stays home with his/her family or extended family network. Thus, parents in Egypt and in many developing countries are reliant on informal sources of support, as professional services are often poorly represented with lack of training and expertise in ASD among the available staff, doctors, teachers, or therapists [64].

Special education schools for children with learning disabilities and mental retardation have been established in Egypt, Jordan, Lebanon, Saudi Arabia, Tunisia, and the UAE [65]. In terms of vocational rehabilitation and employment support for adults with autism, there are no current training colleges or organizations that support autistic adults across the Arab world. However, in some countries like Saudi Arabia, the Saudi Autistic Society has established a new summer program for adults with autism. This program provides training in computer skills and other technical skills [62]. Unfortunately, it is limited to the period of summer vacation and does not offer a wide variety of training modules. In countries like Egypt, the extended family network offers autistic Egyptians some advantages in terms of old-age income and support, which may not be easily available to their counterparts in industrialized countries [4].

Arab organizations for autism

National organizations for children and families with autism now exist in different Arab countries. These organizations provide workshops, courses, and lectures to elucidate vague aspects of autism aiming to increase public awareness [62]. In Saudi Arabia, although considerable voluntary effort is provided by different charity sectors, there is no clear volunteering system, nor is there information available in the Saudi Autistic Society website [66]. In Egypt, few organizations exist that meet the special needs of people with ASD and other developmental/learning disabilities (e.g. The Egyptian Autistic Society, Learning Resource Center, and others). Most of them are private and nonprofit organizations that possess the relevant expertise and experience. However, the institutional capacities of these few organizations are extremely limited because of underfunding [4].

Research on economic costs of autism

Research on the economic costs of autism in developing or semi-industrialized countries including Arab countries is virtually nonexistent. Only one study tried to address this issue in Egypt [4] using survey data gathered from a probability sample of 165 households in the Greater Cairo Region. Mendoza found that 91.2% of individuals with ASD relied on immediate family for care. Direct financial cost estimates of autism care range from LE 171 368 to 251 303 (US\$31 300–45 900). Most of the expenditure is for nonmedical items such as special education, skills training, or camps rather than for medical services, prescription medication, or behavioral therapy. As for indirect costs of caring for an ASD member, Mendoza reported that the median extra time spent by surveyed family caregivers on autistic individuals was ~1211–1239 h a year. Also, lost income, productivity, and leisure time constitute the indirect cost consequences of ASD for individual caregivers in Egypt. However, the economic impact of these losses could vary significantly depending on the particular economic and social circumstances of the caregiver.

Discussion

Our results showed that autism in most Arab countries except for Egypt and Saudi Arabia is not yet a priority, neither with respect to research nor with respect to services. This might be because the field of child psychiatry is relatively new in these countries [6]. According to our results, prevalence studies are lacking in this region. This might be because of the lack of funding in economically burdened countries like Egypt [4] or because of lack of concern for research policy in other countries [67].

The difference in the clinical profile of patients between countries might be attributed to cultural factors, which play an important role in shaping some dimensions of the illness behavior with respect to symptom recognition and response to illness. Arab cultures are generally characterized by the high rate of consanguineous marriages, high support for nuclear families by their extended families, and consequently high tolerance rate for taking care of mentally ill individuals, especially children. Arabic cultures and families are more tolerant to behaviors in children that would be seen by western societies as 'abnormal'. However, any claims remain speculative as little or no research has been carried out to investigate the effects of culture on autism [64].

A lot remains to be learned about autism-related costs in developing countries. Worldwide, families bear a significant portion of the financial burden of ASD, with virtually all of it being borne by families in developing countries. The portions of the caregiving burden that the family cannot sustain will inevitably spill over to society in one form or another [1]. The direct estimates reported by Mendoza were considerably lower than similar estimates obtained in developed countries. The direct nonmedical costs, along with some physician and outpatient services,

accounted for the higher proportion of cost in Egyptian families, which would bear about 79.0–88.3% of these costs in the absence of private health insurance coverage or aid for developmental/learning disabilities. In contrast, indirect costs of autism in Egypt were significantly higher compared with countries like Sweden, where the estimated annual family expenditure of extra time amounts to about 1000 h [68].

Most of the research in Arab countries was concerned with etiology of autism rather than with services and treatment outcome. This might indicate that medical fields are far more developed than educational and rehabilitation fields with respect to this type of disorder. It raises the awareness of policy makers about the need to implement measurable evidence-based services in their countries, which also abide by regulations for documentation and supervision to prevent malpractice. Further, there are more studies on autoimmune and chemical biomarkers of the disorders than there are on imaging and genetics. This might reflect the difficulty of this type of research, which needs extensive funding beyond the capabilities of individual researchers. In addition, we found that results of etiology studies did not seem different from those of western countries, which indicate that no specific environmental or ethnic factors have been proved to cause autism yet. This is in accordance with previous research by Bristol *et al.* [69]. Genetic studies are probably the most desperately needed. It is evident that most genetic studies in the region are just case reports or with very limited sample size. Large sample studies are, however, essential to prove or disprove these reported findings. Recently, there has been growing interest in the region in genetic research because of the specific cultural characteristics of the Arab community, especially in Saudi Arabia. Al-Salehi *et al.* [2] found that almost one-third of a cohort of Saudi children with autism had a history of consanguinity. Most consanguineous marriages in Arab countries are between first cousins. They can be quite prevalent, ranging from 34 to 80% of all marriages in Saudi Arabia, depending on location – higher in rural communities than in urban and suburban settings. Although the findings from Saudi Arabia do not directly link consanguinity with autism in Arab countries, they suggest that there is a higher incidence of autism among families in Saudi Arabia, making them ideal candidates for screening studies for any genetic variations with the aim of implicating biological processes. Accordingly, Walsh's team turned to the Middle East due to increase in odds of finding rare genes. They recruited 88 families with consanguineous marriages and a high incidence of autism from Jordan, Saudi Arabia, Kuwait, Oman, Pakistan, Qatar, Turkey, and the UAE. They compared the DNA of family members to search for recessive mutations. In some of the families, they found large chunks of missing DNA regions that followed the recessive rule. The missing regions varied among families, but they affected at least six genes that play a role in autism [70].

Imaging studies are very scarce in Arab countries. A possible explanation might be the procedural difficulty

in carrying out this type of research, as patients in most cases need to be anesthetized. This does not mean that patients do not undergo imaging studies. They often come to the center carrying a report from an MRI or computed tomography scan that they had undergone some time back, but lack of well-planned pathways to services and lack of documentation lead to loss of data in most cases.

Conclusion

Currently, there is growing interest in autistic disorders in the Arab world, particularly in Egypt and Saudi Arabia, as evidenced by the increasing research in this field in the last few years. Scientists should highlight the magnitude of the problem and raise public awareness as well as direct the attention of policy makers to the need to implement evidence-based services for this group of patients, which is drastically needed. Research on autism in Arab countries is still in its infancy and needs organization efforts to be fruitful. Further research is needed to determine the most effective and efficient means of improving diagnosis and service delivery in the context of a given country, culture, and governmental structure.

Strengths and limitations

To the best of our knowledge, this is one of the first studies to comprehensively investigate the problem of ASD in the Arab world. This article reviewed all internationally published studies from different Arab countries in different aspects of ASD. However, the main limitation that faced authors was the difficulty in accessing studies published in different national periodicals in different Arab countries. This limited our review to only internationally published articles.

Recommendations

At the governmental level, the relevant governmental agencies should provide and ensure affordability of and accessibility to autism resources, including educational services for autistic children and their caregivers. The various ministries of higher education should initiate training programs for teachers to educate them on the appropriate skills needed to give every child with autism the best care. More importantly, there is a desperate need for national policy formulation to care for autistic children in different Arab societies.

At a professional level, there is a marked need to train pediatricians in the core features of autism and relevant differential diagnosis and management options. Initiatives for early detection and intervention are considered medical priority. It is necessary to include diagnosis and management of autism in the curriculum of medical schools. At present, there is lack of focus on psychiatric

education across the Arab world, specifically pediatric psychiatric disorders.

At the caregiver level, caregivers should be involved in planning and evaluating autism policies and programs, such as school integration. Family training and education is important in passing knowledge and experiences to others through informal contacts. The formation of local associations is very important for promoting parental empowerment and for providing formal support services to assist the children and their families.

At the research level, a research foundation is needed to integrate research efforts from different Arab countries for standardization of screening and diagnostic tools across countries and cultures. Extensive research is needed to determine management recommendations and treatment modalities that best suit various Arab cultures.

At the level of organizations, more centers for treating autism are needed. The current autism centers have to increase their capacity to accept more children in their programs and adopt various educational programs. Special schools for severe conditions are also needed. Vocational rehabilitation for adults with autism is also needed to minimize the costs on families and caregivers. This can be achieved by establishing training colleges and organizations specialized in vocational rehabilitation for raising employers' awareness about the working ability of autistic people.

Finally, the public and private sectors have to cooperate to ensure that more organized and effective efforts are provided.

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Conflicts of interest

There are no conflicts of interest.

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مقارنة أوضاع اضطراب طيف التوحد في الدول العربية

يعد مجال طب نفس الأطفال جديد نوعا في الدول النامية و منها الوطن العربي. كما ان اضطراب التوحد لم يحظ بالأهمية في المنطقة حتي منتصف التسعينات. استشعرا من الباحثين بالحاجة الي سد الفجوة بين احتياجات مرضي التوحد و الخدمات المتاحة من خلال توجيه نظر مخططي السياسات العلاجية و البحثية في المنطقة كانت اهمية هذا البحث الذي يهدف الي تحديد حجم المشكلة في الوطن العربي و استعراض الأبحاث المنشورة في هذا المجال و القاء الضوء علي الخدمات المتاحة لمرضي التوحد و نوبهم مع التركيز علي دور الثقافة العربية و الخصائص الاقتصادية. اجراءات البحث: تم جمع المعلومات عن طريق الاستعراض المنهجي للأبحاث المنشورة باللغة الانجليزية في دوريات عالمية في الفترة من 1992 الي 2012 عن طريق شبكة الأنترنت عبر محرك البحث MEDLINE. نتائج البحث: تم العثور علي 75 بحث عن التوحد منشورة في الدوريات العالمية في هذه الفترة معظمهم في آخر 4 سنوات (73.3%) اغلبهم عن اسباب حدوث المرض و أقلها عن الأساليب العلاجية و مآل المرض. و كانت السعودية (30.6%) و مصر (21.3%) في مقدمة البلاد التي تنشر في مجال التوحد. نستنتج من البحث أن هناك ازدياد في الاهتمام بالتوحد في الوطن العربي و خاصة في مصر و المملكة العربية السعودية و لكن البحث يحتاج الي التنظيم بحيث يكون مثمرا و مؤثرا و ما زال هناك احتياج الي الأبحاث في مجال التشخيص و الخدمات.