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Prevalence and risk factors of autism spectrum disorders in preschool children in Sharkia, Egypt: a community-based study

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Abstract

Background: Lateness in the diagnosis of autism spectrum disorders (ASD) results in significant disability and pressure on affected children and their families. We aimed to detect the preschool children who have high-risk criteria for ASD in Sharkia Governorate in Egypt and assess the prevalence and risk factors of ASD. A cross-sectional community-based study was done in 39 kindergartens throughout Sharkia Governorate, Egypt, using a multi-stage random sampling technique. The study included two phases, the screening phase, where 3722 preschool children were screened by Modified Check List for Toddlers/Revised (M-CHAT-R), and the diagnostic phase where the diagnosis of ASD among the high-risk children was made according to the research diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) of ASD administrated by experienced psychiatrists and the Childhood Autism Rating Scale (CARS).

Results: This study showed that 2.8% of children were at high risk for ASD. The prevalence of ASD in Sharkia Governorate was 5.4/1000. The significant risk factors for the disorder were the presence of factories near the house, first and middle child order, congenital anomalies, child medication during the first year of life, child chronic medical condition, child attachment to TV, a medical condition affecting mother during pregnancy, and psychiatric disorders history in the family.

Conclusion: Autism spectrum disorder is prevalent in preschool children in Sharkia, Egypt, and multiple risk factors contribute to this prevalence.

Keywords: Prevalence, Autism spectrum disorders, Preschool children

Background

According to “Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5),” autism spectrum disorders (ASD) are neurodevelopmental disorders described by deficits in social communication and social interaction and the presence of restricted, repetitive behaviors [1].

ASD represents a complex lifelong developmental incapability that usually appears during the initial years of

life, even though the diagnosis is not habitually made until later in a child’s life, especially when it is mild and perhaps moderate in severity [2].

Children with ASD cannot live independently. Parents of ASD children said that their kids could not live independently without support. Less than 10% can do the most basic tasks: shopping, cooking, washing clothes, paying bills, and managing money without having help. Also, ASD cases had trouble making companions. ASD also influences numerous parts of family life, not just prompting physical and psychological impairment of parents, additionally creating significant unemployment and monetary problems [3].

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Early detection of ASD is critical as early intervention leads to significant improvement in intellectual capability and behavioral performance of an increasing proportion of children with ASD. When children are diagnosed in school-age or teens where the brain is more developed, the intervention becomes more challenging along with much less usefulness [4].

Risk factors of ASD are not clearly identified till now. Genetic risk factors are the most significant, and it seems that it is not a single gene. Instead, various genes are included [5]. Some prenatal and perinatal problems were considered as possible risk factors for ASD [6].

Therefore, the current study aimed to identify the preschool children at high risk for ASD in Sharkia Governorate in Egypt and assess the prevalence and risk factors of ASD. That will help in subsequent early diagnosis and intervention.

Method

Study design and setting

A community-based cross-sectional study was conducted from the first of March 2017 to the end of January 2018, in 39 kindergartens throughout Sharkia Governorate, Egypt, using a multi-stage random sampling technique as follow:

- 1st stage: We selected five out of 17 districts throughout Sharkia Governorate randomly, which were Zagazig, Minia-Alkamh, Hehia, Kenayat, and Abo-Hamad districts.
- 2nd stage: We selected 39 kindergartens divided into 19 from urban areas and 20 from rural areas randomly from the previously selected communities.
- 3rd stage: All the preschool children in each kindergarten chosen were involved in the study as a cluster sample.

Study subjects

The sample size was calculated by computer software Epi-info version 6 according to the following: the estimated prevalence of ASD was 2.24% according to CDC [7], and the total number of preschool children in Sharkia governorate is 595,422 [8], the power of the test is 80% at 95% confidence interval (CI). The estimated sample size was 3722 subjects.

- a) Inclusion criteria
According to the M-CHAT-R, only the children who were classified as high risk for ASD were included in the diagnostic phase.
- b) Exclusion criteria

Children who had an intellectual disability were excluded clinically by the researchers during the diagnostic phase.

Data collection tools

Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) [9]: Arabic version [10]

The parents filled this screening tool to examine the risk for ASD. It is composed of 20 (yes or no) questions, which are scored as follows: The "NO" response implies ASD risk, with respect to all the items other than 2, 5, and 12; the "YES" answer shows for items 2, 5, and 12 ASD risk.

The following algorithm maximizes the psychometric properties of the M-CHAT-R:

- Low risk: Cumulative score is 0-2; if the infant is less than 24 months, test again after the second birthday. No further intervention is taken until monitoring suggests the risk of ASD.
- Medium risk: Overall score is 3-7; prescribe the follow-up to the risk response system (second level of the M-CHAT-R/F). The child screened positive if the M-CHAT-R/F score stays at two or more. Action needed: transfer the child to the early intervention for diagnostic assessment and eligibility tests. The kid has tested negatively if the follow-up result is 0-1. Almost no action is appropriate until testing reveals ASD risk. At potential infant appointments, the child should be screened.
- High risk: Overall score is 8-20; the follow-up is appropriate to be circumvented and automatically refer to early detection diagnostic assessing and eligibility determination. Children evaluated by the researchers and the diagnosis of ASD was done according to research diagnosis criteria of DSM-5 of ASD and CARS in that division during the diagnostic phase.

Clinical interview for the diagnosis of ASD

The diagnosis of ASD was made according to research diagnostic criteria of DSM-5 of ASD that were administrated by experienced psychiatrists (two professors and two assistant professors of the psychiatric department of the University Hospital) using DSM-5 criteria for ASD.

In May 2013, the DSM-5 replaced the previous manual (DSM-IV). The DSM-5 made some significant changes to the way autism is diagnosed. There is now a single diagnosis of autism spectrum disorder, which replaces the formerly used subcategories of autistic disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS) [11].

The Childhood Autism Rating Scale (CARS) questionnaire

This tool helps screen youngsters with ASD and determines symptom severity via quantifiable ratings depending on direct observation. It consists of 15 domains evaluating autism-related behaviors and the overall experiences of autism. Each domain is graded on a scale ranging from one to four; higher scores are correlated with higher disability levels. The child may also be given scores of 1.5, 2.5, or 3.5 if his/her behavior is indicated to be between two descriptions. According to the total score, the child is diagnosed as non-autistic: scores 15-29; mildly/moderately autistic: scores 30-36; and severely autistic: scores 37-60 [12].

The risk factor assessment questionnaire

A semi-structured questionnaire was adapted from Moussa et al. [13] and modified by the researcher, then tested by a pilot study. This questionnaire was used to obtain information about the following:

- Demographic data: This domain consisted of 16 items; all were close-ended questions except two open-ended ones.
- Child's perinatal history: This domain was composed of 36 items divided into 28 close-ended questions and eight open-ended ones.
- Developmental history: This domain asked about five areas of child development which were motor (three items), language (two items), cognitive (one item), social, and psychological development (three items).
- Family history: (two close-ended, yes or no questions).

The reliability of the risk factor assessment questionnaire was tested by measuring their internal consistency. It demonstrated an excellent level of reliability (Cronbach's $\alpha = 0.80$).

Operational design**Pilot study**

It was carried out in February 2017 on parents of 10 preschool children from a kindergarten in Zagazig City to test the risk factor assessment questionnaire regarding clarity, understanding, consistency, and the time needed to fill it out. Those children were excluded from the main study sample. The pilot study findings showed that the questions were clear and relevant then the questionnaire was ready for use.

Fieldwork

It was carried out from the first of March 2017 to the end of January 2018. It passed through two phases:

- 1) Screening phase: Using M-CHAT-R, which took 6 months where the following was done:
 - After obtaining official permissions, the researchers interviewed the teachers of the selected kindergartens explaining the purpose of the study and asked them to help distribute the checklists among the parents.
 - The checklists were given to the parents by the teachers at the end of the school day when they took their children back home. After telling them about the purpose of the study, they were asked to fill in the checklists, return them on the next day, and be informed about the results.
 - The researchers interviewed the parents who refused to fill in the checklists or returned them blank or invalid. They discussed the purpose and importance of this study and offered assistance in filling in the checklist. This was a trial to decrease the nonresponse and the number of invalid checklists.
 - The collected checklists were scored by the researchers and classified into low, medium, and high risk.
- 2) Diagnostic phase: This took 3 months. The researchers interviewed the high-risk group of studied subjects; children evaluated by the researchers and the diagnosis of ASD was done according to research diagnosis criteria of DSM-5 of ASD and CARS at the psychiatry outpatient clinic in Zagazig University Hospital. The risk factors assessment questionnaires were filled for each of the participants.

Statistical analysis

Collected data were recorded then analyzed statistically by SPSS version 25. Data were summarized as mean \pm standard deviation for quantitative variables, number, and percentage for qualitative variables. The appropriate statistical tests such as Chi-square, Fisher exact, and student t tests were used. Binary logistic regression analysis for the significant risk factors for ASD among the studied group was done [14].

Results

The current study is a cross-sectional study that included 3722 preschool children, with 1973 (53%) of the studied group were from 2 to 3 years, and 1749 (47%) were from 4 to 5 years. Regarding sex distribution, 1887

(50.7%) were males, and 1835 (49.3%) were females. By using Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R), 2691 (72.3%) of the studied group were of low risk for ASD, 927 (24.9%) were of medium risk, and 104 (2.8%) were at high risk for ASD (Table 1).

The researcher included four experienced psychiatrists who assessed one hundred four participants (2.8%) who were high risk for ASD using the research diagnostic criteria of DSM-5 and CARS questionnaire, which showed that 20 children (19.2%) diagnosed with ASD and 84 (80.8%) were non-autistic. CARS score among the high-risk group ranged from 16 to 43 (mean 22.73). About 13 children (65%) had mild to moderate autism, and seven children (35%) had severe autism.

So, the prevalence of ASD was estimated to be 5.4 per 1000 children (20 children from 3702) (Fig. 1).

Table 2 shows that there was a statistically significant difference between autistic and non-autistic children in age group 4-5 years, mother education (university), presence of factories near the house, and child order. Also, it shows that 15 (75%) of the autistic children mainly were males.

Table 3 shows a statistically significant difference between autistic and non-autistic children in the type of feeding, type of milk, the onset of weaning, and consuming artificial food with 8 (40%) of the autistic children were artificially fed, 8 (53.3%) of the autistic children who were on artificial or combined feeding received powdered milk, 19 (95%) of all autistic children started to be weaned before 6 months, and 12 (60%) of them consumed artificial food.

As shown in Table 4, there was a statistically significant difference between autistic and non-autistic children in congenital anomaly, medical condition, GIT troubles, and taking medication with all non-autistic children had no congenital anomalies, GIT troubles, or

history of taking medication versus [15% (3children), 25% (5 children), and 10% (2 children)] in the autistic group respectively.

The results showed a statistically significant difference between autistic and non-autistic children in duration of watching TV, and attachment to TV with autistic group had a mean duration of watching TV 6.75 ± 2.83 h and 12 (60%) of them had a strong association with TV (Table 5).

Table 6 shows a statistically significant difference between autistic and non-autistic cases in language, early cognitive, and social development.

Table 7 illustrated a statistically significant difference between autistic and non-autistic children in consuming preserved food during pregnancy, a medical condition during pregnancy, and psychiatric disorder history in the family.

As shown in Table 8, the significant risk factors for ASD among the studied group were factories near the house. First and middle child order, congenital anomalies, child medication during the first year of life, chronic medical condition of the child, child attachment to TV, medical condition affecting mother during pregnancy, and psychiatric disorder history in the family.

Discussion

ASD is a complex lifelong developmental incapability that causes a burden to affected kids and their families. Early detection and early intervention of this problem lead to a better prognosis with fewer burdens on the family. So, our research aimed to detect preschool children in Sharika Governorate who have a high risk for ASD to assess prevalence and risk factors of ASD among them.

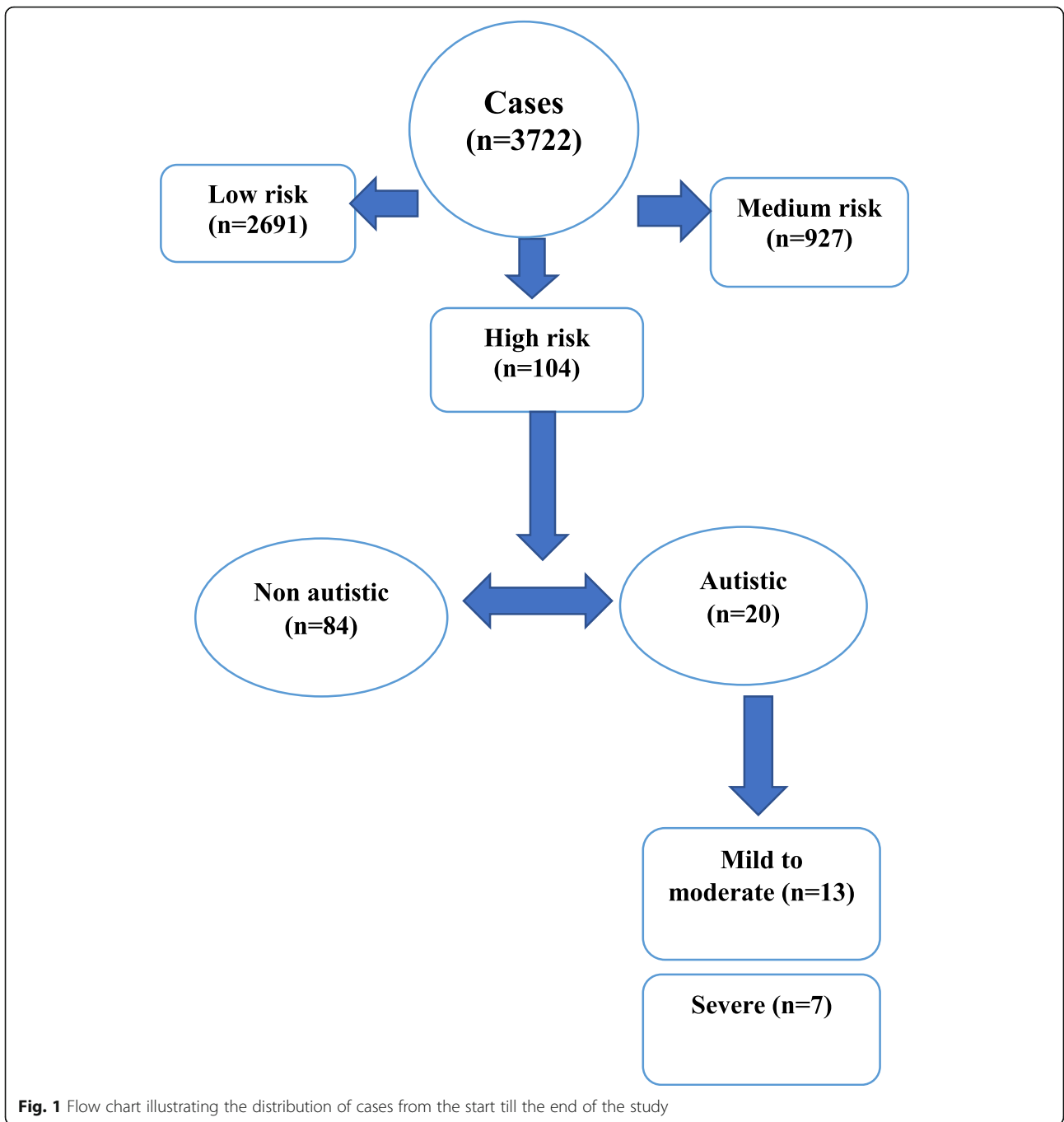
In this study, the sex distribution of the studied subjects in the screening phase was 50.7% males and 49.3% females. That is similar to the sex distribution in a cross-sectional study performed in Lebanon to assess the prevalence of ASD in kindergartens toddlers in Beirut and Mount-Lebanon [15].

Our results showed that 2.8% of children assessed using M-CHAT-R during the screening phase were at high risk for ASD, which is in line with the cross-sectional descriptive study of Moussa S and his colleagues, who found that 2% of children showed an increased risk for ASD [13].

However, this was different from a study that was conducted in India to screen children aged 16–30 months for ASD using M-CHAT-R, and to find an association between maternal, birth, and postnatal risk factors of ASD, and found that 9.4% of children were at high risk for ASD [16]. This difference could be explained by the difference in the locality and age group of research participants.

Table 1 Demographic and clinical characteristics of the studied group

| Variable | Cases (n = 3722) | |
|------------------|---------------------|------|
| | No. | % |
| Age group | | |
| 2-3 years | 1973 | 53 |
| 4-5 years | 1749 | 47 |
| Sex | | |
| Male | 1887 | 50.7 |
| Female | 1835 | 49.3 |
| Risk | | |
| Low risk | 2691 | 72.3 |
| Medium risk | 927 | 24.9 |
| High risk | 104 | 2.8 |



In our study, the mean score on CARS used in the diagnostic phase was 22.73 (SD = 6.99) with a range of 16-43. That was not consistent with the study of Reszka S and colleagues, which performed in the USA and showed that the CARS mean score was 33.37 (SD = 7.31) with a range of 15–55.5. This difference may be attributed to the difference in purpose and sampling technique. In our study, CARS was used for diagnosis of ASD among the high-risk children, with more than 80% of them were non-autistic (score < 30), while in the

American study, most of the children were autistic (score > 30) [17].

Our study showed that 65% of autistic children were mild to moderate ASD, and 35% were severe ASD. That was comparable in Saudi Arabia, where 66.7% of autistic children had mild to moderate ASD, and 33.3% had severe ASD [18].

An Egyptian study found that 43% of cases had mild to moderate degree of ASD, and 57% of them had a severe degree of ASD [19], also different from our study, a

Table 2 Comparison between autistic and non-autistic children in demographic data

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ^2 | P |
|--------------------------------|----------------------|------|---------------------------|------|---------------|----------------|
| | No. | % | No. | % | | |
| Age group | | | | | | |
| 4-5 years | 16 | 80 | 39 | 46.4 | Fisher | 0.006** |
| Sex (Male) | 15 | 75 | 53 | 63.1 | 1.01 | 0.32 (NS) |
| Father education | | | | | | |
| Read and write | 0 | 0 | 2 | 2.4 | | |
| Middle education♦ | 6 | 30 | 44 | 52.4 | Fisher | 0.13 |
| University | 14 | 70 | 38 | 45.2 | | NS |
| Mother education | | | | | | |
| Read and write | 0 | 0 | 2 | 2.4 | | |
| Middle education♦ | 2 | 10 | 41 | 48.8 | Fisher | 0.005** |
| University | 18 | 90 | 41 | 48.8 | | |
| Father occupation | | | | | | |
| Employee | 7 | 35 | 33 | 39.3 | | |
| Private work | 13 | 65 | 32 | 38.1 | Fisher | 0.06 |
| Vocational worker | 0 | 0 | 15 | 17.9 | | NS |
| Professional | 0 | 0 | 4 | 4.8 | | |
| Mother occupation | | | | | | |
| Housewife | 9 | 45 | 55 | 65.5 | 2.86 | 0.09 |
| Working | 11 | 55 | 29 | 34.5 | | NS |
| Who care | | | | | | |
| Father | 5 | 45.4 | 5 | 17.2 | | |
| Grand mom and pap | 3 | 27.3 | 8 | 27.6 | Fisher | 0.25 |
| Kinder garden | 3 | 27.3 | 14 | 48.3 | | NS |
| Other | 0 | 0 | 2 | 6.9 | | |
| Duration | | | | | | |
| < 4 h | 3 | 27.3 | 2 | 6.9 | Fisher | 0.11 |
| ≥ 4 h | 8 | 72.7 | 27 | 93.1 | | NS |
| Social state of parents | | | | | | |
| Married | 20 | 100 | 82 | 97.6 | Fisher | 0.65 NS |
| Residence | | | | | | |
| Urban | 13 | 65 | 38 | 45.2 | 2.52 | 0.11 |
| Rural | 7 | 35 | 46 | 54.8 | | NS |
| Factories near home■ | | | | | | |
| No | 16 | 80 | 84 | 100 | | |
| Yes | 4 | 20 | 0 | 0 | Fisher | 0.001** |
| Home environment | | | | | | |
| Extended | 0 | 0 | 2 | 2.4 | Fisher | 0.65 |
| Nuclear | 20 | 100 | 82 | 97.6 | | NS |
| Smoker inside home | | | | | | |
| Yes (father) | 9 | 45 | 41 | 48.8 | 0.09 | 0.76 NS |
| Sibling number | | | | | | |

Table 2 Comparison between autistic and non-autistic children in demographic data (Continued)

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ ² | P |
|-----------------------|-------------------|----|------------------------|------|----------------|-----------|
| | No. | % | No. | % | | |
| ≤ 2 | 10 | 50 | 58 | 69 | 2.59 | 0.11 |
| <2 | 10 | 50 | 26 | 31 | | NS |
| Order of child | | | | | | |
| First | 10 | 50 | 41 | 48.8 | Fisher | < 0.001** |
| Middle | 8 | 40 | 6 | 7.1 | | |
| Last | 2 | 10 | 37 | 44 | | |

#Non-autistic children included here were those of the high-risk group

♦Middle education refers to primary, preparatory, secondary, and vocational education

Who care for the child during mother's absence for working

■Any industries that could emit air pollutants and toxins such as sulfur dioxide (SO₂), nitric oxides (NO_x), and volatile organic compounds (VOC) like petrochemical industries, iron smelters, oil refineries, polypropylene plants, power companies and methanol industries, formaldehyde plants and urea industries, heavy industries, and metal industries

No answer means that the distance of the child home from the factory is > 20 km

Yes answer means that the distance between the home of the child and the factory is ≤ 20 km

**Statistically significant

study in Rome, Italy, where 44% of autistic children were with mild to moderate ASD, and 56% of them were with severe ASD [20]. Those differences were because of the variations in methodology and age groups studied.

In this research, 20 out of 3722 children were diagnosed with ASD using the research diagnostic criteria of DSM-5 and CARS which means Sharkia Governorate ASD prevalence was 5.4/1000 children. The estimated global prevalence was 7.6 per 1000, according to the systematic review [21].

In the United Arab Emirates, it was 2.9/1000 [22], and in Oman, it was 0.14/1000 [21]. In the UK, the prevalence of ASD was 1.1% [22], and in the USA, it was 2.24% [7].

The differences in localities could explain the difference in the prevalence rates of ASD. Diagnosing autism is more common to clinicians in developed countries. Mental health services for autistic children are more available, and families often are more aware of the disorder. These aspects make the diagnosis of ASD more convenient in developed countries than in developing ones. Also, the time difference between this study and the older studies might be responsible for the different prevalence rates. There was an increasing prevalence rate of ASD over the last decade. Additionally, the wide age group interval included in the American study (3-17 years) in comparison to the limited age group interval of this study (2-5 years) was responsible for the prevalence difference from that of American studies.

In our study, most autistic children (80%) diagnosed by the research diagnostic criteria of DSM-5 and CARS were from 4 to 5 years old, which was in line with Iranian research results [23]. In which ASD patients detected mainly were males (75%). That was similar to the studies in the USA, which found that 75% of children having

ASD were males [7] and also with that one which was conducted in Oman to determine ASD prevalence among 0–14 years subjects and found that ASD was more prevalent among boys (75%) [21]. It was different from the Lebanese study, which found that male: female ratio was 1.05 in Beirut and 1.2 in Mount Lebanon.

This difference might be due to the small sample size of that Lebanese study and the age group difference between the two studies [15]. Ninety percent of mothers of autistic children were university graduates in comparison to 49.4% of non-autistic children, and this difference was statistically significant. That is consistent with the research undertaken in Saudi Arabia to establish potential risk factors for autism and found a statistically significant disparity between the autistic patients and the control group in mothers' university education [18]. That was also consistent with the study conducted in Assiut City in Egypt to recognize the risk factors for ASD and found that 61.7% of mothers of autistic children had a university level of education [24].

Our results also showed a statistically significant association between ASD and the presence of factories near the house. We used a proximity method to classify the existence of the child's home from factories with industries that could emit air pollutants and toxins to be near or not. The proximity approach is widely used in many influential environmental epidemiology studies [25–28]. In addition, this method is used frequently in many environmental investigation studies such as in the environmental impact assessment and environmental justice studies [25]. The threshold distance used in the studies assessing the effects of air pollutant industrial complex was up to 20 km [25]. To determine the most appropriate definition of the minimum distance for exposure, we reviewed several examples of international housing

Table 3 Comparison between autistic and non-autistic children in natal and perinatal data

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ ² | P |
|------------------------------|-------------------|------|------------------------|------|----------------|-----------|
| | No. | % | No. | % | | |
| Type of pregnancy | | | | | | |
| Natural | 20 | 100 | 84 | 100 | -- | -- |
| Gestational age | | | | | | |
| Full term | 20 | 100 | 84 | 100 | -- | -- |
| Place of delivery | | | | | | |
| ZUH | 2 | 10 | 0 | 0 | | |
| Private hospital | 12 | 60 | 78 | 92.9 | Fisher | 0.60 |
| Clinic | 4 | 20 | 4 | 4.8 | | NS |
| Home | 2 | 10 | 2 | 2.4 | | |
| Mode of delivery | | | | | | |
| NVD | 12 | 60 | 35 | 41.7 | 2.19 | 0.14 |
| CS | 8 | 40 | 49 | 58.3 | | NS |
| Birth weight | | | | | | |
| Mean ± SD | 3.25 ± 0.33 | | 3.37 ± 0.22 | | 1.92 | 0.06 |
| Range | 2.6-3.5 | | 3-3.5 | | | NS |
| Complication at birth | | | | | | |
| No | 20 | 100 | 78 | 92.9 | Fisher | 0.41 |
| Yes | 0 | 0 | 6 | 7.1 | | NS |
| Incubator | | | | | | |
| No | 20 | 100 | 80 | 95.2 | Fisher | 0.42 |
| Yes | 0 | 0 | 4 | 4.8 | | NS |
| Feeding | | | | | | |
| Breast feeding | 5 | 25 | 50 | 59.5 | | |
| Artificial | 8 | 40 | 18 | 21.4 | 7.73 | 0.02* |
| Combined | 7 | 35 | 16 | 19 | | |
| Type of milk | | | | | | |
| Fresh animal | 7 | 46.7 | 0 | 0 | Fisher | < 0.001** |
| Powdered milk | 8 | 53.3 | 34 | 100 | | |
| Onset of weaning | | | | | | |
| ≤ 6 months | 19 | 95 | 50 | 59.5 | Fisher | < 0.001** |
| ≥ 6 months | 1 | 5 | 34 | 40.5 | | |
| Artificial food | | | | | | |
| No | 8 | 40 | 73 | 86.9 | 20.63 | < 0.001** |
| Yes | 12 | 60 | 11 | 13.1 | | |

#Non-autistic children included here were those of the high-risk group
**Statistically significant

policies upon that we considered that if the distance of the child home from the factory is > 20 km so it is not near the home and if the distance is ≤ 20 km, so the home of the child is near the factory. Factories were sources of air pollution leading to perinatal exposure of those children to the hazardous chemicals and fumes emitted from those factories. That was consistent with

Table 4 Comparison between autistic and non-autistic children in child medical history

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ ² | P |
|-----------------------------|-------------------|-----|------------------------|------|----------------|-----------|
| | No. | % | No. | % | | |
| Congenital anomalies | | | | | | |
| No | 17 | 85 | 84 | 100 | Fisher | 0.006** |
| Yes | 3 | 15 | 0 | 0 | | |
| Chronic medical | | | | | | |
| No | 14 | 70 | 79 | 94 | 9.88 | 0.002** |
| Yes | 6 | 30 | 5 | 6 | | |
| Neonatal infection | | | | | | |
| No | 20 | 100 | 5 | 6 | Fisher | 0.34 |
| Yes | 0 | 0 | 79 | 94 | | NS |
| GIT troubles | | | | | | |
| No | 15 | 75 | 84 | 100 | Fisher | < 0.001** |
| Yes | 5 | 25 | 0 | 0 | | |
| Sleeping troubles | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | -- |
| Take medication | | | | | | |
| No | 18 | 90 | 84 | 100 | Fisher | 0.04* |
| Yes | 2 | 10 | 0 | 0 | | |
| Allergy | | | | | | |
| No | 17 | 85 | 81 | 96.4 | Fisher | 0.06 |
| Yes | 3 | 15 | 3 | 3.6 | | NS |
| Hospitalization | | | | | | |
| No | 20 | 100 | 82 | 97.6 | Fisher | 0.65 |
| Yes | 0 | 0 | 2 | 2.4 | | NS |
| Operation | | | | | | |
| No | 17 | 85 | 80 | 95.2 | Fisher | 0.08 |
| Yes | 3 | 15 | 4 | 4.8 | | NS |
| Child abuse | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | -- |

#Non-autistic children included here were those of the high-risk group
**Statistically significant

the research performed in the USA to examine the theory that perinatal air pollutants exposure is correlated with ASD [29].

In our study, a statistical difference between autistic and non-autistic children in birth orders where 40% of autistic children were first born while 50% were of middle birth order. That was inconsistent with the finding of the meta-analysis study of Gardener and his colleagues that aimed at providing the first quantitative review and meta-analysis of the association between maternal pregnancy complications, and pregnancy-related factors, and risk of Autism, and found that being firstborn versus third or later was significantly increased autism risk [5]. That was also inconsistent with the finding of the other

Table 5 Comparison between autistic and non-autistic children in watching TV

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ^2 | P |
|--|----------------------|----|---------------------------|------|--------------------|---------------------|
| | No. | % | No. | % | | |
| Age of beginning TV (in months) | | | | | | |
| Mean \pm SD | 18.1 \pm 8.6 | | 18.83 \pm 6.7 | | MW 1.22 | 0.22 NS |
| Range | 8-36 | | 8-36 | | | |
| Duration of TV watch | | | | | | |
| Mean \pm SD | 6.75 \pm 2.83 | | 2.55 \pm 1.64 | | MW 4.82 | < 0.001** |
| Range | 1-11 | | 0.5-9 | | | |
| Attachment to TV | | | | | | |
| Weak | 3 | 15 | 47 | 56 | Fisher | < 0.001** |
| Intermediate | 3 | 15 | 33 | 39.3 | | |
| Strong | 12 | 60 | 2 | 2.4 | | |
| Very strong | 2 | 10 | 2 | 2.4 | | |

#Non-autistic children included here were those of the high-risk group

The degree of the attachment of the child to TV was assessed by the degree of irritability of the child when restrained from viewing TV detected by the caregiver

**Statistically significant

meta-analysis study that aimed at identifying pre-, peri-, and neonatal risk factors for pervasive developmental disorders (PDD), including autism and found that being firstborn was significantly associated with risk ASD [30].

This difference might be due to the difference in locality and population characteristics, as all the studies included in the meta-analysis of both studies were from developed foreign countries. This study showed a statistically significant association between ASD and artificial feeding and early weaning. This was consistent with the Indian study, which showed that delayed initiation of breastfeeding was significantly associated with the risk of ASD. In contrast, exclusive breastfeeding in the first 6 months of life was associated with decreased risk [16]. The systematic review study in Arab Gulf countries findings found that delayed breastfeeding and no colostrum ingestion were linked to a higher risk of autism. Extended breastfeeding (up to 24 months) significantly decreased the likelihood of developing it [31].

In this study, 60% of autistic children consumed artificial, preserved, and canned food in comparison to 13.1% of non-autistic, and this difference was statistically significant. That was consistent with a study conducted in Turkey to examine the connection between ASD development and exposure to MEHP, DEHP, and BPA which are used in some food like meat products and canned beef, also in drink packaging, and to coat metal products such as food cans and bottle tops. This Turkish study found that autistic children showed elevated serum MEHP, DEHP, and BPA levels. Significantly, compared to healthy control subjects, they might play a part in autism spectrum disorder pathogenesis [32].

Our results showed a significant increase in congenital anomalies in autistic children compared to non-autistic children. This finding is similar to that of the meta-analysis study that aimed at providing the first review and meta-analysis of the correlation between perinatal and neonatal factors and autism risk and found that congenital deformities have been linked with the risk of ASD [6].

Our results showed that chronic medical conditions (mainly epilepsy) and GIT troubles were significantly correlated with autism in the affected children, consistent with the study in Iran, which showed that ADHD and epileptic disorders were the leading comorbidities [33]. And also, an American study showed that functional constipation was the most prevalent form of GIT in autistic children (85.0%), GIT was not correlated with specific feeding habits or medical status in children with ASD, and the likelihood of constipation was associated with younger age, more social impairment, and lack of expressive language [34].

This study showed a statistically significant difference between autistic and non-autistic children in the duration of watching TV and attachment to TV. The mean time spent in TV watching by the ASD cases was more than 6 h per day, and 60% of those autistic children were firmly attached to a TV compared to only 2.4% of non-autistic. These findings were consistent with the study conducted in Bangladesh to clarify the association between risk and autism for families, communities, and the environment. They found that the diagnosis of autism is closely connected to excessive watching of TV and the insufficient ability to social interaction and poor contact with family members in early childhood [35].

Table 6 Comparison between autistic and non-autistic children in immunization and developmental history

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | χ^2 | P |
|---------------------------------|----------------------|-----|---------------------------|------|---------------|---------------------|
| | No. | % | No. | % | | |
| Hypothyroidism screening | | | | | | |
| Yes | 20 | 100 | 84 | 100 | -- | -- |
| Immunization | | | | | | |
| Complete | 20 | 100 | 84 | 100 | -- | -- |
| Motor development | | | | | | |
| Head support | | | | | | |
| Normal | 18 | 90 | 78 | 92.9 | Fisher | 0.84 |
| Delayed | 2 | 10 | 6 | 7.1 | | NS |
| Sitting without support | | | | | | |
| Normal | 20 | 100 | 80 | 95.2 | Fisher | 0.92 |
| Delayed | 0 | 0 | 4 | 4.8 | | NS |
| Walking without support | | | | | | |
| Normal | 19 | 95 | 81 | 96.4 | Fisher | 0.87 |
| Delayed | 1 | 5 | 3 | 3.6 | | NS |
| Language | | | | | | |
| Babbling | | | | | | |
| Normal | 7 | 35 | 84 | 100 | Fisher | < 0.001** |
| Delayed | 13 | 65 | 0 | 0 | | |
| Dada and mama | | | | | | |
| Normal | 7 | 35 | 78 | 92.9 | Fisher | < 0.001** |
| Delayed | 13 | 65 | 6 | 7.1 | | |
| Early cognitive | | | | | | |
| Hidden object | | | | | | |
| Normal | 7 | 35 | 82 | 97.6 | Fisher | < 0.001** |
| Delayed | 13 | 65 | 2 | 2.4 | | |
| Social and psychological | | | | | | |
| Social smile | | | | | | |
| Normal | 10 | 50 | 84 | 100 | Fisher | < 0.001** |
| Delayed | 10 | 50 | 0 | 0 | | |
| Recognize mother | | | | | | |
| Normal | 17 | 85 | 84 | 100 | Fisher | < 0.001** |
| Delayed | 3 | 15 | 0 | 0 | | |
| Assist in dress | | | | | | |
| Normal | 14 | 70 | 84 | 100 | Fisher | < 0.001** |
| Delayed | 6 | 30 | 0 | 0 | | |

#Non-autistic children included here were those of the high-risk group

**Statistically significant

Also, in agreement with these findings, the study conducted in Thailand to analyze the level and degree of television consumption in children with ASD relative to typically developed subjects identified a greater incidence of television viewing in autistic children than children with typical development. And that there was an

early initiation of TV exposure in autistic children compared to children with typical developments [36].

We found a statistically significant delay in language, early cognitive, social, and psychological development among children with ASD in our study. On the other hand, there was no statistically significant delay in motor

Table 7 Comparison between autistic and non-autistic children in parents and family history

| Variable | Autistic (n = 20) | | Non autistic# (n = 84) | | t | P |
|--|-------------------|-----|------------------------|------|-------------|---------------------|
| Father age at ges. | | | | | | |
| Mean ± SD | 31.9 ± 4.58 | | 30.27 ± 4.68 | | 1.40 | 0.16 |
| Range | 25-40 | | 23-43 | | | NS |
| Mother age at ges. | | | | | | |
| Mean ± SD | 26.75 ± 4 | | 26.36 ± 4.21 | | 0.38 | 0.71 |
| Range | 22-34 | | 19-39 | | | NS |
| Variable | No. | % | No. | % | χ^2 | P |
| Drug intake during Pregnancy | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | -- |
| Progesterone during pregnancy | | | | | | |
| No | 17 | 85 | 80 | 95.2 | Fisher | 0.10 |
| Yes | 3 | 15 | 4 | 4.8 | | NS |
| Alcohol during pregnancy | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | -- |
| Smoking during pregnancy | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | --- |
| Preserved food during pregnancy | | | | | | |
| No | 7 | 35 | 53 | 63.1 | 5.22 | 0.02* |
| Yes | 13 | 65 | 31 | 36.9 | | |
| Complication during pregnancy | | | | | | |
| No | 20 | 100 | 82 | 97.6 | Fisher | 0.65 |
| Yes | 0 | 0 | 2 | 2.4 | | NS |
| Medical condition during pregnancy | | | | | | |
| No | 10 | 50 | 84 | 100 | Fisher | < 0.001** |
| Yes | 10 | 50 | 0 | 0 | | |
| HPT | 7 | 35 | ---- | ---- | | |
| Celiac disease | 3 | 15 | | | | |
| ASD in family | | | | | | |
| No | 20 | 100 | 84 | 100 | -- | -- |
| Psychiatric disorders in the family | | | | | | |
| No | 18 | 90 | 84 | 100 | Fisher | 0.04* |
| Yes | 2 | 10 | 0 | 0 | | |

#Non-autistic children included here were those of the high-risk group

**Statistically significant

development. That was similar to the Saudi study findings that did not show a significant difference between cases and controls in motor milestones (sitting and walking) [18].

Meanwhile, we found a statistically significant difference between autistic children and the control group in delayed language development and mother recognition. That was inconsistent with the Egyptian study; El-Baz F and his colleagues examined the potential risk factors of autism and found that all the developmental milestones analyzed were delayed in the autistic children than the

control group [19]. This difference might be because 55% of autistic patients in that study had an intellectual disability, while those with intellectual disability were excluded from our research.

The Egyptian study of El-Baz F and his colleagues also showed a statistically significant difference for autistic children and controls in the elevated maternal age (mother = 35 years) at birth, advanced parent age (father = 35 years) at birth, and positive family history of autism [19] that was in contrast to the results of our study which showed no differences. This difference might be

Table 8 Binary logistic regression analysis for the significant risk factors for ASD among the studied group

| Variable | B | S.E. | Wald | Sig. | OR | 95.0% C.I. | |
|--------------------------------|-------------|-------------|-------------|--------------|-------------|-------------|-------------|
| Age group 4-5 years | 0.42 | 0.05 | 1.00 | 0.76 | 1.52 | 0.76 | 3.21 |
| University educated mother | 3.09 | 0.13 | 1.93 | 0.08 | 1.99 | 0.82 | 4.65 |
| Factories near house | 74.08 | 0.99 | 13.89 | < 0.001** | 14.90 | 4.72 | 34.76 |
| First and middle child | 32.74 | 0.68 | 8.28 | < 0.001** | 16.28 | 6.73 | 45.87 |
| Not exclusive breast feeding | 0.60 | 0.03 | 2.29 | 0.89 | 1.83 | 0.56 | 3.85 |
| Fresh milk in feeding | 0.46 | 0.06 | 3.07 | 0.93 | 1.59 | 0.45 | 2.99 |
| Artificial food | 2.94 | 0.16 | 1.12 | 0.45 | 1.65 | 0.56 | 3.74 |
| Congenital anomalies | 33.38 | 0.54 | 8.52 | < 0.001** | 31.55 | 19.43 | 65.41 |
| Chronic medical condition | 37.66 | 0.84 | 7.71 | < 0.001** | 22.68 | 12.47 | 42.84 |
| GIT troubles | 3.38 | 0.12 | 1.81 | 0.08 | 1.57 | 0.30 | 6.76 |
| Medication intake | 33.58 | 0.83 | 5.56 | < 0.001** | 30.45 | 18.45 | 59.32 |
| Strong attachment to TV | 36.32 | 0.82 | 8.61 | < 0.001** | 29.82 | 7.45 | 53.29 |
| > 6 h watching TV | 2.01 | 0.12 | 1.51 | 0.07 | 1.49 | 0.53 | 4.56 |
| Canned food during pregnancy | 1.47 | 0.09 | 0.14 | 0.12 | 0.95 | 0.23 | 3.45 |
| Medical condition in pregnancy | 6.21 | 0.34 | 2.64 | 0.03* | 10.53 | 3.23 | 26.23 |
| Psychiatric disorder in family | 23.45 | 0.51 | 6.23 | 0.01* | 16.78 | 5.67 | 31.83 |

**Statistically significant

due to the methodological difference between the two studies.

Our study showed a statistically significant increase in the maternal consumption of artificial, preserved, and canned food during pregnancy among the mothers of autistic children (65%) compared to (36.9%) mothers of non-autistic, consistent with the study of De Cock M and his colleagues which was conducted to provide a review of research on perinatal human sensitivity to endocrine disrupting chemicals (EDCs) in relation to ASD and ADHD and identified significant correlations between ASD and the exposure to the examined chemicals, including toxic air contaminants, pesticides, and bisphenol [37].

We found a statistically significant difference between autistic and non-autistic children in the presence of a history of chronic medical condition during pregnancy where 35% of autistic children had a history of maternal hypertension with pregnancy, and 15% had a history of maternal celiac disease. This was in line with the findings of the research of Walker Ch and his colleagues in the USA, which found that preeclampsia was associated with the development of ASD [38], and in Denmark, a study of Atladóttir HO1 and his colleagues found that maternal history of rheumatoid arthritis and celiac disease elevated the like hood of developing autism [39].

In our study, 10% of autistic children had a family history of psychiatric disorders than 0% of non-autistic children, which was statistically significant. This is similar to the study of Alsulaimani A and his colleagues in Saudi Arabia [18].

The statistically significant risk factors for ASD among the studied group by using binary logistic regression analysis were the presence of factories near the house, first and middle child order, congenital anomalies, child medication during the first year of life, chronic medical condition of child, child attachment to TV, medical condition affecting mother during pregnancy, and psychiatric disorders history in the family.

The statistically significant risk factors for ASD in that Saudi study were the older age of the fathers, positive family history of the psychiatric disorder including autism, history of maternal diabetes mellitus, and the mother's exposure to stress during pregnancy. Also, Gardener H and his colleagues in their meta-analysis research revealed that advanced paternal age at birth, maternal prenatal medication usage, gestational diabetes, bleeding, and firstborn were associated with ASD risk were [6].

Our present study had some limitations; first, we included only the children with high risk for ASD in the diagnostic phase due to limited time and resources. Second, the preschool children who go to kindergartens were only included in this study without including household preschoolers. This study did not include those younger than two years of age. Third, The MCHA T-R has a high false-positive rate. Fourth, the risk factors assessment questionnaires included items that were very subjective like the attachment to TV. Fifth, the nonresponse rate was increased by about 40% due to the refusal of many parents to participate in the study, refusal of some school managers to perform the study on their

children, illiteracy and low educational level of many parents, and neglect of some parents to fill in the checklist. Some parents refused to complete the second diagnostic phase of the study, causing some dropouts among the high-risk group, and we excluded them from the second diagnostic phase's statistical analysis. This might be attributed to the fear of stigma perceived by some parents if their children were diagnosed with ASD and the feeling of some parents that the study was not useful for them.

Conclusion

Autism spectrum disorder is prevalent in preschool children in Sharkia, Egypt, and multiple risk factors contribute to this prevalence.

Abbreviations

ASD: Autism spectrum disorders; CARS: Childhood Autism Rating Scale; DSM-5: Diagnostic and Statistical Manual of Mental Disorders 5th edition; M-CHAT-R: Modified Checklist for Autism in Toddlers, Revised; CARS: Childhood Autism Rating Scale; SO₂: Sulfur dioxide; NO_x: Nitric oxides; VOC: Volatile organic compounds; ADOS: Diagnostic and observation schedule; SRS: Social Responsiveness Scale; UK: United Kingdom; USA: United States of America; PDD: Pervasive developmental disorders; MEHP: mono-(2-Ethylhexyl) phthalate; DEHP: di-(2-Ethylhexyl) phthalate; BPA: Bisphenol A; GIT: Gastrointestinal tract; GID: Gastrointestinal dysfunction; ADHD: Attention deficit hyperactivity disorder; EDCs: Endocrine disrupting chemicals

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Authors' contributions

AMY, NRA, AEM, and EHR designed the work and made the diagnosis of ASD among the high-risk group and applied the psychometric assessment. RMS and MMA shared in designing the study, collection of data, and put the sequence of work phases. EMH helped in collecting the data. All authors contributed to the conception, preparation, and writing of this article. AMY gave the paper a final review and then forwarded the report for publication. The authors read and approved the final manuscript.

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Availability of data and materials

Upon request

Declarations

Ethics approval and consent to participate

We had an approval from the Ethical Committee of the Faculty of Medicine, Zagazig University, Egypt (IRB# 2016). The necessary official permissions to carry out the study were obtained from the Educational and Social Solidarity directorates.

We obtained a written informed consent from parents of the children of the high-risk group before filling the questionnaires. They were reassured about the strict confidentiality of any received information, and that the study results would be used only for research. The study procedures were free from any harmful effects on the participants.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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