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## Assessment of Toxoplasma Seropositivity in Children Suffering from Attention Deficit Hyperactivity Disorder

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### Abstract

**Background:** Toxoplasmosis, a protozoan infection caused by *Toxoplasma gondii*, is suggested to be a risk factor for many psychological disorders such as schizophrenia and depression. Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders among children. Previous studies have assessed the correlation between ADHD and infectious diseases like toxoplasmosis. So we aimed to investigate the possible correlation between Toxoplasma seropositivity and ADHD in children. **Materials and Methods:** In this cross-sectional study children with signs of ADHD were regarded as patients and underwent clinical assessments. Diagnosis of these patients was based on DSM-IV-TR system which was performed by a pediatric psychiatrist. Forty-eight Children without signs of ADHD or other psychic disorders were considered as control, and 48 patients were considered as case group. Parents were asked to answer a questionnaire including demographic, pregnancy and habitual questions. Blood samples were taken from all individuals and assessed for anti-Toxoplasma IgM and IgG antibodies. **Results:** Ninety-six male and female patients with a mean age of 8.12 years underwent analysis. Seropositivity rate for anti-T.*gondii* IgG antibody was 4.2% in the case and 2.1% in control individuals (P=0.92). Anti-T.*gondii* IgM antibodies were not found in control individuals while it was found in 2.1% of case individuals (P=0.74). There was no statistically significant association between seroprevalence of IgM (P=0.74) and IgG (P=0.92) antibodies and ADHD in study individuals. **Conclusion:** Our findings showed that the toxoplasmosis seropositivity has no significant difference between children with and without ADHD. Further studies are needed with a larger amount of individuals. [GMJ. 2016;5(4):188-93]

**Keywords:** Attention Deficit Hyperactivity Disorder; Toxoplasmosis; *Toxoplasma Gondii*; Children

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## Introduction

Toxoplasmosis, a protozoan infection caused by *Toxoplasma gondii*, has congenital and acquired forms that can be deployed in the brain, heart, and lung. Initial establishment of *T.gondii* in children leads to central nervous system (CNS) dysfunction [1, 2]. Toxoplasmosis is transmitted through oocytes, tissue cysts, tachyzoites or congenital transmission as main, and blood transfusion, laboratory contamination, milk consumption, Birds and Insects and genital transmission as secondary ways.

Attention Deficit Hyperactivity Disorder (ADHD), characterized by inattention, impulsive disruptive behavior, impaired concentration, and motor restlessness, is one of the most common psychiatric disorders [3, 4]. These children have many problems with parents and are strangers to peers so that they will suffer social isolation later [5]. The prevalence of ADHD among Iranian children has been reported 3 to 6 percent in ages between 7 to 12 years [6]. The ADHD may begin during infancy, rarely diagnosed during the toddler age though [7].

It has been mentioned that *T. gondii* directly interacts with neurons in CNS and that they are the primary target of *Toxoplasma* [8]. Some previous studies have confirmed the correlation of cognitive and behavioral disorders [9] like ADHD and schizophrenia with infectious diseases like toxoplasmosis and herpes [10-14]. While there are no studies on the investigation of immunoglobulins (IgG and M levels in children with ADHD and its possible correlation with toxoplasmosis [15]. So we aimed to investigate the prevalence of anti-*Toxoplasma* IgG and IgM antibodies and *T. gondii* morbidity in children with ADHD.

## Materials and Methods

### Participants

This cross-sectional study was conducted between September 2011 and May 2012 on children of both genders referring to child psychiatric and pediatrics clinic of Baqiatalah Hospital. At first, all individuals were examined by both pediatrician and child psy-

chiatrist. Children with signs of ADHD were regarded as patients and underwent clinical assessments. Diagnosis of these patients was confirmed by child psychiatrist applying DSM-IV-TR system. Healthy children were regarded as controls. Children with underlying disorders and those similar to other mental disorders were excluded from the study.

One hundred and ten children participated in this study. Participants with ADHD and healthy individuals were divided into case and control groups respectively. These two groups were matched for age according to case group so that in each group the youngest age was 4 and the oldest age was 12 years old. After signing an informed consent from parents were asked to answer a questionnaire including information about their age, family ownership of domestic animals, demographic information, positive family history of psychiatric disorders, characteristics and problems of children at birth such as weight, term or preterm and associated disorders that were recorded for each of the children on a special chart.

### Ethical Statement

Our institutional review board approved the present study. All the terms of Helsinki Declaration were followed, and all the personal information was kept anonymous. All the parents signed an informed consent form.

### Serological Techniques

Blood samples (5ml) were collected from each patient under sterile conditions and were labeled and stored at -80°C. Samples were sent to the laboratory to determine *T. gondii* antibodies (IgG and IgM) using ELISA technique. Sensitivity and specificity of applied kits for this experiment were high (>98%).

### Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 16.0 Windows (SPSS Inc. Chicago, IL). Normally distributed variables (approved by 1-sample Kolmogorov-Smirnov test) were compared using independent sample t-test between the groups and paired sample t-test within the groups. Chi-square test was used to compare

categorical variables in the 2 groups. Also, fisher's exact test, the correlation coefficient, ANOVA, and covariance analysis was used for statistical analysis. A P-value of less than 0.05 was considered as statistically significant.

## Results

Eventually, 96 cases with a mean age of 8.12 years underwent analysis. Both case and control groups were consisted of 32 (66.7%) males and 16 (33.3%) females (Table-1).

As showed in Table-2, case group had a mean birth weight of 2981gr and control group had a mean birth weight of 3221.88 gr. There was a significant difference between two groups for birth weight ( $P=0.028$ ).

The preterm birth history was reported by 4 (8.3%) patients of case group and 3 (6.2%) individuals in the control group. There was no significant difference between case and control groups for birth age ( $P=0.537$ ).

Regarding the positive familial history of psychiatric problems, there was no significant relation between case and control groups ( $P=0.537$ ). In case group and control group 7(14.6%) patients and 5 (10.4%) individuals mentioned a type of psychiatric disorders in their family. There was no significant difference between two groups for problems in infancy and pregnancy ( $P=0.232$ ). In case group 14(29.2%) patients and control group 9(18.8%) individuals had a type of problems like hyperbilirubinemia, prematurity, etc.

The percentage of anti-*T.gondii* IgG antibodies positivity in the case and 48 (100%) control individuals was 4.2% and 2.1% respectively. The difference in Toxoplasma IgG seropositivity between case and control individ-

uals was not statistically significant ( $P=0.920$ , Table-3).

Anti-*T.gondii* IgM antibodies were not found in control individuals, while its seropositivity was 2.1% in case group (Table-3). The difference in Toxoplasma IgM seropositivity between case and control individuals was not statistically significant ( $P=0.745$ ).

## Discussion

We found that Toxoplasmosis infection has no direct effect on the incidence of ADHD in the individuals of the present study. Birth weight in patients with ADHD was significantly lower in comparison with the healthy control children.

Previous studies demonstrated that latent infection of *T. gondii* effects on behavior and learning capacity of patients and that is associated with higher incidence of ADHD [16]. Brynska *et al.* in a review article, assessing the progressive effect of toxoplasmosis on nine psychological and neurological disorders, reported that *T. gondii* reacts with about 3000 genes and host proteins. Genes that make the patient predisposed to various diseases like ADHD [2]. In the present study, there was no significant association between seropositivity of Toxoplasma *gondii* and ADHD.

Elgen *et al.* assessing eleven-year-old children with low birth weight, concluded that these individuals have significantly more mental disorders comparing with normal birth weight controls [17] which is in concordance with the present study.

It has been demonstrated that toxoplasmosis has a positive effect on dopamine production in the brain and causes an increase in its level [18].

**Table 1.** Demographical Characteristics of Case and Control Groups

Demographical characteristics	Case group (N=46)	Control group (N=46)
Male N(%)	32 (66.7%)	32 (66.7%)
Female N(%)	16 (33.3%)	16 (33.3%)
Age (Mean, years)	8.12±3.25	8.12±2.40
Residency (Iran, Tehran)	46 (100%)	46 (100%)

**Table 2.** Assessed Factors Considered to Be Probably Related with Disease

Parameters	Case group (N=46) n(%)	Control group (N=46) n(%)	P-value
Postpartum diseases	14 (29.2)	9(18.8)	0.23
Preterm birth	4 (8.3)	3(6.2)	0.78
Toxoplasmosis-like Symptoms in past	1 (2.1)	0(0.0)	0.45
Ocular symptoms	2 (4.2)	1 (2.1)	0.65
Mother's infectious diseases during pregnancy	1 (2.1)	1(2.1)	0.34
Familial history of psychiatric problems	7 (14.6)	5(10.4)	0.53
Undercooked meats consumption	2 (4.2)	2(4.2)	0.43
Raw vegetables consumption	31 (64.6)	33(68.7)	0.35
History of contact with animals	2 (4.2)	2(4.2)	0.65
Drinking water health	46 (100)	46(100)	0.66
The economic situation	Average	4 (8.3)	5 (10.4)
	Poor	42 (87.5)	41 (85.4)
	Excellent	2 (4.2)	2 (4.2)
Weight (mean, kg)	15-41 (27.48)	15-42 (29.4)	0.94
Birth weight (mean, gr)	1800-4200 (2981)	1800-4100 (3221.8)	0.02
Diagnosis time of ADHD (mean, y)	2-9(6.06)	-	NC*

\*Not Calculated

**Table 3.** Comparison of IgG and IgM Levels in Both Case and Control Groups

Anti-toxoplasma anti-body level in serum	Case group (N=46) n(%)	Control group (N=46) n(%)	P-value
IgG level	Positive	1 (2.1)	0.92
	Negative	46 (95.8)	
IgM level	Positive	0 (0)	0.74
	Negative	46 (95.8)	

According to the obvious relation between dopamine level and behavior, attention, motivation and sleep patterns, *T. gondii* can be effective in causing dopamine-related diseases like schizophrenia, Parkinson, and ADHD. Torrey *et al.* mentioned that *T. gondii* causes mental disorders and behavioral changes by the same mechanism, but the proving documents are controversial [19].

There are no prospective studies in which the researchers assess the individuals before and after getting infected by *T. gondii* for behavioral changes. However, it is obvious that behavioral changes induced by *T. gondii* result from its relation with dopamine level [20]. In previous assessments by Edrisian *et al.*, seropositivity of toxoplasmosis in the general population and different regions of Iran has a high prevalence. In the north of country 55%, in western regions 12.8 to 18.3%, in southern areas 9 to 49% and in Tehran and central districts 42 to 86% of prevalence have been reported that demonstrates a high prevalence in general population [21] which is in concordance with recently published meta-analysis by Daryani *et al.* [22]. However, in the present study, the majority of participants are Tehran residents and the prevalence of toxoplasmosis is 2.1% in children without ADHD, 4.2% in patients with ADHD and 3.1% for both groups. These results showed a significant difference with the previous studies on the general population of the country and can be an indicator of more exposure in remaining years of life as reported by Daryani *et al.* [22]. Also, this evident decreases in toxoplasmosis seropositivity may be because of general health improvement, increased the tendency for urban life and decrease of animal contact [21].

In the present study, there is no statistically

significant association between toxoplasmosis seropositivity, gender, and age in both case and control groups. In contrast, there is a highly significant difference between case and control groups for birth weight.

Comparing the different related variables such as birth time (term & preterm), infectious diseases in mothers during pregnancy, raw vegetable and meat consumption, contact with cat and animals, unrefined water consumption and positive family history for psychological diseases demonstrates no statistically significant difference between case and control groups. Assessing the children with congenital toxoplasmosis, Kern *et al.* concluded that the median score on sustained attention was in the 14th percentile in comparison with the anticipated group which had the average of 50th percentile based on DSM-IV test [23].

### Conclusion

Finally, there is no statistically significant difference between case and control groups for toxoplasmosis seropositivity, but low birth weight may be an indicator of affliction by ADHD in future. We suggest that in future research, more extend studies with a larger amount of individuals are needed. Also, by following the children with low birth weights in prospective studies, assessing the incidence of ADHD in them and comparing it with the children with normal birth weights, the relation between the ADHD and birth weight can be found in a more accurate way.

### Conflict of Interest

There are no conflicts of interest regarding the present manuscript.

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