Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.47750/jptcp.2023.30.07.034

Risk and Protective Factors for ADHD in Damietta, Egypt

Amir Soliman[1], Safy Eldin Mahmoud AboAli[2], Dania Abdelhady Mohammed[3], Ahmed E. Sarhan[4], Mohamed Elsheikh[5], Asmaa M. Al-Emrany[6], Omnia Saeed Mahmoud Ahmed[7]

[1]Assistant Professor of Public Health and Community Medicine, Faculty of Medicine, Delta University for Science and Technology.

[2]Lecturer of Physical Therapy at Pediatrics Department, Faculty of Physical Therapy, October University for Modern Sciences and Arts (MSA).

[3]Department of Physiology, Faculty of Medicine, Benha University.

[4]Department of Neurology, Faculty of Medicine, Al-Azhar University.

[5]Department of Psychiatry, Al-Azhar University, Cairo, Egypt.

[6]Lecturer of Physical Therapy for Internal Medicine and Geriatrics, Faculty of Physical Therapy, October University for Modern Sciences and Arts.

[7]Lecturer of Physical therapy for internal medicine and geriatrics, Faculty of Physical therapy, October university for Modern Sciences and Arts.

***Corresponding author:** Amir Soliman, Assistant Professor of Public Health and Community Medicine, Faculty of Medicine, Delta University for Science and Technology,
Email: amirsoliman0004@gmail.com

Submitted: 11 February 2023; Accepted: 17 March 2023; Published: 14 April 2023

ABSTRACT

Background: With the world widely increasing burden of neurodevelopmental disorders in general and ADHD in particular the need for more studies about its risk and protective factors becomes urgent, working in this research area will enable us to find better ways to reduce incidence of ADHD.

Results: To assess possible risk and protective factors of ADHD in children in Damietta governorate this case-control study included100 ADHD patients and 100 matched controls, 70% males and 30% females, aged between 3 and 18 years, patients were recruited from specialized institutions and controls from regular schools in Damietta in a period of 6 months, the study suggested some risk factors for ADHD as residence in urban areas, parental consanguinity, prenatal maternal active or passive exposure to tobacco smoke, regular maternal psychoactive drugs intake, maternal high intake of sugar, family exposure to furniture paints, family regular intake of food additives, having a sibling with ADHD, and some protective factors which are regular maternal iron intake, folic acid intake, and omega3 intake during pregnancy.

Conclusion: Risk factors revealed by the study for ADHD are residence in urban areas, parental consanguinity, prenatal maternal active or passive exposure to tobacco smoke, regular maternal psychoactive drugs intake, maternal high intake of sugar, family exposure to furniture paints, family regular intake of food additives, having a sibling with ADHD and protective factors are regular maternal iron intake, folic acid intake, and omega3 intake during pregnancy.

Keywords: *protective factors; risk factors; ADHD; neurodevelopmental; Damietta*

J Popul Ther Clin Pharmacol Vol 30(7):e279–e292; 14 April 2023.

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by excessive amounts of inattention, carelessness, hyperactivity, and impulsivity that are prevalent, damaging, and otherwise age-inappropriate (1).

ADHD is a prevalent condition affecting 6.7 to 7.8% of children worldwide. This percentage is higher in Middle East countries, reaching 9.4–21.8% in Egypt and 11.6% in Saudi Arabia (2).

Although the area of detecting the specific cause(s) and risk factors for ADHD is still to some extent virgin, researches try diligently to reach cause(s) and risk factors of ADHD in an effort to determine best ways to manage and minimize the chances of having this disorder, some recent researches tried to describe associations of some factors as genetic factors(3), exposure to environmental pollutants during pregnancy or at a young age, maternal bad dietary habits, parental smoking during pregnancy, premature delivery, and Low birth weight With ADHD(4) (5).

ADHD in children is still a wide fertile field for researches. More studies are needed to highlight risk and protective factors associated with it, which helps to encircle this global disorder with its agonizing clinical, social and economic burdens.

Aim of the study

To raise awareness level in the fields of child health and reproductive health

Objectives

To assess possible risk and protective factors of ADHD in children in Damietta governorate

Methods

Technical Design

Site of Study

Damietta governorate, Egypt.

Sample Size

A representative sample of 200 participant, a case group containing 100 children with ADHD and a matched control group containing an equal number, age of all participants ranges between 3 and 18 years , 70% of those participants were males and 30% females, patients were recruited from specialized institutions in Damietta, Egypt. Open Epi I program was used to calculate the suitable sample size, at confidence interval of 95% and power of 80%. The ability to detect a difference of at least 15% in risk and protective factors between the case and control groups was wanted; so, the minimum required number of participants in each group was 50 participants, Diagnosis of ADHD cases was based on DSM V).

Subjects included in the study

Inclusion criteria

Male or female community-dwellers.

Age between 3 and 18 years.

Exclusion criteria

Mental disability

Severe cognitive impairment

Tools

A pretested questionnaire about socio-demographic, possible risk and protective factors of ADHD (Appendix2), to be filled by the parents of children included in the study in presence of researcher, with commitment of the highest levels of confidentiality, to evaluate association between these factors and ADHD in children.

Operational design

Type of study

Comparative case-control study

Method

Recruitment and data collection

The researcher attended specialized local organizations caring for ADHD children in Damietta, meetings with in charge administrators were arranged to explain research objectives, and

similar meetings with families of candidate children were arranged for the same purpose , an informed consent forms (appendex1) were offered to parents who accept the participation invitation to sign the questionnaire to be filled (appendex2).

Simultaneously, we follow more or less similar procedures for recruitment of the control group from age and sex matched children attending regular schools in Damietta and have no neurodevelopmental disorders.

100 cases and 100 controls with age ranges between 3 and 18 years were assigned, diagnosis of cases was based on (DSM V), and the study was conducted in 6months (from June to December, 2022). The study objectives and design were explained thoroughly by a team member to parents of every candidate then offered an informed consent to be signed in case of acceptance before beginning of the study to insure complete satisfaction (Appendix 1).

Statistical Analysis

Descriptive statistics in the form of frequencies and percentages for qualitative variables, while the mean and standard deviation were used to present the numeric variables. Chi square test, Monte Carlo test and multiple logistic regression were used to study socio-demographic factors associated with ADHD. IBM SPSS 28 software for windows (IBM SPSS Inc., Chicago, IL, USA) for the statistical analysis. P-value is considered statistically significant when < 0.05.

Administrative design

A prior ethical approval from the relevant IRB was obtained(DFM-IRB 00012367-22-5-007), the committee's date was 31 May 2022. All methods were performed in accordance with the relevant guidelines and regulations, the study objectives and design were explained thoroughly by researcher to parent(s)/legal guardian(s) of every candidate then he/she sign an informed consent in case of acceptance before beginning of the study to insure complete satisfaction (Appendix 1).

RESULTS

TABLE 1: comparison of socio-demographic characteristics and history of the studied groups (n=200)

	Total number =200	**Cases n=100(%)**	**Control n=100(%)**	**Test of significance**
Age of mothers at start of pregnancy(years)				
<20	10	10(100)	0	χ2MC=36.58
20-<30	146	84(57.5)	62(42.5)	p<0.001*
≥30	44	6(13.6)	38(86.4)	
Mean ± SD		23.07±3.14	28.64±4.02	t=10.92 p<0.001*
Age of fathers at start of pregnancy(years)				
20-<30	58	34(58.6)	24(41.4)	χ2=2.43
≥30	142	66(46.5)	76(53.5)	p=0.119
Mean ± SD		33.16±5.69	33.32±5.69	t=0.199 p=0.843
Sex				
Male	140	70(50.0)	70(50.0)	χ2=0.0
Female	60	30(50.0)	30(50.0)	p=1.0
Residence				
Urban	132	76(57.6)	56(42.4)	χ2=8.91
Rural	68	24(35.3)	44(64.7)	p=0.003*

J Popul Ther Clin Pharmacol Vol 30(7):e279–e292; 14 April 2023.

Parental consanguinity				
yes	36	26(72.2)	10(27.8)	$\chi2$=8.68
no	164	74(45.1)	90(54.9)	p=0.003*
Maternal active or passive exposure to tobacco smoke during pregnancy				
yes	106	66(62.3)	40(37.7)	$\chi2$=13.57
no	94	34(36.2)	60(63.80	p<0.001*
Regular maternal psychoactive drugs intake during pregnancy	51	38(74.5)	13925.5)	$\chi2$=16.45
yes	149	62(41.6)	87(58.4)	p<0.001*
no				
Regular maternal iron intake during pregnancy	104	20(19.2)	84(80.8)	$\chi2$=82.05
yes	96	80(83.30	16(16.7)	p<0.001*
no				
Regular maternal folic acid intake during pregnancy				
yes	130	38(29.2)	92(70.8)	$\chi2$=64.09
no	70	62(88.6)	8(11.4)	p<0.001*
Regular maternal omega3 intake during pregnancy				
yes	124	38(30.6)	86(69.4)	$\chi2$=48.89
no	76	62(81.6)	14(18.4)	p<0.001*
Family exposure to furniture paints				
yes	118	86(72.9)	32(27.1)	$\chi2$=60.27
no	82	14(17.1)	68(82.9)	p<0.001*
Family regular intake of food additives				
yes	144	86(59.7)	58(40.3)	$\chi2$=19.44
no	56	14(25.0)	42(75.0)	p<0.001*
Maternal high intake of sugar during pregnancy	102	82(80.4)	20(19.6)	$\chi2$=76.91
yes	98	18(18.4)	80(81.6)	p<0.001*
no				
Preterm birth				
yes	34	24(70.6)	10(29.4)	$\chi2$=6.95
no	166	76(45.8)	90(54.2)	p=0.008*
LBW				
yes	48	36(75)	12(25)	$\chi2$=15.79
no	152	64(42.1)	88(57.9)	p<0.001*
Having a sibling with ADHD				
yes	36	32(88.9)	4(11.1)	$\chi2$=26.56
no	164	68(41.5)	96(58.5)	p<0.001*
Birth order				
First	44	26(59.1)	18(40.9)	$\chi2$=3.234
Second	68	30(44.1)	38(55.9)	P=0.357
Third	60	28(46.7)	32(53.3)	
Fourth	28	16(57.1)	12(42.9)	
Delivery type				
Vaginal delivery	42	18(42.9)	24(57.1)	$\chi2$=1.09
CS	158	82(51.9)	76(48.1)	p=0.298

$\chi2$:Chi-square test MC: Monte Carlo test *:statistically significant

According to table (1): Maternal age at start of pregnancy showed a statistically significant difference as mean age of mothers of control children (28.64±4.02) was higher than mean age

of mothers of ADHD cases (23.07±3.14), (t = 10.92, p-value<0.001).Percentage of cases was 100% among children of mothers who get pregnancy at an age< 20 years, and 57.5% of children of mothers who get pregnant at an age from 20 to less than 30 years and 13.6% of children of mothers who get pregnant at age of 30 years and more, (χ2MC = 36.58, P-value <0.001).

Paternal age at start of pregnancy showed a statistically non-significant difference as mean age of fathers of cases was (33.16±5.69) and mean age of fathers of ADHD controls was (33.32±5.69), (t = -0.199, P-value=0.843). Percentage of cases was 58.6% among children of fathers whose age was 20 - <30years at start of pregnancy, and 46.5% of children of fathers whose age was 30 years and more at start of pregnancy, (χ2=2.43, P- value =0.119).

There was a statistically significant difference in ADHD cases per residence as the percentage of ADHD cases was 57.6% among those living in urban areas, while the percentage was 35.3% among those living in rural areas, (χ2= 8.91, p-value =0.003).

We found also a statistically significant difference in parental consanguinity among ADHD cases and controls, the percentage of cases in consanguineous parents was 72.2% versus 45.1% in non-consanguineous parents, (χ2= 8.68, p-value =0.003).

Maternal active or passive exposure to tobacco smoke during pregnancy showed also a significant difference between case and control groups, the percentage of cases among exposed mothers was 62.3% in cases and 36.2% in non-exposed, (χ2= 13.57, p-value <0.001).

As regards maternal intake of psychoactive drugs, the results shows a statistically significant difference between case and control groups, the percentage of cases was 74.5% in users group and 41.6% in non-users group,, (χ2= 16.45, p-value <0.001).

The study revealed also a statistically significant difference in maternal iron intake during pregnancy among ADHD cases and controls, the percentage of cases was 19.2% and 83.3% respectively in children of mothers who were taken and who were not take iron regularly during pregnancy , (χ2= 82.03, p-value p<0.001).

Regarding maternal folic acid intake during pregnancy there was also a statistically significant difference among cases and controls, the percentage of cases was 29.2% and 88.6% respectively in children of mothers who were taken and who were not take folic acid regularly during pregnancy, (χ2= 64.09, p-value<0.001).

The results showed also a statistically significant difference in maternal omega 3 intake during pregnancy among ADHD cases and controls, the percentage of cases was 30.6% in regular omega 3 consumer mothers group and 81.6% in non-consumers group, (χ2 = 48.89, p-value<0.001).

As regards family exposure to furniture painting, the results shows a statistically significant difference between case and control groups, the percentage of cases was 72.9% in kids of exposed families and 17.1% in non-exposed families, (χ2= 60.72, p-value<0.001).

There was a statistically significant difference between case and control groups in intake of food additives, the percentages of cases were 59.7% among families who intake food additives and 25% among families which do not have this nutritional habit, (χ2= 19.44, p-value <0.001).

The difference between case group and control group in maternal high intake of sugar during pregnancy (more than 6 teaspoonful per day) was also statistically significant, the percentages of children with ADHD was 80.4% among mothers who highly intake sugar during pregnancy and 18.4% among others, (χ2= 76.91, p-value <0.001).

Also the difference between case group and control group as regards history of pre-term labour was statistically significant, the percentages of cases was 70.6% among pre-term babies and 45.8% among others, (χ2=6.95, p-value =0.008).

LBW showed a statistically significant difference between case and control groups, the percentage of ADHD cases was 75% of LBW babies and 42.1% in others, (χ2= 15.79, p-value <0.001).

Having a sibling(s) with ADHD had also a significant difference between case and control

groups, the percentage of cases was 88.9% in families who had a sibling with ADHD and 412.1% in families who had not, (χ2= 25.56, p-value <0.001).

There was a statistically non-significant difference between case and control groups in birth order. The percentage of cases was 59.1% among first order kids, 44.1% among second order kids, 46.7% among third order and 57.1% among fourth order kids (χ2= 3.23, p-value =0.357).

And finally there was a statistically non-significant difference in ADHD cases and controls per mode of delivery, ADHD cases were 51.9% of children delivered by CS and 42.9% of those who were delivered thorough SVD, and the rest by spontaneous vaginal delivery (χ2= 1.09, p-value =0.298).

TABLE 2: Univariate and multivariate analysis for prediction of ADHD

Predictors	**Univariate analysis**		**Multivariate analysis**		
	p	Crude Odds ratio (95% CI)	β	p	Adjusted odds ratio (95% CI)
Residence **Urban** **Rural (r)**	0.003*	2.49(1.36-4.56)	1.86	<0.001*	6.40(2.62-16.66)
Parental consanguinity	0.004*	3.16(1.43-6.98)	1.21	0.01*	3.36(1.33-8.48)
Age of mothers at start of pregnancy(years) **<20 (r)** **20-<30** **≥30**	 1 0.999 0.999	 undefined undefined			
Maternal active or passive exposure to tobacco smoke during pregnancy	<0.001*	2.91(1.64-5.18)	1.83	<0.001*	6.23(2.60-14.91)
Regular maternal psychoactive drugs intake during pregnancy	<0.001*	4.10(2.02-8.34)	1.54	<0.001*	4.68(1.98-11.05)
Regular maternal iron intake during pregnancy	<0.001*	0.048(0.023-0.098)	-1.56	0.006*	0.209(0.069-0.635)
Regular maternal folic acid intake during pregnancy	<0.001*	0.053(0.023-0.122)	-1.95	0.003*	0.142(0.039-0.512)
Regular maternal omega3 intake during pregnancy	<0.001*	0.10(0.05-0.20)	-2.3	<0.001*	0.099(0.041-0.238)
Family exposure to furniture paints	<0.001*	13.05(6.46-26.39)	3.92	<0.001*	50.2(10.1-249)
Family regular intake of food additives	0.003*	4.45 (1.68-11.81)	0.722	0.011*	5.25 (1.45-18.97)
Maternal high intake of sugar during pregnancy	<0.001*	18.22(8.98-36.97)	4.23	<0.001*	68.77(14.91-317.2)
Preterm birth	0.01*	2.84(1.28-6.32)	0.385	0.631	1.24(0.58-9.5)
LBW	<0.001*	4.13(1.99-8.55)	0.643	0.285	1.90(0.586-6.19)
Having a sibling with ADHD	<0.001*	11.29(3.82-33.42)	2.42	<0.001*	11.29(3.82-33.42)
overall % predicted=86.0%					

r: reference group , β : regression coefficient

Multiple logistic regression was done and showed some risk factors associated with ADHD: residence in urban areas, parental consanguinity, maternal active or passive

exposure to tobacco smoke during pregnancy, regular maternal psychoactive drugs intake during pregnancy, family exposure to furniture paints, family regular intake of food additives, maternal high intake of sugar during pregnancy, having a sibling with ADHD.

The results showed also some protective factors which are: regular maternal iron intake during pregnancy, regular maternal folic acid intake during pregnancy, and regular maternal omega3 intake during pregnancy.

For residence, kids who live in urban areas are more likely to have ADHD as compared to kids who live in rural areas, (OR=6.40), p-value=<0.001.

Consanguineous parents tend to have a greater chance to get kids with ADHD (OR=3.36), p-value=0.01, Maternal active or passive exposure to tobacco smoke during pregnancy (OR=6.23), p-value<0.001, regular maternal psychoactive drugs intake during pregnancy(OR=4.68), p-value<0.001,family exposure to furniture paints(OR=50.2), p-value<0.001, family regular intake of food additives(OR=5.25), p-value=0.011, maternal high intake of sugar during pregnancy(OR=68.77), p-value<0.001, having a sibling with ADHD(OR=11.29), p-value<0.001, are also risk factors of ADHD.

The results showed also some protective factors which are: regular maternal iron intake during pregnancy (OR=0.209), p-value=0.006, regular maternal folic acid intake during pregnancy (OR=0.142), p-value=0.003, and regular maternal omega3 intake during pregnancy (OR=0.099), p-value<0.001.

DISCUSSION

Our study found that residents in urban areas have more risk for having ADHD kids than those who residing in rural areas, this is in agreement with results of study of Zablotsky and colleagues. 2017(6) who discovered a significant increases in the prevalence of ADHD (8.5%-9.5%, P < .01) in children residing in urban areas than those residing in rural ones, but this is in disagreement with the results of the study of El Gendy, and colleagues 2016(7) that revealed that the students residing urban areas had less risk to have ADHD.

The results of our study showed that that ADHD cases have been subjected to highly statistical significant parental rates of consanguinity, these results were consistent with those of Bishary and colleagues.(8) on risk factors for ADHD in a sample of Egyptian adolescents, and also anothe study on phenotypic subtypes in ADHD in an isolated Dutch population conducted by Croes and colleagues.(9), who found that 81% of those patients of the inattentive subtype were derived from consanguineous marriages. These results are consistent also with different studies that suggest that genes predispose individuals to ADHD as that of Rickel and Brown (10).

Regression analysis of our study failed to detect an association between maternal age and the risk of having an ADHD baby, this association is controversial among different studies, for example, the large population-based study of Halmøy and colleagues. (11) which revealed that: first birth order and younger age of the mother at time of pregnancy are risk factors of having ADHD babies, also the study of Clements and colleagues. (12) reported that the younger the age of the mother at time of pregnancy the higher the chance of getting an ADHD baby (OR = 0.97). Chang and colleagues. (13) conducted a cohort study all over the whole Sweden (N = 1,495,543; 30,674 having ADHD) to study the association between age of pregnant mothers and ADHD through analyses of sibling- and cousin-comparison. In the whole population children of teenage mothers have a higher risk for ADHD (HR = 1.78). On the contrary, multivariable logistic regression analyses of results of the study of Park at al. (14) stated that advanced age of pregnant mothers is a risk factor for inattentive (OR = 1.6) and combined types (OR = 1.4) of ADH, and in contrast with the results of our study they revealed that younger age of father at pregnancy is a risk factor for (inattentive, OR = 0.7 and combined, OR = 0.8 subtypes of ADHD. Another study of EL-Gendy and colleagues, 2016(7) found that increased maternal age increases the risk of delivering children suffering from ADHD (27.55± 4.60 vs. 26.50± 3.76; P=0.03).

Our study found a statistically significant association between maternal active or passive exposure to tobacco smoke during pregnancy and

risk of ADHD, the study of Silva and colleagues (15) revealed that paternal(OR = 1.9) and maternal(OR = 1.7) smoking during pregnancy is a risk factor of ADHD ,this may be due to the effect of nicotine on serotonin and dopaminergic systems, development of CNS, and synthesis of DNA and RNA in brain of fetus (16,17) . Another study of Langley and colleagues. (18) attributed the link between ADHD and pregnant mothers smoking to genetic risk factors and found that both mothers ($\beta = 0.25$) and fathers ($\beta = 0.21$) smoking in pregnancy increase the possibility of ADHD manifestations at age 7.6 years through a large prospective cohort research (N = 8234). These results are in agreement with results of another study of Zhu and colleagues. (19) who reported an association between parental smoking during pregnancy and ADHD, the risk is stronger in cases of maternal smoking and even exposed of pregnant mothers to nicotine.

The cohort study of Skoglund and colleagues. (20) (N = 813,030; 19,891 ADHD cases) found that pregnant mothers smoking predicted ADHD status initially (HR ranged from 1.89 to 2.50 for moderate to high smoking, respectively). While other studies (21, 22) did confirm neither pregnant mother smoking nor alcohol intake as risk factors for ADHD in the children.

Our results showed that there is a significant representation of regular psychoactive drugs intake by mothers during pregnancy in the ADHD cases group compared with their healthy counterparts, this is consistent with results of numerous other studies revealing a higher prevalence of psychoactive drugs intake in parents of children and adolescents with ADHD (8, 23, and 24).

In contrast, four case–control studies including about 1500 of participants did not show a relationship between psychoactive drugs intake during pregnancy and ADHD (25) in these studies the number of mothers who reported using psychoactive substances during pregnancy was small. Langley and colleagues. (26) reported that alcohol intake (for example) by pregnant mothers has an association with increased ADHD manifestations but the study did not discuss this point thoroughly because it was not its key focus of interest. The study of Sundquist and colleagues. (27) reported higher prevalence of ADHD in kids of alcohol user parents compared to that in kids of non- user parents, the risk was even more in children of parents who were diagnosed with alcohol use disorder before start of pregnancy (incidence ratio is 2.70; 95% CI 2.59–2.81) , the study attributed this mutation in germ cells which increases the ADHD risk.

Our study found that regular iron intake by pregnant mothers is a Protective factor against ADHD, the study of Weigersma and colleagues. (28) explained about the potential relationship between anemia and neurodevelopmental issues, the brain needs a lot of energy and oxygen so normal blood iron levels ensures transport of enough oxygen to the brain and protect fetus against neurodevelopmental disorders.

Our findings are in accordance with results of Jasveer and colleagues. (29) study, which revealed that early multivitamin supplementation intake by mothers during the first 4 to 8 weeks of pregnancy decreases the risk of ADHD in offspring. The same study of (29) and in accordance with our results revealed that there is an essential role of regular micronutrients intake by pregnant mother on brain development of the fetus. Which decreases the risk of neurodevelopmental disorders in offspring, the study investigated the roles of Folic acid, vitamin D, omega-3 fatty acids, and choline intake by pregnant mothers in normal development of fetal CNC. The positive impact of prenatal folic acid supplementation in reduction of the risk of neurodevelopmental disorders is now established. The same results was reached in the study of Li and Freedman (30) in the year 2020.

Another research of (Kohlboeck and colleagues., 2011) (31) has reported that there is negative correlation between cord blood DHA level and possibility of ADHD in offspring at age ten years.

A study (32) conducted in 2021 showed the association between omega-3 polyunsaturated fatty acids deficiency and ADHD, the study attributed this association to involvement of numerous biological systems such as inflammation, malfunctioning of the hypothalamic-pituitary-adrenal axis and autonomic nervous system and imbalance of gut-microbiota , so, the biomarkers from the formerly

mentioned biological systems are good predictors of response to omega-3 polyunsaturated fatty acids in children with ADHD.

As regard exposure to furniture paintings which is a common industrial practice in Damietta, our study revealed that exposure of pregnant moms to such air pollutants is a risk factor for ADHA which is similar to results of another study (33) that reported that this risky health effect arises through VOCs resulting from the use of furniture coatings (33). Indoor air VOCs are among important causes of building-related symptoms (BRSs), pregnant mothers exposure to VOCs in indoor air has been proven to have harmful effects on fetal and children development (Chang and colleagues., 2017; Franck and colleagues., 2014; Till and colleagues., 2001)(34,35,36). The study of Guxens and colleagues. (2012) (37) reported that prenatal exposure to air pollutants such as NO2 and benzene can unfavorably interfere with normal neuronal development in children. Some researches discussed the effect of exposure of pregnant mothers to occupational VOCs on nervous system of their babies , as the study of(Nakaoka and colleagues. 2021)(38) which revealed a strong association between pregnant mothers occupational exposure to formalin/formaldehyde and CNS development in twelve months old children, the study reported a neurodevelopmental delays related to problem-solving and personal-social skills in the aforementioned age group which increases with pregnant mothers occupational exposure to formalin/formaldehyde, according to the JECS survey. Also the study of (choi and colleagues 2021)(39) which discovered that exposure of pregnant moms to organophosphate esters present in furniture coatings as DPHP and BDCIPP intensifies the risk of ADHD in offspring.

Our study accused family food additives intake (as artificial flavors, colors and preservatives such as preservative sodium benzoate, present in carbonated drinks, dairy products, fruit juices, jams) to be a risk factor of ADHD, this is in accordance with results of a randomized placebo controlled trial conducted on 297 children with age from 3-9 years and showed increase in hyperactive behavior in children after they ate a mixture of food coloring materials and a preservative (sodium benzoate)(40) , the children participating in this trial were from the general population and did not have ADHD, the study reported negative behavioral impacts of the mixture as measured by a global hyperactivity aggregate score, the daily dose approximated that found in two 56 g bags of sweets.

Our study revealed a relationship between high maternal sugar intake during pregnancy (more than 6 teaspoons per day) and increased ADHD risk in children, this is similar to the results of (Cecil and colleagues. 2016)(41) study which found that intake of foods with high-sugar and fat has a strong association not only with high risk for non-communicable diseases as obesity and diabetes, but also for neurodevelopmental disorders, as ADHD via epigenetic modifications of the insulin-like growth factor gene.

Our multiple logistic regression did not found history of preterm delivery and LBW as risk factors associated with ADHD, our result is in accordance with those of a study conducted in the USA and failed to find an association between gestational age and ADHD (42). Another case–control study (43) did not show a difference between children with ADHD (N = 2243) and controls (N = 5631) regarding premature birth. Other studies reported that prematurity is a risk factor for ADHD, because premature delivery does not allow the required time for normal neural development , increased incidence of obstetric complications that may result in neural insult (44) and genetic factors that may be common risk for both premature birth and ADHD. Some studies (45, 46, 13, and 47) in addition to a meta-analysis (25) reported that lower BW is associated with higher risk of ADHD. In contrast with these findings, another study (12) found that there is no relationship between LBW and ADHD. Some population based studies (11, 15 and 48) reported that LBW is a significant risk for ADHD. Some previous studies of Soheilipour and colleagues.(49), Wüstner and colleagues.(50) ,Anderson and colleagues.(51) , Franz and colleagues.(52) ,Heinonen and colleagues.(53)and El Marroun and colleagues.(54) included PTM labour and LBW as risk factors for ADHD.

The results of our study shows no statistically significant differences in birth order of ADHD cases, this is in agreement with the study of Berger and colleagues (55), while some other studies found different results, as that of Bishary and colleagues.(10), Sami and colleagues.(56), who reported that 66.7% of children with ADHD in the Egyptian population had the first birth order, and that of Barakat (57), who found thae same result in 42% of children with ADHD and Pressman and colleagues. (58) Who explained this result by that the family reaction to the first kid is more prominent and results in impairment this is due to the relative deficiency of parenting and child rearing experiences.

Our study revealed that siblings of an ADHD child have a higher possibility to have this disorder in comparison to controls, this is similar to results of another study (59) conducted in 2019 (OR =11.4 - 13.5), and ADHD prevalence = 26 - 45.2% among these siblings.

The difference between cases and controls regarding delivery type was statistically non-significant, which is consistent with results of another case control study (12) that found no association between mode of delivery and ADHD and also recent reports (60, 61) of similar results, but in contrast to Talge and colleagues that reported that term children - delivered by CS delivery preceded by induced labour – have more symptoms of ADHD (62).

CONCLUSIONS

ADHD is widespread neurodevelopmental disorder in children. Our study suggested some factors to be risk factors associated with ADHD: residence in urban areas, parental consanguinity, maternal active or passive exposure to tobacco smoke during pregnancy, regular maternal psychoactive drugs intake during pregnancy, family exposure to furniture paints, family regular intake of food additives, maternal high intake of sugar during pregnancy, having a sibling with ADHD. The results showed also some protective factors which are: regular maternal iron intake during pregnancy, regular maternal folic acid intake during pregnancy, and regular maternal omega3 intake during pregnancy.

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder
DSM V: The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders
OR: Odds Ratio
RR: Relative Risk
PTM: Pre-term
SGA: Small for Gestational Age
CNS: Central Nervous System
LBW: low Birth Weight
RCT: Randomized Controlled Trial
DHA: Docosahexaenoic Acid
VOCs: Volatile Organic Compounds
DPHP : Diphenyl phosphate
BDCIPP : Bis(1,3-dichloro-2-propyl) phosphate
JECS: Japan Environment and Children's Study

Declarations

Ethical approval and consent to participate

A prior ethical approval from IRB of Faculty of medicine, Al Azhar University was obtained. All methods were performed in accordance with the relevant guidelines and regulations. The study objectives and design were explained thoroughly by a team member to sponsor of every candidate then he/she signed an informed consent in case of acceptance before beginning of the study to insure complete satisfaction.

Consent for publication

The author provide a consent for publication of this manuscript, appendices and details in this journal.

Availability of data and materials

The author declare the availability of all necessary data and materials for conducting the study.

Competing interests

The author declare no competing interests nor conflict of interest.

FUNDING

The study was funded by the authors.

Author's contributions

Conceptualization, questionnaire designing, and methodology, data analysis , data collection, writing, original draft preparation, reviewing and editing then reading and agreement on the final version of the manuscript was done by the author.

ACKNOWLEDGEMENTS

Sincere thanks to all the participant children, their families, institutions and organizations that care for them and facilitated our mission in conducting this research.

REFERENCES

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders .5th Ed. Arlington, American Psychiatric Publishing.2013; pp. 59–65
2. Hanan Azzam : Perceived parenting attitudes in relation to ADHD symptoms and aggressive behaviors in a sample of Egyptian children with ADHD, Middle East Current Psychiatry. 2021volume 28, Article number: 18
3. Stephen V. Faraone , Henrik Larsson : Genetics of attention deficit hyperactivity disorder, Molecular Psychiatry .2019; 24:562–575
4. The World Federation of ADHD International Consensus Statement: 208 evidence-based conclusions about the disorder, Neuroscience & Biobehavioral Reviews, j.neubiorev. 2022; doi:10.1016
5. CDC ADHD fact sheet 2022: website :https://www.cdc.gov/ncbddd/adhd/index.html , cited on 1/09/2022
6. Zablotsky B, Black LI, Maenner MJ, Schieve LA, Danielson ML, Bitsko RH, Blumberg SJ, Kogan MD, Boyle CA . Prevalence and Trends of Developmental Disabilities among Children in the United States: 2009-2017. Pediatrics 2019 Oct;144(4):e20190811. doi: 10.1542/peds.2019-0811. PMID: 31558576; PMCID: PMC7076808.
7. Soad D, EL-Gendy, Eman A, El-Bitar, Mona A, El-Awady, Hanaa E, Bayomy , Eman M, Agwa .Attention-Deficit/Hyperactivity Disorder: Prevalence and risk factors in Egyptian primary school children. The Egyptian Journal of Public Health 2017 ; Article 1, Volume 35, Issue 1, January 2017, Page 1-16
8. Zeinab Bishry, Hisham A, Ramy, Mona M, El-Sheikh, Ahmed A, El-Missiry , Marwa A . Risk factors for attention deficit hyperactivity disorder in a sample of Egyptian adolescents: A case-control study, Middle East Current Psychiatry 2013 ; 20(3):131-139, July 2013, DOI:10.1097/01.XME.0000430425.13729.e6
9. Croes EA, El Galta R, Houwing-Duistermaat JJ . Phenotypic subtypes in attention deficit hyperactivity disorder in an isolated population, European Journal of Epidemiology 2005; vol. 20,pp789–794
10. Rickel A, and Brown R . Attention-deficit/hyperactivity disorder in children and adults, Hogrefe & Huber Publishers 2007;website: https://psycnet.apa.org/record/2007-05952-000
11. Anne Halmøy, Kari Klungsøyr, Rolv Skjærven, Jan Haavik . Pre- and Perinatal Risk Factors in Adults with Attention-Deficit/Hyperactivity Disorderد Biological Psychiatry 2016; vol. 71, issue 5, P474-481, March 01, 2012
12. Clements CC, Castro VM, Blumenthal SR, Rosenfield HR, Murphy SN, Fava M. Prenatal antidepressant exposure is associated with risk for attention-deficit hyperactivity disorder but not autism spectrum disorder in a large health system, Mol. Psychiatry 2015 ;20(6):727–34
13. Chang Z, Lichtenstein P, D'Onofrio BM, Almqvist C, Kuja-halkola R, Sjölander A . Maternal age at childbirth and risk for ADHD in offspring: a population-based cohort study, Int. J. Epidemiol. 2014;43(6):1815–24
14. Park S, Cho S-C, Kim J-W, Shin M-S, Yoo H-J, Oh SM . Differential perinatal risk factors in children with attention-deficit/hyperactivity disorder by subtype, Psychiatry Res. 2014; 2;219(3):609–16. doi:10.1016/j.psychres.2014.05.036
15. Silva D, Colvin L, Hagemann E, Bower C . Environmental risk factors by gender associated with attention-deficit/hyperactivity disorder. Pediatrics. 2014;133(1):e14–22
16. Biederman J, Petty CR, Bhide PG, Woodworth KY, Faraone S . Does exposure to maternal smoking during pregnancy affect the clinical features of ADHD? Results from a controlled study. World J Biol Psychiatry. 2012;13(1):60–4. doi:10.3109/15622975.2011.562243.
17. Wakschlag LS, Lahey BB, Loeber R, Green SM, Gordon RA, Leventhal BL. Maternal smoking during pregnancy and the risk of conduct disorder in boys. Arch Gen Psychiatry. 1997;54(7):670–6.
18. Langley K, Heron J, Smith GD, Thapar A . Maternal and paternal smoking during pregnancy and risk of ADHD symptoms in offspring: testing

for intrauterine effects. Am J Epidemiol. 2012;176(3):261–8.
19. Zhu JL, Olsen J, Liew Z, Li J, Niclasen J, Obel C . Parental smoking during pregnancy and ADHD in children: the Danish national birth cohort, Pediatrics. 2014;134(2):e382–8.
20. Skoglund C, Chen Q, D'Onofrio BM, Lichtenstein P, Larsson H . Familial confounding of the association between maternal smoking during pregnancy and ADHD in offspring. J Child Psychol. 2014;55(1):61–8. doi:10.1111/jcpp.12124.
21. Thapar A, Rice F, Hay D, Boivin J, Langley K, van den Bree M . Prenatal smoking might not cause attention-deficit/hyperactivity disorder: evidence from a novel design. Biol Psychiatry 2009;66(8):722–727. pmid:19596120
22. Schlack R, Goebel K, Hoelling H, Petermann F, Romanos M.Predictors of stability of parent report on ADHD lifetime prevalence and incidence of parent-reported ADHD diagnosis in the developmental course over six years, Zeitschrift für Psychiatrie, Psychologie und Psychotherapie, 2018;66:233–247.
23. Chronis AM, El Galta R, Houwing-Duistermaat JJ, Ferdinand RF, Leo´ n SL, Rademaker TAM. Phenotypic subtypes in attention deficit hyperactivity disorder in an isolated population, Europe J Epidemiol 2005; 20 (Suppl 9):789–794.
24. Lahey BB. Should the combined and predominantly inattentive types of ADHD be considered distinct and unrelated disorders? Not now, at least.Clin Psychol-Sci Pr 2001; 8:494–497.
25. Sciberras E, Mulraney M, Silva D, Coghill D . Prenatal Risk Factors and the Etiology of ADHD-Review of Existing Evidence. Current Psychiatry Reports 2017; Jan;19(1):1. DOI: 10.1007/s11920-017-0753-2. PMID: 28091799.
26. Langley K, Heron J, Smith GD, Thapar A . Maternal and paternal smoking during pregnancy and risk of ADHD symptoms in offspring: testing for intrauterine effects. Am J Epidemiol. 2012;176(3):261–8.
27. Sundquist J, Sundquist K, Ji J. Autism and attention-deficit/hyperactivity disorder among individuals with a family history of alcohol use disorders, eLife 2014;3, e02917.
28. Aline Marileen Wiegersma, Christina Dalman, Brian K. Lee, Håkan Karlsson, Renee M. Gardner. Association of Prenatal Maternal Anemia With Neurodevelopmental Disorders, JAMA Psychiatry 2019 Dec; 76(12): 1294–1304.
29. Jasveer Virk,Zeyan Liew,Jørn Olsen,Ellen A Nohr,Janet M Catov , Beate Ritz.Pre-conceptual and prenatal supplementary folic acid and multivitamin intake, behavioral problems, and hyperkinetic disorders: A study based on the Danish National Birth Cohort (DNBC), Nutritional Neuroscience 2018; Volume 21, Issue 5, Pages 352-360
30. Ying Li,Robert Freedman. Prospects for improving future mental health of children through prenatal maternal micronutrient supplementation in China, Pediatr Investig. 2020; Jun 24;4(2):118-126. doi: 10.1002/ped4.12199
31. Kohlboeck G, Glaser C, Tiesler C, Demmelmair H, Standl M, Romanos M. Effect of fatty acid status in cord blood serum on children's behavioral difficulties at 10 y of age: Results from the LISAplus Study,American Journal of Clinical Nutrition, 2011;94(6):1592–1599.
32. Jane Pei-Chen Chang.Personalised medicine in child and Adolescent Psychiatry: Focus on omega-3 polyunsaturated fatty acids and ADHD,Brain, Behavior, & Immunity - Health,Volume 16,2021,100310.
33. Gould J.F., Treyvaud K., Yelland L.N., Anderson P.J., Smithers L.G., McPhee A.J., Makrides M . Seven-year follow-up of children born to women in a randomized trial of prenatal DHA supplementation. J. Am. Med. Assoc. 2017;317:1173–1175. doi: 10.1001/jama.2016.21303.
34. United States Environmental Protection Agency.Volatile Organic Compounds' Impact on Indoor Air Quality 2020; website: https://www.epa.gov/indoor-air-quality-iaq/volatile-organic-compounds-impact-indoor-air-quality
35. M. Chang, H. Park, M. Ha, Y.C. Hong, Y.H. Lim, Y. Kim, Y.J. Kim, D. Lee, E.H. Ha .The effect of prenatal TVOC exposure on birth and infantile weight: the Mothers and Children's Environmental Health study, Pediatr. Res. 2017; pp. 423-428, 10.1038/pr.2017.55
36. U. Franck, A. Weller, S.W. Röder, G. Herberth, K.M. Junge, T. Kohajda, M. von Bergen, U. Rolle-Kampczyk, U. Diez, M. Borte, I. Lehmann .Prenatal VOC exposure and redecoration are related to wheezing in early infancy, Environ. Int. 2014; 73, pp. 393-401, 10.1016/j.envint.2014.08.013
37. C. Till, G. Koren, J.F. Rovet.Prenatal exposure to organic solvents and child neurobehavioral performance,Neurotoxicol. Teratol. 2001; 23, pp. 235-245, 10.1016/S0892-0362(01)00141-6
38. M. Guxens, I. Aguilera, F. Ballester, M. Estarlich, A. Fernández-Somoano, A. Lertxundi, N. Lertxundi, M.A. Mendez, A. Tardón, M. Vrijheid, J. Sunyer . Prenatal exposure to

residential air pollution and infant mental development: modulation by antioxidants and detoxification factors,Environ., Health Perspect 2012; 120, pp. 144-149, 10.1289/ehp.1103469

39. Hiroko Nakaoka, Aya Hisada, Daisuke Matsuzawa, Midori Yamamoto, Chisato Mori, Michihiro Kamijima, Shin Yamazaki, Yukihiro Ohya, Reiko Kishi, Nobuo Yaegashi, Koichi Hashimoto, Chisato Mori, Shuichi Ito, Zentaro Yamagata, Hidekuni Inadera, Takeo Nakayama, Hiroyasu Iso, Masayuki Shima, Youichi Kurozawa, Narufumi Suganuma, Koichi Kusuhara, Takahiko Katoh . Associations between prenatal exposure to volatile organic compounds and neurodevelopment in 12-month-old children. The Japan Environment and Children's Study (JECS). Science of The Total Environment 2021;Volume 794,2021,148643,ISSN 0048-9697.
40. Giehae Choi, Alexander P. Keil, David B. Richardson, Julie L. Daniels, Kate Hoffman, Gro D. Villanger, Amrit K. Sakhi, Cathrine Thomsen, Ted Reichborn-Kjennerud, Heidi Aase, Stephanie M. Engel. Pregnancy exposure to organophosphate esters and the risk of attention-deficit hyperactivity disorder in the Norwegian mother, father and child cohort study,Environment International 2021;Volume 154,2021,106549,ISSN 0160-4120.
41. Kemp A . Food additives and hyperactivity, BMJ, 2008 May 24;336(7654):1144. doi: 10.1136/bmj.39582.375336.BE. PMID: 18497374; PMCID: PMC2394588.
42. Cecil CA, Walton E, Barker ED. Prenatal diet and childhood ADHD: exploring the potential role of IGF2 methylation, Epigenomics, 2016 Dec;8(12):1573-1576. doi: 10.2217/epi-2016-0131, Epub 2016 Nov 18. PMID: 27855496.
43. Harris MN, Voigt RG, Barbaresi WJ, Voge GA, Killian JM, Weaver AL. ADHD and learning disabilities in former late preterm infants: a population-based birth cohort. Pediatrics 2013;132(3):e630–6.
44. Clements CC, Castro VM, Blumenthal SR, Rosenfield HR, Murphy SN, Fava M . Prenatal antidepressant exposure is associated with risk for attention-deficit hyperactivity disorder but not autism spectrum disorder in a large health system. Mol Psychiatry 2015;20(6):727–34. doi:10.1038/mp.2014.90.
45. Getahun D, Rhoads GG, Demissie K, Lu SE, Quinn VP, Fassett MJ.In utero exposure to ischemic-hypoxic conditions and attention-deficit/hyperactivity disorder. Pediatrics. 2013;131(1):e53–61.
46. Tole F, Kopf J, Schröter K, Palladino VS, Jacob CP, Reif A (2019): The role of pre-, peri-, and postnatal risk factors in bipolar disorder and adult ADHD. J Neural Transm (Vienna) 2019;126:1117–1126.
47. Wüstner A, Otto C, Schlack R, Hölling H, Klasen F, Ravens-Sieberer U. Risk and protective factors for the development of ADHD symptoms in children and adolescents: Results of the longitudinal BELLA study. PLoS One. 2019;14:e0214412.
48. Hanć T, Szwed A, Słopień A, Wolańczyk T, Dmitrzak-Węglarz M, Ratajczak J. Perinatal risk factors and ADHD in children and adolescents: a hierarchical structure of disorder predictors. J Atten Disord. 2018;22:855–863.
49. Henriksen L, Wu CS, Secher NJ, Obel C, Juhl M . Medical augmentation of labor and the risk of ADHD in offspring: a population-based study, Pediatrics 2015;135(3):e672–7.
50. Fahimeh Soheilipour, Sareh Shiri, Hamid Reza Ahmadkhaniha, Ebrahim Abdollahi, and Fatemeh Sadat Hosseini-Baharanchi. Risk factors for attention-deficit/hyperactivity disorder: a case-control study in 5 to 12 years old children, Med Pharm Rep. 2020 April, 93(2): 175–180.
51. Wüstner A, Otto C, Schlack R, Hölling H, Klasen F, Ravens-Sieberer U. Risk and protective factors for the development of ADHD symptoms in children and adolescents: Results of the longitudinal BELLA study. PLoS One 2019;14:e0214412.
52. Anderson PJ, De Luca CR, Hutchinson E, Spencer-Smith MM, Roberts G, Doyle LW. Attention problems in a representative sample of extremely preterm/extremely low birth weight children. Dev Neuropsychol. 2011;36:57–73.
53. Franz AP, Bolat GU, Bolat H, Matijasevich A, Santos IS, Silveira RC. Attention Deficit/Hyperactivity Disorder and Very Preterm/Very Low Birth Weight: A Meta-analysis. Pediatrics 2018;141:e20171645.
54. Heinonen K, Räikkönen K, Pesonen AK, Andersson S, Kajantie E, Eriksson JG . Behavioural symptoms of attention deficit/hyperactivity disorder in preterm and term children born small and appropriate for gestational age: a longitudinal study. BMC Pediatr. 2010;10:91.
55. El Marroun H, Zeegers M, Steegers EA, van der Ende J, Schenk JJ, Hofman A . Post-term birth and the risk of behavioral and emotional problems in early childhood. Int J Epidemiol. 2012;41:773–781
56. Berger I, Felsenthal-Berger N.Attention-deficit hyperactivity disorder (ADHD) and birth order. J

Child Neurol. 2009 Jun;24(6):692-6. doi: 10.1177/0883073808330763.
57. Sami Noha . Effect of psychosocial Factors on Childhood ADHD (MD thesis) 2006; Faculty of medicine, Ain Shams University, Department of Psychiatry
58. Barakat DM. Prenatal and perinatal risk factors in ADHD in a sample of Egyptian ADHD children (MD thesis); Faculty of Medicine, Ain Shams University, Department of Psychiatry
59. Pressman L, Loo S, Carpenter E, Arasnow JR, Lynn D, McCracken JT. Relationship of family environment and parental psychiatric diagnosis to impairment in ADHD. J AM Acad Child Adolesc Psychiatry 2006; 45 (Suppl3): 346–354.
60. Hidalgo-López C, Gómez-Álzate AM, García-Valencia J, Palacio-Ortiz JD . Risk of Attention Deficit/Hyperactivity Disorder (ADHD) and Other Psychiatric Disorders in Siblings of ADHD Probands. Rev Colomb Psiquiatr (Engl Ed). 2019 Jan-Mar;48(1):44-49. English, Spanish. doi: 10.1016/j.rcp.2017.06.002. Epub 2017 Jul 26. PMID: 30651172.
61. Curran EA, O'Neill SM, Cryan JF, Kenny LC, Dinan TG, Khashan AS . Research review: Birth by caesarean section and development of autism spectrum disorder and attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. J Child Psychol Psychiatry. 2015;56:500–508.
62. Curran EA, Cryan JF, Kenny LC, Dinan TG, Kearney PM, Khashan AS .Obstetrical mode of delivery and childhood behavior and psychological development in a British cohort. J Autism Dev Disord. 2016;46:603–614.
63. Talge NM, Allswede DM, Holzman C . Gestational age at term, delivery circumstance, and their association with childhood attention deficit hyperactivity disorder symptoms. Paediatr Perinat Epidemiol. 2016;30:171–180