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ASSOCIATION BETWEEN PARENTAL OCCUPATIONAL SOLVENTS EXPOSURES AND AUTISM SPECTRUM DISORDERS

By

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Abstract

Introduction: Autism Spectrum Disorders (ASD) is a heterogenous group of conditions for which there is no single explaining theory, however, might be attributed to many risk factors. These conditions affect brain development, communication, and social interactions. Parents' age, smoking status, health conditions, medications intake, type of work, and occupational exposures represent an ongoing area of research as risk factors of ASD. **Aim of Work:** To study the association between parental occupational solvents exposures and the occurrence of ASD in their children. **Materials and Methods:** This is a case control study that was performed in Psychiatry and Children's outpatient clinic, Mansoura University Hospital including 75 cases with ASD and 75 controls attending for other health problems.Both groups were subjected to a structured questionnaire including personal and medical histories of the study participants and their parents, pregnancy related data, and parental occupational history. Data were collected through a face-to-face interview with the children's caregivers. **Results:** Paternal age, smoking, manual work, chemical, and solvents exposures were independent predictors of ASD (OR = 1.94, 2.13, 2.28, 2.32, and 4.44 respectively). Maternal work duration three years or more was positively related to ASD (OR = 12.92). These associations were statistically significant. **Conclusion and Recommendations:** Parental occupational exposure to chemicals and solvents in the 12 months before and during the index pregnancy are among the risk factors of ASD on bivariate analysis. Effective environmental control and personal protective measures are necessary to decrease the risk of ASD occurrence

Key words: Autism spectrum disorders, Parental, Occupational exposure and Solvents

Introduction

Autism spectrum disorders (ASD) is a term used to describe early appearing social communication deficits with or without repetitive behaviors (Lord et al., 2018). ASD include autism, Asperger syndrome, Rett syndrome, unidentified pervasive developmental disorders, and childhood disintegrative disorder (Paris, 2015). Current epidemiological studies suggest that prevalence of ASD is about 1.5 - 3.62 % even though methods used in surveys estimating autism are not standardized yet worldwide (Lyall et al., 2017). ASD are estimated to be 4 to 5 times more common in males than females but camouflaging and severity are more in females (Cook et al., 2021). Prevalence is generally higher in higher income countries (Lord et al., 2020). ASD have multiple risk factors including gene environment interactions during intrauterine and early childhood developments but the main pathology remains unclear (Chaste and Leboyer 2022). ASD are highly heritable neurodevelopmental disorders but studies suggest that fraction of affected people that could be attributed to heredity is small and that the disorder is largely due to interactions of multiple risk factors (Palladino et al., 2019). Through epigenetic mechanisms, environmental risk factors can affect quantity and quality of gene expression ending in ASD (Perera and Herbstman, 2011). Several environmental exposures have been investigated for their relatedness to ASD such as solar radiation (suggesting some birth seasonality of ASD children) and electromagnetic fields (Lee et al., 2019). Several environmental and occupational chemical exposures of the parents have been linked to ASD in offspring (Dickerson et al. 2014). Chemical such as pesticides, phthalates, polychlorinated biphenyls, solvents, air pollutants, fragrances, glyphosate and heavy metals, especially aluminum all have been studied and links of variable degrees of strength have been found with ASD (Sealey et al., 2016). Parental exposures to solvents, paints, and other chemicals are reported as risk factors of ASD before and during the index pregnancy (Grossi et al., 2018). Occupational solvents exposure include xylene, toluene, benzene, methyl ethyl ketone (MEK), ethanol, ethyl acetate, ethyl benzene, etc…. exposure to which occurs commonly upon contact with paints, paint thinners, lacquers, and inks (Hormozi et al., 2017). According to authors' knowledge, parental

occupational chemical (solvents) exposure has not yet been studied in relation to ASD in Egypt. This study aims to test this association. This might be a basis for future plans to minimize workplace exposure, especially for parents with a previous affected child.

Aim of Work

To study the association between parental occupational solvents exposures and the occurrence of ASD in their children.

Materials and Methods

Study design: This is a case control study.

Place and duration of the study: It was conducted in Psychiatry outpatients' clinics and Children outpatients' clinics in Mansoura University Hospitals, Egypt from November 2022 to September 2023.

Study sample/ inclusion and exclusion criteria:

The study population were attendants of Psychiatry outpatients' clinics, Mansoura University Hospitals, only patients diagnosed with ASD were recruited (cases group), and attendants of Children outpatients' clinics, Mansoura University Hospitals (control group). The exclusion criteria are children with diagnosed psychiatric or neurological health problems, physical, mental, or language developmental delay, learning difficulties, and łess than 3 years old.

Study methods:

Study participants underwent clinical interviews by the psychiatrists then referred to clinical psychologists. A comprehensive autistic assessment approach was followed including A) child and adolescent psychiatric sheet for history taking and mental status examination, B) clinical diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) criteria for autism (Biederman et al., 1994), C) diagnosis and severity assessment of autism using the Arabic version of the Childhood Autism Rating Scale (CARS) which contains fifteen domains of child autistic behavior (scores:1 - 4 for each item ranging from normal to severely abnormal) (Schopler et al., 1988), (El-Shemry and Al-Saratawy, 2002), D) Gilliam Autism Rating Scale (GARS) items are fifty six items to assess the severity of autism, the higher the score, the worse the autistic condition, (Gilliam, 1995), (Abdelrahman and Hasan, 2004), E) psychological

assessment of IQ according to DSM-IV criteria for mental retardation (Biederman, 1994). Children who did not respond to IQ testing according to DSM-IV were assessed using Vineland Adaptive Behavioral Scale (VABS) which is formed of four sub domains: communication, daily living, social, and motor abilities. Higher scores indicated better developmental adaptation (Sparrow et al, 1984), (Eletibi, 2004).

A questionnaire was constructed to include the following items: Patient related information: such as age, sex, birth order, and average daily hours spent on smart devices, pregnancy related information: such as maternal diseases or drug intake during pregnancy, parents' general information: such as age and consanguinity, and parents' occupational history information the 12 months before and during the index pregnancy such as job description and solvents exposures. Questionnaires were completed from parents or caregivers of the study participants during a face-to-face interview.

Center for Disease Control and Prevention (CDC) (2022), defined occupational exposures as: physical exposures; those which transmit energy to body such as pressure and radiation, mechanical exposures; those which may include injuries such as falls and hits, biological exposures; those resulting from transmission of pathogens, psychological exposures; factors causing stress or interpersonal problems, chemical exposures; resulting from handling any type of chemical by any means such as toxic gases and solvents. CDC (2018) defined organic solvents as carbon-based chemicals that can dissolve other substances such as benzene, carbon tetrachloride, and toluene.

A previous case control study documented that solvents exposure among parents of ASD cases was 29.6% and among parents of their matched controls was 16.7%, and that the Odds Ratio (OR) was 3.1 (McCanlies et al., 2012) . Based on this, sample size was calculated using the Open Epi program to be 75 cases and 75 controls (https://www.openepi.com/SampleSize/SSPropor.htm) with alpha error of 0.05 and study power of 80%.

Consent

Informed verbal consent was taken from all parents of study participants before questionnaire administration.

Ethical Approval

Study protocol was submitted to and approved by the Institutional Research Board (IRB), Faculty of Medicine, Mansoura University. The code number is (R.22.09.1835).

Data Management

Data were entered and statistically analyzed using the Statistical Package for Social Sciences version 23 (SPSS. V. 23). Qualitative variables were presented as numbers and percentages. Chi square and Fischer Exact tests were used for comparison. Regression models were performed using stepwise forward Wald method for patients' data, pregnancy-related, and parental occupational information detect the independent predictors of ASD. Data were presented by tables. The statistical significance level was $p \leq 0.05$.

Results

Table 1: Psychometric characters of the cases group.

Test performed	Mean ± SD	Median	Mode	Min	Max
Vineland ABS	47.65 ± 8.99	45	40	35	69
IQ test	50.41 ± 15.84	45	35	20	87
CARS test	37.66 ± 5.20	38	39	29	49.5
GARS	91.81 ± 18.17	91.5	70	30	131

SD = Standard Deviation. Vineland ABS = Vineland Adaptive Behavior Scale.IQ test = Intelligence Quotient test. CARS test = The childhood autism rating scale. GARS = Gilliam Autism Rating Scale. Min = Minimum. Max = Maximum.

The mean scores of Vineland ABS show a low level of functioning among the cases group. The mean IQ score indicates low cognitive and reasoning abilities. The mean CARS test scores show a low degree of autistic traits. The mean GARS scores show moderate degree of ASD among the cases group.

Table 2: Socio demographic characteristics of the studied patients.

Parameters		Cases (75)	Control (75)	p value	COR (95%CI)	AOR (95%CI)
Age groups [a]	≤ 8 years	36 (48.0)	26 (34.7)	0.097	1 (r)	–
	≥ 8 years	39 (52.0)	49 (65.3)		0.55 (0.10 - 1.11)	
Sex	Female	19 (25.3) 56	21 (28.0)		1 (r)	
	Male	(74.7)	54 (72.0)	0.712	1.15 (0.56 - 2.37)	–
Residence	Rural	55 (73.3)	37 (49.3)		1 (r)	–
	Urban	20 (26.7)	38 (50.7)	**0.003***	0.35 (0.18 - 0.70)	
First child	NO	41 (54.7) 34	34 (45.3)		1 (r)	
	Yes	(45.3)	41(54.7)	0.253	0.69 (0.36 - 1.31)	-
Less than 12 months breastfed						
	NO	61 (81.3)	71 (94.7)		1 (r)	1 (r)
	Yes	14 (18.7)	4 (5.3)	**0.012***	4.07 (1.27 - 13.03)	5.40 (1.29 - 22.69)
Mode of delivery	Normal	21 (28.0)	38 (50.7)		1 (r)	
	Cesarean section	54 (72.0)	37 (49.3)	**0.004***	2.64 (1.34 - 5.20)	–
Preterm	NO	58 (77.3)	74 (98.7)		1 (r)	1 (r)
	Yes	17 (22.7)	1 (1.3)	**≤ 0.001***	21.69 (2.80 - 167.80)	27.67 (3.13 - 244.97)
ASD condition in the family	NO	62 (82.7)	73 (97.3)		1 (r)	1 (r)
	Yes	13 (17.3)	2 (2.7)	**0.003***	7.65 (1.66 - 35.22)	8.44 (1.47 - 48.64)
Smart devices use	NO	46 (61.3)	14 (18.7)		1 (r)	-
	Yes	29 (38.7)	61 (81.3)	**≤ 0.001***	0.14 (0.07 - 0.30)	
Hours spent on smart devices [a]	< 2	53 (70.7)	18 (24.0)		1 (r)	1 (r)
	≥ 2	22 (29.3)	57 (76.0)	**≤ 0.001***	0.13 (0.06 - 0.27)	0.13 (0.06 - 0.31)
Health problem after birth	NO	61 (81.3)	74 (98.7)		1 (r)	1 (r)
	Yes	14 (18.7)	1 (1.3)	**≤ 0.001***	16.98 (2.17 - 132.80)	8.67 (0.94 - 80.19)

[a] Grouping is based on data median. COR = Crude Odds Ratio. CI = Confidence Interval. (r) is reference category. AOR = Adjusted Odds Ratio. Regression model χ^2 = 69.578 (P ≤ 0.001). % correctly predicted = 79.3%. Constant = 0.345. *: Statistically significant.

In table 2, factors like urban residence, smart device use, and spending more than 2 hours on smart devices, are associated with lower risk of developing ASD. Less than 12 months breastfeeding, cesarean delivery, being a preterm, having an ASD condition in the family, and getting health problems after birth revealed higher risk of ASD. Regression analysis indicated 79.3% of ASD can be predicted by time spent on smart devices, breast feeding duration, being preterm or not, having an ASD condition in the family, and getting health problems after birth. The difference between cases and control groups was not statistically significant regarding congenital syndromes and chronic medical conditions (results are not tabulated).

Table 3: Pregnancy related information.

Parameters		Cases (75)	Control (75)	p value	COR (95%CI)	AOR (95%CI)
Consanguinity	NO	63 (84.0)	69 (92.0)		1 (r)	
	Yes	12 (16.0)	6 (8.0)	0.132	2.19 (0.78 - 6.18)	-
First Para	NO	41 (54.7)	30 (40.0)		1 (r)	
	Yes	34 (45.3)	45 (60.0)	0.072	0.55 (0.29 - 1.06)	-
Interpregnancy interval						
	< 3 years	54 (72.0)	61 (81.3)		1 (r)	
	> 3 years	21 (28.0)	14 (18.7)	0.177	1.69 (0.79 - 3.66)	-
Maternal obesity	NO	51 (68.0)	41 (54.7)		1 (r)	
	Yes	24 (32.0)	34 (54.3)	0.094	1.69 (0.79 - 3.66)	-
Radiation exposure	**NO**	68 (90.7)	70 (93.3)		1 (r)	
	Yes	7 (9.3)	5 (6.7)	0.547	1.44 (0.44 - 4.76)	-
Maternal drugs intake	NO	74 (98.7)	69 (92.0)		1 (r)	1 (r)
	Yes	1 (1.3)	6 (8.0)	**0.053***	0.16 (0.02 - 1.32)	0.16 (0.02 - 1.32)
Maternal use of pesticides	NO	49 (65.3)	47 (62.7)		1 (r)	
	Yes	26 (34.7)	28 (37.3)	0.734	0.89 (0.46 - 1.74)	-

COR = Crude Odds Ratio. CI = Confidence Interval. (r) is reference category. AOR = Adjusted Odds Ratio. Regression model χ^2 = 4.137 (P = 0.042). % : correctly predicted = 53.3%. Constant = 0.070. *: Statistically significant.

Maternal use of medications during pregnancy decreased the risk of ASD in table 3, and this can predict 53.3% of ASD cases. The difference between cases and control groups was not statistically significant regarding maternal infections, emotional problems, makeup, and fragrances use (results are not tabulated).

Table 4: Paternal general information and occupational characters (in the 12 months before and during the index pregnancy).

Parameters	Cases (75)	Control (75)	p value	COR (95%CI)	AOR (95%CI)
Age at childbirth [a] < 30	26 (34.7)	38 (50.7)	**0.048***	1 (r)	-
> 30	49 (65.3)	37 (49.3)		1.94 (1.00 - 3.73)	
Education Before secondary/secondary	45 (60.0)	24 (32.0)	**0.001***	1 (r)	1 (r)
University/postgraduate	30 (40.0)	51 (68.0)		0.31 (0.16 - 0.61)	0.29 (0.14 - 0.57)
Smoking NO	31 (41.3)	45 (60.0)	**0.022***	1 (r)	-
Yes	44 (58.7)	30 (40.0)		2.13 (1.11 - 4.09)	
Chronic medical conditions [b] NO	63 (84.0)	68 (90.7)	0.220	1 (r)	-
Yes	12 (16.0)	7 (9.3)		1.85 (0.69 - 5.00)	
Job Professional/unemployed	41 (54.7)	55 (73.3)	**0.017***	1 (r)	-
Manual worker/farmer	34 (45.3)	20 (26.7)		2.28 (1.15 - 4.52)	
Physical exposures [c] NO	43 (57.3)	49 (65.3)	0.314	1 (r)	-
Yes	32 (42.7)	26 (34.7)		1.40 (0.73 - 2.71)	
Mechanical exposures NO	50 (66.7)	60 (80.0)	0.065	1 (r)	-
Yes	25 (33.3)	15 (20.0)		2.00 (0.95 - 4.20)	
Biological exposures NO	62 (82.7)	49 (65.3)	**0.016***	1 (r)	1 (r)
Yes	13 (17.3)	26 (34.7)		0.40 (0.18 - 0.85)	0.34 (0.15 - 0.77)
Chemical exposures NO	42 (56.0)	56 (74.7)	**0.016***	1 (r)	-
Yes	33 (44.0)	19 (25.3)		2.32 (1.16 - 4.63)	
Solvents exposures NO	60 (80.0)	71 (94.7)	**0.007***	1 (r)	-
Yes	15 (20.0)	4 (5.3)		4.44 (1.40 - 14.09)	

[a] Calculated based on data median. [b] Such as diabetes mellitus type II or hypertension. [c] Occupational exposures were inquired about. COR = Crude Odds Ratio. CI = Confidence Interval. (r) is reference category. AOR = Adjusted Odds Ratio. Regression model $\chi^2 = 19.112$ ($P \leq 0.001$). % correctly predicted = 66%. Constant = 0.950. *: Statistically significant.

The risk of ASD was found to be lower among children with paternal university or postgraduate degree, and biological occupational exposures as seen in table 4. Paternal age 30 years and older, smoking, being a manual worker or farmer, having chemical or solvents occupational exposures increased ASD risk. About 66% of cases can be predicted from paternal educational degree and occupational biological exposures. No hobbies that might add extra-solvents exposure were reported by fathers (not presented in the table). The difference between cases and control groups was not statistically significant regarding paternal psychological exposures, shift work, duration of work by years, and daily working hours (results are not tabulated).

Table 5: Maternal general information and occupational characters (in the 12 months before and during the index pregnancy).

Parameters	Cases (75)	Control (75)	p value	COR (95%CI)	AOR (95%CI)
Age at childbirth [a] < 25	23 (30.7)	23 (30.7)		1 (r)	
≥ 25	52 (69.3)	52 (69.3)	1.000	1 (0.50 - 2.00)	-
Education Before secondary/secondary	49 (65.3)	28 (37.3)	**0.001***	1 (r) 0.32 (0.16 - 0.62)	-
University/ postgraduate	26 (34.7)	47 (62.7)			
Chronic medicalconditions					
[b] NO	61 (81.3)	74 (98.7)	≤	1 (r)	
Yes	14 (18.7)	1 (1.3)	**0.001***	16.98 (2.17 - 132.80)	-
Job Housewife	61 (81.3)	49 (65.3)	**0.027***	1 (r) 0.43 (0.20 - 0.92)	-
Professional/manual worker/farmer	14 (18.7)	26 (34.7)			
Duration of working (years) [c]					1 (r)
< 3	1 (7.7)	14 (51.9)		1 (r)	12.92
≥ 3	12 (92.3)	13 (48.1)	**0.013***	12.92 (1.47 - 113.80)	(1.47 - 113.77)

[a, d] Calculated based on data median. [b] Such as diabetes mellitus type II or hypertension. [c] Calculated only for working mothers. COR = Crude Odds Ratio. CI = Confidence Interval. (r) is reference category. AOR = Adjusted Odds Ratio. Regression model $\chi^2 = 8.481$ (P = 0.004). % Correctly predicted = 67.5 %. Constant = -2.639. *: Statistically significant.

Table 5 showed lower risk of ASD among children with maternal university or postgraduate educational degree, and maternal work, while chronic maternal health conditions and more than 3 years' work duration increased the risk. Duration of work can predict up to 67.5% of cases. No maternal smoking, alcohol, occupational psychological or solvents exposures were reported.

Only 2 study participants had maternal solvents exposure through hobbies and recreational activities. The difference between cases and control groups was not statistically significant regarding maternal physical, mechanical, biological, chemical exposures, and shift work (results are not tabulated).

Discussion

ASD is defined by the American Psychiatric Association (APA) as a neurodevelopmental pathology that affects social interaction and language development and is characterized by repetitive patterns of activities. The evidence that this group of disorders might be attributed to parental occupational and environmental exposures is growing (Alibek et al., 2019). Investigating the occupational parental exposures of ASD children, and their association with ASD occurrence was aimed at in the current study.

The current study detected that urban residency has a lower risk for developing ASD (Table 2). A review performed in India showed lower pooled estimate of ASD in urban than rural areas (Chauhan et al., 2019). In the Chinese research conducted by Dong et al. (2021), smart device use increased ASD risk especially with longer hours of use, contrary to the findings in the current study, smart device use and spending more than 2 hours daily had lower association with the development of ASD (Table 2). This can be explained by the effect of treatment because most cases were previously diagnosed many years ago (prevalent cases) and are already on treatment that includes limitation of smart devices use.

Insufficient breastfeeding and other ASD conditions in the family increased the risk of ASD among the studied group (Table 2); and this was in accordance with an Iranian study conducted by Malek et al. (2019) who reported that insufficient breastfeeding and other ASD condition in the family increased ASD risk. Also there was an association between being a preterm child and occurrence of ASD (Table 2) which agreed with the work performed by Bokobza et al. (2019) who explained this by inflammatory brain insult. Caesarean delivery increases the risk of occurrence of ASD among the studied group (Table 2) which was in accordance with a population-based birth-cohort analysis in Taiwan (Chien et al., 2015), but authors believe that this finding should be re-investigated because of the abrupt increase in cesarean section rates in Egypt in the recent years (Betran et al., 2021). The present study emphasized that neonatal health problems can increase ASD risk (Table 2). This was in harmony with Alibek et al. (2019) who conducted a study on children from Kazakhstan and Ukraine. They specified neonatal

asphyxia, hypoxia, infection, and nervous system insults as ASD risk factors. The most important patient - related factors according to the current study are time spent on smart devices, breast feeding duration, being preterm or not, having an ASD condition in the family, and getting health problems after birth and 79.3 % of cases can be predicted based on these factors (Table 2).

History of maternal use of medication before and during the index pregnancy was associated with lower rates of ASD and regression model signified that this could predict up to 53.3% of ASD cases among the studied group (Table 3). This is opposing some studies like the Turkish case control study performed by Güneş et al. (2023) which reported a statistically significant difference between ASD and control groups regarding maternal antidepressant and anti-epilepsy medications use. An American retrospective cohort study emphasized on maternal medications use and neonatal epilepsy as risk factors for development of ASD (Hisle - Gorman et al., 2018). Authors think that this point might be under reported and believe it should undergo further research focusing on medications categories and their duration of use.

Having a parent with high educational degree (university or postgraduates) was associated with lower risk of ASD among the studied group (Tables 4 and 5); and this agreed with an Egyptian nationwide cross-sectional survey done by Metwally et al., 2023.

A Swedish population - based case control study claimed ASD being falsely overrepresented in higher socioeconomic classes which is against the gradient of most health conditions. The mentioned study expected that ASD might be more prevalent among lower socioeconomic classes (Rai et al., 2012). This finding may meet our findings in some points where parents' educational degree is one of the socioeconomic status covariates.

Paternal age advancement was detected to be a risk factor for ASD among the studied children (Table 4); which was in concurrence with the Iranian cross-sectional study conducted by Manzouri et al. (2019). Also, father smoking increased the risk of ASD, which is the same finding in many other studies like the South Korean study conducted by Kim et al. (2021). Occupational solvents exposure was proved to be a risk factor of ASD (OR

is 4.44) (Table 4); which was similar with a population based Danish study that analyzed patients' registries and concluded that the OR of paternal occupational solvents exposure can be as high as 3.07 for benzene and 1.66 for toluene one year before conception (Dickerson et al., 2022). In the current study, a significant proportion of manual workers worked in construction and vehicle repair, and these jobs are usually associated with strong solvents exposure. Farmers were among the strongly exposed occupational categories to chemicals. Farming as a paternal job is a risk factor for ASD whereas another study was conducted in Vietnam and concluded that farming as a maternal job leads to higher risk of occurrence of ASD eventhough the same study concluded that urban rather than rural residence was a risk factor. It was suggested that environmental exposure to hazardous pollutants during pregnancy and early childhood contributed to increased risk of ASD and to this disparity (Hoang et al., 2019).

ASD risk was lower among the studied children of working mothers (Table 5). Authors think that might be attributed to sending the children to day care centers where using smart devices is unlikely, and interaction with other children is more which helps more intellectual development. An interesting finding was that mothers who worked for more than three years are at increased risk of having an ASD child. Here, the children are older, and the beneficial effects of day care centers fade away. Mothers working for long years might have established an almost fixed lifestyle for her own and her children, and this lifestyle may include long hours where the child is alone with excess smart device use and less interaction with others in the same age. Duration of mother's work can predict up to 67.5% of ASD cases, so this should be further investigated in future research.

Chronic maternal medical conditions were risk factors for development of ASD among the studied children (Table 5). This was in contrary with a nation - wide Taiwanese cohort study followed up all live births between 2001 and 2012 that were born to mothers with systemic lupus and rheumatoid arthritis and concluded that the mentioned diseases are not risk factors for ASD development (Tsai et al., 2018). A more recent cohort study was conducted in

Taiwan as well and included many chronic and autoimmune disorders in both fathers and mothers of ASD and attention deficit hyperactivity disorders (ADHD) children. It concluded that paternal and maternal chronic medical conditions are risk factors of ADHD and only paternal chronic diseases can increase the risk of ASD development in children (Lee et al., 2023).

In the current study, some other ASD risk factors were investigated but authors found only very few numbers among the cases group such as asphyxia during birth, low birth weight, inadequate maternal - neonate relation, paternal alcohol intake, and paternal and maternal psychiatric diseases.

Study limitations

The present study may be limited by the subjective nature of some questions where parents reply from their own perspective. Also, recall bias might impair the accuracy of some answers. No actual workplace environmental assessment was performed, but hazard evaluation was based on parents' knowledge about their own workplaces.

Conclusion and Recommendations

There are many risk factors for ASD among the studied group such as less than 12 months breastfeeding, being a preterm, another ASD condition in the family, neonatal health problems, and mother work for more than 3 years. Authors recommend screening for early detection, especially including preterm children, those who had neonatal health problems, and families having ASD conditions. Health education should be directed to mothers about the protective value of breast feeding. Further multi-center studies should be performed.

Conflict of Interest

Authors declared there were no conflicting interests.

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