Risk Factors of Autistic Spectrum Disorders (ASDs) in a group of Egyptian Children Attending Psychiatric Clinic of Postgraduate Childhood Studies Institute, Ain Shams University

Thesis
Master Degree in Epidemiology

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بسم الله الرحمن الرحيم

﴿وَقُل رَّبِّ زِدْنِي عِلْماً﴾

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Contents

List of Abbreviations

AAP	American Academy of Pediatrics
ABC	Autism Behaviour Checklist
ADDM	Autism and Developmental Disabilities Monitoring Network
ADHD	Attention Deficit Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview—Revised
AOSI	Autism Observation Scale for Infants
APA	American Psychiatric Association
ASD	Autistic Spectrum Disorder
ASIEP	Autism Screening Instrument for Educational Planning
BCG	Bacillus Calmette–Guérin Vaccine
CARS-2	Childhood Autism Rating Scale (2nd edition)
CARS2-HF	Childhood Autism Rating Scale (2nd edition) - High functioning form
CARS2-ST	Childhood Autism Rating Scale (2nd edition) - The Standard form
CDC	Center of Disease Prevention and Control
CDD	Childhood Disintegrative Disorder
CHAT	Checklist for Autism in Toddlers
CI	Confidence Interval
CS	Ceserian Section
DHEA	Dehydro- epiandrosterone
DHEA-S	Dehydro- epiandrosterone sulfate
DPT	Diphtheria, Pertussis and Tetanus Vaccine
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th Edition
DSM-IV-	Diagnostic and Statistical Manual of Mental Disorders 4th Edition – Text Revision

List of Abbreviations (Cont.)

DSM-V	Diagnostic and Statistical Manual of Mental Disorders 5th Edition
ESAT	Early Screening of Autistic Traits
ETS	Environmental Tobacco Smoking
GARS-3	Gilliam Autism Rating Scale-Third Edition
GFCF	Gluten -free and Casein- free diet
HBW	High Birth Weight
HPA	hypothalamic/pituitary/adrenal axis
IQ	intelligence quotient
LBW	Low Birth Weight
M.	Months
M-CHAT-F	Modified Checklist for Autism in Toddlers, Revised with Follow-Up
M-CHAT-R	Modified Checklist for Autism in Toddlers, Revised
MECP2	Methyl CpG Binding Protein 2
MMR	Measles, Mumps and Rubella Vaccine
NBW	Normal Birth Weight
NICU	Neonatal Intensive Care Unit
No.	Number
OR	Odds Ratio
PDD-NOS	Pervasive Developmental Disorders – Not Otherwise Specified
PET	Preeclampsia
RR	Relative Risk
SCQ	Social Communication Questionnaire
SD	Standard Deviation
SRIs	serotonin reuptake inhibitors

List of Abbreviations (Cont.)

STAT	Screening Tool for Autism in Two-Year-Old
UAE	United Arab of Emirates
VLBW	Very Low Birth Weight
WHO	World Health Organization

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ABSTRACT

Autism spectrum disorder (ASD) is characterized by difficulties in social interaction, verbal and nonverbal communication and repetitive behaviours. ASD is caused by a combination of genetic and environmental factors. The aim of the study is identify possible risk factors of ASD and impact of autistic child on his/ her family. The current study is a case-control study. Seventy one of autistic children were recruited from Postgraduate Childhood Studies Institute affiliated to Ain Shams University, and 71 typically developing children were recruited from outpatient Pediatric clinics of Ain Shams University. Both cases and controls were matched regarding age and sex. The total 142 caregivers of all children answered an interview questionnaire about risk factors for ASD and only cases answered an interview questionnaire of the Impact on Family Scale. The main findings are advanced paternal age at the time of conception, hypertension during pregnancy, postnatal hypoxia, positive family history of psychiatric diseases, and artificial feeding are risk factors for ASD. Also, folic acid supplementation during 1st trimester is protective from autism. On the other hand, order of birth, age of mother at conception, consanguinity, parity, birth weight and prematurity were of no significance difference. Factors affecting the Impact on Family Scale were order of birth of autistic child, number of siblings, marital status, ability of autistic child to say a word, admission to school, sad autistic child, and autistic child improvement. It is recommended that folic acid supplementation before pregnancy and at the first trimester of pregnancy (at least 600 mcg per day), financial support for families and ensuring their emotional and physical health.

Key words: Autism spectrum disorder, ASD, social interaction, communication, repetitive behaviours, advanced paternal age, the Impact on Family Scale, folic acid supplementation.

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Introduction

Autistic spectrum disorders (ASDs) are group of complex neurodevelopmental disorders characterized by impairments in social and communication skills as well as repetitive body movements and behaviors. ASDs include autistic disorder (AD), Asperger's syndrome, childhood disintegrative disorder and pervasive developmental disorder - not otherwise specified. **(American Psychiatric Association, 2013)**

Autism is a lifelong complex disorder that affects practically every aspect of the diagnosed person's life. It is first described by Leo Kanner in 1943; autism is usually diagnosed before age 3 and is characterized by impairments in social interactions, delayed speech and language development, and restrictive repetitive behaviors. Individuals with ASD may also have difficulties in responding to others, motor planning, and visual processing. While there are core similarities, it should be noted that individual presentations can vary considerably. **(Elder, 2008)**

The number of reported cases of autism increased dramatically in the 1990s and early 2000s. This increase is largely attributable to changes in diagnostic practices, referral patterns, availability of services, age at diagnosis, and public awareness. **(Chawarska and Volkmar, 2005)**

The most recent estimates from the Centers for Disease Control reveal that one in 68 children in the United States have some type of ASD. This represents a marked increase since 2000

when prevalence rates were approximately one in 150 children. Boys are disproportionally affected with rates approximately five times higher than girls (1:42 boys versus 1:189 girls). **(CDC, 2014)**

In a study from the United Arab of Emirates (UAE) to measure the prevelance of autistic spectrum disorders in a sample of 694 three-year old children by using an autism screening questionnaire, 58 per 10,000 children were noted to have autistic features. The presence of autistic features was associated with male gender. **(Eapen et al., 2007)**

The etiology of autism is unknown. Although the estimated 60% to 92% concordance rate in monozygotic twins compared with the 0% to 10% rate in dizygotic twins shows the importance of genetic influences, the incomplete concordance in monozygotic twins also indicates a role of environmental factors. It is now believed that the mechanism underlying autism etiology is most likely polygenic and that environmental factors may interact with genetic factors to increase risk**. (Gardener et al., 2011)**

Several studies have focused on perinatal risk factors for autism. Some studies found an increased risk of autism associated with the presence of one or more unfavorable obstetric events. Studies focusing on single perinatal risk factors have reported a positive association for low birth weight (<2,500 g), low Apgar score (<6 or <7) at 5 minutes, being small for gestational age, gestational age at birth of less than 37 weeks, cesarean section, and congenital malformations**.** Prenatal exposure to valproic acid, thalidomide, rubella, and alcohol has been associated with an increased risk of ASDs. A gender stratification in one study indicated an increased risk of autism among boys, but not girls, of low birth weight (<2,500 g) **(Larsson et al., 2004).**

Compared with parents of children with other handicaps, parents of autistic children more frequently have schizoid personality traits and women with schizophrenia are at increased

risk of an adverse pregnancy outcome. Most studies on perinatal factors and autism have not been able to adjust for socioeconomic status. Socioeconomic status may be associated with adverse pregnancy outcomes as well as autism **(Larsson et al., 2004).**

Environmental factors such as mercury and radiation have been proposed as possible causes of autism spectrum disorders. Several studies provided strong evidence against the hypothesis that MMR vaccination causes autism**.** Prior research suggests that parental characteristics, such as age and level of education, may be associated with a risk of autism. Parental age has been shown to be associated with many disorders, such as schizophrenia, childhood cancer and fetal death; however, results from studies of parental age and autism are inconsistent **(El-Baz et al., 2011).**

A case control study had been conducted to determine the possible risk factors of autism at pediatric hospital, Ain Shams University. High maternal age (mother ≥ 35 years) at birth was found in 23% of autistic children in comparison to 9.5% of controls. Also advanced paternal age (father ≥ 35 years) at birth was found in 91% of cases in comparison to 83.5% of control group and the difference was statistically significant. Positive family history was found to be statistically significantly associated with the risk of autism (16% of cases versus 1% of controls). As regards natal factors, history of low birth weight and delivery by ceserian section were significantly higher among cases than controls. Also postnatal factors as history of hypoxia, resuscitation and history of jaundice were considered significantly risk factors for autism **(El-Baz et al., 2011)**.

Despite significant research on prenatal, perinatal, neonatal, and other risk factors in autism, the causal nature of these associations is still disputed due to several current methodological limitations of studies.**(Gardener, 2009)**

The impact of autistic children on their families is well researched. Autistic child can severely affect his family causing

greater parental anxiety and stress than other disabilities. **(White and Hasting, 2004)**

These families may suffer from Children's difficulties in eating, toileting, inappropriate social behavior and sleep problems such as not falling asleep in their own bed, multiple night time awakenings and early waking. Also, fixed routines and behavioral problems may severely restrict families' abilities to undertake routine community activities of daily life, such as shopping and eating out. **(Preece and Almond, 2008)**

Siblings of autistic children also may be affected by one or more of the following risks like loneliness, behavioral disturbances, vulnerability to stress and depression, anger towards the sibling with ASD (particularly if that sibling is aggressive) .**(Petalas et al., 2012)**

Studies from the Middle East on this topic have been particularly rare. In a survey on mental health research in the Arab world over a 25 years period, publications on child psychiatry, in particular, on topics such as autism, were found to be under-represented. **(Afifi, 2005)**