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# Frequency of helminthes infection and iron deficiency in children with autism and its association with severity of symptoms in ASD

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**Abstract**

*Autism spectrum disorder (ASD) represents a group of disorders characterized by impairment in three developmental areas: social interaction, communication, and restricted and repetitive behaviors. Though the precise cause of autism has not yet been confirmed, but the experts suspect gene mutation, environmental pollution and other micro-nutrient deficiencies are the major factors fostering autism. In micro-nutrient deficiencies iron is one of them. High prevalence of iron deficiency anemia (IDA) was reported in children with ASD. In developing countries one of the major cause of iron deficiency anemia for children is helminthes infection. But for ASD children insufficient dietary iron intake was considered to be associated with food selectivity which is commonly seen in this*

*population. But negligence or stigma in ASD children for deworming are seen in our society. In Bangladesh the highest prevalence of A. lumbricoides (42.11%) was observed among the children aged 10 -12 years though deworming program has been running for the school going children round the year by Bangladesh government. For cognitive, behavioral, and motor development iron plays an important role. A reduction of iron levels in the brain may be accompanied by changes in serotonergic and dopaminergic systems, cortical networks, and myelination. In iron deficiency, learning, attention, memory, and psychomotor functions may be affected due to functional deficits in these biological processes. Thus, it can be considered that iron deficiency or anemia due to helminthes infection may increase the severity of symptoms of autism.*

***Materials and Methods:*** *This was a Case- Control study, 30 children were taken in each group and age range were 1 to 12 years. Random sampling method was used. ASD children were selected from out-patient department of Institute of Paediatric Neurodisorder and Autism (IPNA) Bangabandhu Sheikh Mujib Medical University (BSMMU), where the patients regularly visited for diagnosis, assessment and management. On the other hand same number of controlled children were selected with age group 1-12 years from randomly selected regular schools in Dhaka city. After selecting cases and controls, sample of blood and stools were collected and examine for detecting helminthes infection. If any group were found with helminthes infection then associate it with blood haemoglobin level. If the ASD children had iron deficiency (anemia) then again associate it with their symptoms of severity using Autism Diagnostic Check List (ADCL).*

***Result:*** *The result showed that selected ASD children had no ova count in their stool sample, but still they had low level of Hemoglobin in their blood sample (60% ). On the other hand blood Ferritin level is normal in most of them (76.7%). In case of Non-ASD children (16.7%) had ova in their stool sample and most of them had low level (70%) hemoglobin in their blood sample with normal blood Ferritin (86.7%) level. In this study Helminths infestation or blood hemoglobin level was not associated with Autism severity (P-value .25).*

***Conclusion:*** *Because of presence of low level of hemoglobin in blood sample of ASD and Non-ASD children it would be necessary to*

*find out the causes.So many more research will be helpful to find out the cause.*

**Key words:** Autism Spectrum Disorder, Helminthes infection, Iron deficiency anemia, Symptoms of Autism

## INTRODUCTION

Autism spectrum disorder (ASD) is defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*[10] as a persistent impairment in social interaction and communication across multiple contexts that presents in early development that causes clinically significant social, educational, and occupational deficits. Autism affects information processing in the brain by altering the way nerve cells and their synapses connect and organize. However how does this occur is not well understood.[11]The first appearance of autism starts during infancy or childhood, and generally follows a steady course without remission.[12] Overt symptoms gradually begin after the age of six months, become established by age two or three years,[13]and tend to continue through adulthood, although often in more muted form.[14] It is distinguished not by a single symptom, but by a characteristic triad of symptoms. Other aspects, such as atypical eating, are also common although not essential for the diagnosis. [15] Autism also implies difficulties in learning societal and linguistic skill apart from excessively following repetitive routines and behaviors. For example, a person with autism may have an obsession with a certain topic, such as airplanes, and have high-energy temper tantrums. A person with autism may also have problems making eye contact, or may show he or she is happy by spinning around instead of smiling[16]. Autism has three defining core features: (1) Problems with social interactions; (2) Impaired verbal and nonverbal communication and (3) A pattern of repetitive behavior with narrow, restricted interests.[17]

The cause of autism has not yet been confirmed, but the experts suspect gene mutation, environmental pollution and other micro-nutrient deficiencies are the major factors fostering autism. In micro-nutrient deficiencies iron is one of them. High prevalence of

iron deficiency anemia (IDA) was reported in children with ASD[4-6].In developing countries one of the major cause of iron deficiency anemia for children is helminthes infection. But for ASD children insufficient dietary iron intake was considered to be associated with food selectivity which is commonly seen in this population[3]. But negligence or stigma for deworming these children are commonly seen in our society.

The prevalence of intestinal helminth parasites such as *Ascaris lumbricoides* and *Trichuris trichiura* are major public health concern both in rural and urban areas reported that 64% of the children of the country suffered from intestinal parasitic infection[7]. In this perspective highest prevalence of *A. lumbricoides* (42.11%) was observed among the children aged 10 -12 years[7] though deworming program has been running for the school going children round the year by Bangladesh government. The Government of Bangladesh is increasing its focus on the disease in the country. The Ministry of Health & Family Welfare (MOHFW) has expanded its targets for deworming from treating children from 5-11 years up to 16 years as part of their expanded efforts to eliminate the health effects of intestinal worm infections nationwide.[18]

For cognitive, behavioral, and motor development iron plays an important role[3,4]. In case of reduced iron levels in the brain may be accompanied by changes in serotonergic and dopaminergic systems, cortical networks, and myelination[10]. In iron deficiency, learning, attention, memory, and psychomotor functions may be affected due to functional deficits in these biological processes [4]. On the other hand, it is discussed that healthy children could be receiving sufficient stimulus and developing new skills [11]. Thus, it can be considered that iron deficiency anemia due to helminthes infection may increase the severity of symptoms of autism.

## RATIONALE FOR THE STUDY

There are so many activities are going on for deworming of the children in Bangladesh. But still now prevalence of helminthes infection is higher. On the other hand awareness of autism in Bangladesh is not covered countrywide. So it is important to see the population with autism have included or not in this deworming

program. This study was fill up the gap by knowing the frequency of infection among them. There is a strong connection between symptoms of autism and iron deficiency anemia. For cognitive, behavioral, and motor development iron plays an important role[3,4]. A reduction of iron levels in the brain may be accompanied by changes in central nervous system [10]. In iron deficiency, learning, attention, memory, and psychomotor functions may be affected due to functional deficits in these biological processes [4]. In developing country like Bangladesh, iron deficiency anemia which will be occurred by helminthes infection could affect the nervous system of the children with ASD as well as intelligence capacity.

## OBJECTIVE OF THE STUDY

General objective was observed the frequency of helminthes infection and presence of anemia among ASD and non-ASD children with its association on symptoms severity of autism. The specific Objectives were seeing frequency of helminthes infection of the children with autism and normal healthy children, seeing presence of helminthes infection mediated iron deficiency anemia present or not among them,doing association between helminthes infection mediated iron deficiency anemia and symptoms severity of autism and measuring nutritional status of both groups if helminthes infection present or not.

## STUDY METHODOLOGY

It was a Case-control study. This study was conducted from May, 2019 to October, 2019 after getting the Research grant and approval of IRB of Bangabandhu Sheikh Mujib Medical University (BSMMU). Children with autism were taken as cases from OPD of Institute of Paediatric Neurodisorder and Autism (IPNA), BSMMU, where the patients regularly visited for diagnosis, assessment and management of different neuro-developmental disorders. On the other hand same number of controls were taken with age group 1-12 years from randomly selected schools of Dhaka city for normal healthy children.

## QUESTIONNAIRE DESIGN

Semi-structured questionnaire used for demographic and anthropometric data collection. For helminthes infection, stool report was included in questionnaire. For detecting anaemia and autism severity, results of Blood report and ADCL (Autism Diagnostic Check List) reports were also included in the questionnaire.

## STUDY PROCEDURE:

The case group were 30 in number and selected from the children (age range 2-12 years) come to outpatient department of IPNA, BSMMU who had confirmed diagnosis of Autism (by DSM-5) with or without comorbidities. On the other hand control group was also 30 in number and selected from randomly selected schools for normal healthy children from Dhaka city with same age group with no psychological problem detected previously, unrelated to an individual with autism (not a brother, sister, parent, aunt, or uncle). After selecting cases and controls consent were taken in a consent paper, specimen of stool and blood were collected to see helminthes infection and presence of Anemia. For BMI calculation height and weight of both groups were recorded in questionnaire.

## STATISTICAL ANALYSIS:

To analyze the data Statistical Package for Social Science (SPSS) version 21.0 was used. After entry, range and consistency were checked. Statistical analysis was done by using descriptive statistics. Continuous variables was present as mean values ± standard deviation (SD), and categorical variables was present as percentages. For data appropriateness significance test $x^2$ tests were done to compare proportions and $p<0.05$ was considered as statistical significance. Logistic regression techniques to identify predictors; odds ratios (ORs) and 95% CIs were calculated.

## RESULT

Demographic Characteristics of ASD participants:
Table 1. presents information on age group (in year) of ASD participant. About 56.7 percent participant were 5-8 years (#17), Male children were more 86.7 percent (#26), most of the mother's hadn't completed graduation (#18), Parents monthly income mostly 20,000 to 39,000taka, their housing status was mostly rented house, Father of the participants were mostly servie holder and mother were mostly house wife. Most of th ASD child was Healthy (#14), on their blood report Hemoglobin level less than normal and Ferritin level was normal limit.

| Baseline characteristics | | N(%) (N=30) |
|---|---|---|
| Children's age group | 1-4 yrs | 12 (40) |
| | 5-8 yrs | 17 (56.7) |
| | 9-12 yrs | 1 (3.3) |
| Children's sex | Male | 26 (86.7) |
| | Female | 4 (13.3) |
| Mother's education | Below Graduation | 18 (60) |
| | Above Graduation | 12 (40) |
| Family monthly income | <20,000 taka | 8 (26.7) |
| | 20,000-39,000 taka | 11 (36.7) |
| | 40,000 & above | 11 (36.6) |
| House status | Rental house | 17(56.7) |
| Father occupation | Service Holder | 20(66.7) |
| Mother occupation | House wife | 21(70) |
| BMI | Healthy | 14(46.7) |
| Hb level | Less than normal | 18(60) |
| Ferritin level | Normal | 23(76.7) |

**Table-1: Demographic Characteristics of ASD participant (n=30)**

Table 2 presents information on age group (in year) of Non-ASD participant. About 66.7 percent participant were 5-8 years (#20), Male children were more 56.7 percent (#17), most of the mother's had secondary education(#11), Parents monthly income mostly 20,000 to 39,000taka, their housing status was mostly rented house, Father of the participants were mostly service holder and mother were mostly house wife. Most of the Non-ASD child was Healthy (#17), on their

blood report Hemoglobin level less than normal and Ferritin level was normal limit.

| Baseline characteristics | | N(%) (N=30) |
|---|---|---|
| Children's age group | 1-4 yrs | 5 (16.7) |
| | 5-8 yrs | 20(66.7) |
| | 9-12 yrs | 5 (16.7) |
| Children's sex | Male | 17 (56.7) |
| | Female | 13(43.3) |
| Mother's education | Secondary | 11 (36.7) |
| Family monthly income | <20,000 taka | 6 (20.0) |
| | 20,000-39,000 taka | 18 (60.0) |
| | 40,000 & above | 6 (20) |
| House status | Rental house | 25(83.3) |
| Father occupation | Service Holder | 18(60) |
| Mother occupation | House wife | 27(90) |
| BMI | Healthy | 17(56.7) |
| Hb level | Less than normal | 21(70) |
| Ferritin level | Normal | 26(86.7) |

**Table-2: Demographic Characteristics of Non-ASD participant (n=30)**

Table 3. shows that both groups had taken anti-helminthes drug more.

| **Helminthes drugs** | **Percent (#)** |
|---|---|
| Drug taken (ASD participants) | 60(18) |
| No drug taken (ASD participants) | 40(12) |
| Drug taken (Non-ASD participants) | 56.7(17) |
| No drug taken (Non-ASD participants) | 43.3(13) |

**Table-3: Helminthes drug ingestion of participants**

Table 4. Shows that no ova present in stool sample of ASD children, but only (#5) sample had ova in stool sample of Non-ASD children.

| **Ova count in Stool** | **Percent (#)** |
|---|---|
| No ova (ASD participants) | 30 (100) |
| Ova present (ASD participants) | 0(0) |
| No ova (Non-ASD participants) | 25(83.3) |
| Ova present (Non-ASD participants) | 5(16.7) |

**Table-2.4: Ova count of participants**

In Table 5 Association present with Autism severity and helminthes drug ingestion, hemoglobin level and blood ferritin level of ASD participants.

| Autism severity | Helminthes drug ingestion | | P-value |
|---|---|---|---|
| | Drug taken | No drug | |
| Low level of Autism | 10 | 6 | .52 |
| Mild level of Autism | 8 | 6 | |
| | Hemoglobin level in blood | | |
| Low level of Autism | 5 | 11 | .25 |
| Mild level of Autism | 7 | 7 | |
| | Blood Ferritin level | | |
| Low level of Autism | 10 | 6 | .06 |
| Mild level of Autism | 13 | 1 | |

**Table-2.5: Anti-helminthes drug ingestion with Autism severity, Hemoglobin level and Blood Ferritin level of ASD participants**

In Table 6 No association present in Non-ASD group also.

| | Anti-helminthes drug | Normal level | Less than normal level | P-value |
|---|---|---|---|---|
| Hemoglobin level | Drug taken | 5 | 12 | .62 |
| | No drug taken | 4 | 9 | |
| Blood Ferritin level | Drug taken | 16 | 1 | .20 |
| | No drug taken | 10 | 3 | |

**Table-6: Anti-helminthes drug ingestion, Hemoglobin level and Blood Ferritin level of Non-ASD participants**

## DISCUSSION

This study aimed to assess frequency of helminthes infection and presence of anemia among ASD and non-ASD children with its association on symptoms severity of autism. About 56.7 percent participant were 5-8 years (#17), Male children were more 86.7 percent (#26), most of the mother's hadn't completed graduation (#18), Parents monthly income mostly 20,000 to 39,000taka, their housing status was mostly rented house, Father of the participants were mostly servie holder and mother were mostly house wife. Most of th ASD child was Healthy (#14), on their blood report Hemoglobin level less than normal and Ferritin level was normal limit. About 66.7 percent participant were 5-8 years (#20), Male children were more 56.7 percent (#17), most of the mother's had secondary education(#11), Parents monthly income mostly 20,000 to 39,000taka, their housing status was mostly rented house, Father of the participants were

mostly service holder and mother were mostly house wife. Most of the Non-ASD child was Healthy (#17), on their blood report Hemoglobin level less than normal and Ferritin level was normal limit. Both groups had taken anti-helminthes drug more. No ova present in stool sample of ASD children, but only (#5) sample had ova in stool sample of Non-ASD children. Association present with Autism severity and helminthes drug ingestion, hemoglobin level and blood ferritin level of ASD participants. No association present in Non-ASD group also.

## CONCLUSION

The result showed that selected ASD children had no ova count in their stool sample, but still they had low level of Hemoglobin in their blood sample (60% ). On the other hand blood Ferritin level is normal in most of them (76.7%). In case of Non-ASD children (16.7%) had ova in their stool sample and most of them had low level (70%) hemoglobin in their blood sample with normal blood Ferritin (86.7%) level. In this study Helminths infestation or blood hemoglobin level was not associated with Autism severity (P-value .25). Because of presence of low level of hemoglobin in blood sample of ASD and Non-ASD children it would be necessary to find out the causes. So many more research will be helpful to find out the cause

### Ethical Consideration

The purpose and procedure of the study were properly explained to the parents of ASD children and or their guardian and informed written consent was taken. The study was not involving any additional burden to the patients. All participants in a research study had a right to have the information they provide to be kept confidential. Additionally, in order to conduct a research study, it was imperative to consider any harm that might occur to participants. Furthermore, the purpose of the study was clearly indicated to participants prior to the study being conducted. An informed consent section was included as the first page of the study.

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