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# MATERNAL CONDITIONS AND INFECTIONS DURING PREGNANCY IN AUTISM SPECTRUM DISORDERS, KHARTOUM SUDAN 2019

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**Abstract**— BACKGROUND: Autism spectrum disorder (ASD) is a developmental disability characterized by social and communication impairments as well as a limited interests and repetitive behaviors, about 1 in 59 children has been diagnosed with ASD. OBJECTIVE: To study maternal infection and other characteristics during pregnancy and its link to autism spectrum disorders in Khartoum locality, Sudan. METHODS: A descriptive cross-sectional study, were parents and guardians of children with ASD were enrolled, the data was collected via an interview by the researcher with a semi-structured questionnaire that was based on previous studies then was modified to meet the objectives of this study. RESULTS: The study included 123 child diagnosed with ASD, 31.7% were males and 68.3% were females, Of all the participants` mothers 64.9% had a significant maternal condition such as diabetes 43.0% and 13.0% had Placenta praevia. 73.2% of the participants' mothers were not hospitalized during pregnancy, and 65.9% did not use antibitotics during pregnancy. Infections during pregnancy were rare, where 82.9% did not suffer a bacterial nor Viral 95.1%. 41.4% delivered by a Caesarean section and 18.6%, emergency CS. CONCLUSION: Our results suggests that DM and CS are risk factors for ASD, also it suggesst that bacterial infections, viral infec-tions, or use of antibiotics during pregnancy are strong risk factors for ASD. The few positive findings are possible con-cidence findings.

**Index Terms**—Antibiotic use, ASD, Autism Spectrum Disorders, Delivery, Hospitalization, Labour, Maternal Infection, Pregnancy.

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## 1 INTRODUCTION

Autism spectrum disorder (ASD) is a developmental disability characterized by social and communication impairments as well as a limited interests and repetitive behaviors [1]. According to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network about 1 in 59 children has been diagnosed with ASD [2]. The first studies of the prevalence of autism were published in the 1960s when autism was believed to be a severe illness, usually accompanied by intellectual disabilities [3]. Autism was first distinguished as a unique clinical diagnosis in 1980 by the American Psychiatric Association in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) [4].

While genetic susceptibility certainly causes autism etiology in many cases [5] non-genetic factors are likely play a role as well, multiple etiological pathways increase the risk for ASD. For example, many monogenic syndromes and other rare de novo variants have been identified to have high penetrance for ASD [6],[7],[8],[9],[10] with theoretically many others that have yet to be discovered [11], ASD are also associated with prenatal exposure to a variety of infectious agents [1],[13],[14],[15] The diversity of potential infectious triggers suggests that activation of maternal immunity, is likely to have a role in the genesis of neuro-developmental consequences [16].

The literature have observed higher levels of inflammatory cytokines in amniotic fluid [17] or maternal mid-gestational serum [18]. Maternal responses to infection for example the timing of fever episodes relative to fetal brain development and measures to alleviate the fever, may influence risk of ASD [19],[20].

Factor known to alter early fetal brain development and increase the risk for ASD is maternal infection during pregnancy [21],[22][,[23],[24],[25],[26],[27], Specifically cases of autism following congenital cytomegalovirus, perinatal herpes simplex virus, and congenital rubella infections have been reported [28],[29],[30],[31]. Gestational exposure to measles, rubella, and mumps and postnatal exposure to mumps and varicella were associated with higher autism risk in a large epidemiologic study [32]. Fever is the main presenting symptoms for these infections, and such fever during pregnancy is supposedly linked to ASD, most recent studies stated that maternal fever during pregnancy has been linked to increased risk of ASD [33].

Another described risk factors arising during the prenatal period are maternal diabetes [34], [35] and preeclampsia [35], [36], [37]; and for the perinatal period, preterm birth [38], [39], [40], [41], [42], low birth weight [38], [43], [44], intra-uterine growth retardation [36], [38]. Despite these suggestions of ASD occurring; a study found it problematic to decisively identify specific factor or risk whether in perinatal or neonatal period that increases the risk of ASD [45].

## 2 PROBLEM STATEMENT

One in every 59 child has been diagnosed with ASD. Fever is the main presenting symptoms for these infections, and such fever during pregnancy is supposedly linked to ASD, are infections during pregnancy linked to ASD?

## 3 OBJECTIVES

### 3.1 General Objective

To study maternal infection and other characteristics during pregnancy and its link to autism spectrum disorders in Khartoum locality, Sudan.
Specifically we wanted to assess the link between history of gestational infection and ASD, and to study some of the maternal characteristics.

## 4 METHODS

### 4.1 Ethics

Ethical clearance was obtained from the Ministry of Health Research Ethical committee.
The protocol, aims and benefits of the study were explained for all the participants in the study, and a written voluntary informed consent was obtained from each.

### 4.2 Population

The study enrolled parents and guardians of children who were 5 years or younger and suffering from ASD. According to Intitute administration there were (180) Child with ASD enrolled at the time of the study. Using the modified Cochran Formula for small populations sample calculation: n= n0 / 1+ ((n0-1)/N). Where n0= Recommended Sample size (384)* and N= Population. n0 = 384/ (1+ (384/180) = 123. The sampling procedure was systematic sampling, with sampling interval of 3. Where a participant was selected after every 2 names were encountered

### 4.3 Procedure and Analysis

The data was collected during the study period between March and July 2019 from the institution by the researcher, the data collection. Data was collected via an interview by the researcher with a semi-structured questionnaire that was based on previous studies then was modified to meet the objectives of this study.

The analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 25.0, SPSS Inc. Chicago, IL. The frequency distributions for independent variable and dependent variable was generated.

## 5 RESULTS

The study included 123 child diagnosed with ASD, 31.7% were males and 68.3% were females, Of all the participants` mothers 64.9% had a significant maternal condition (Table 1) 43.0% had diabetes, 13.0% had Placenta praevia (PP), 6.5% had Asthma, 2.4% had Pregnancy hypertension, and 2.4% had

more than one condition.

TABLE 1
MATERNAL CONDITIONS

| Maternal conditions | F | % |
|---|---|---|
| Maternal diabetes | 53 | 43.0 |
| Pregnancy hypertension | 3 | 2.4 |
| Asthma | 8 | 6.5 |
| Placenta praevia | 16 | 13.0 |
| Placenta Abruptio | 0 | 0 |
| More than one condition | 3 | 2.4 |
| **Total** | **80** | **67.3** |

Most of the participants mothers did not have an infection during pregnancy, neither Bacterial 82.9% nor Viral 95.1%, 12.2% had a bacterial infection the third trimester and 4.9% had one in the second trimester, the viral infection rate in each of the first and second trimesters was 2.4% (Figure 1).
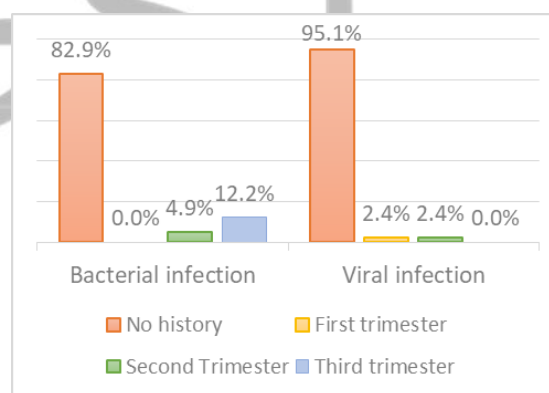


FIGURE 1
INFECTIONS IN PREGNANCY

As for the Hospitalization and antibiotic use (Figure 2); 73.2% of the participants' mothers was not hospitalized during pregnancy, 12.2% reported hospitalization during second trimester, 7.3% reported for both first and third trimester.
Antibiotic during pregnancy was used by 17.1% during second trimester, 9.8% in third trimester and 7.3% in first trimester, and was not used by 65.9% at all during pregnancy (Firgure 2).
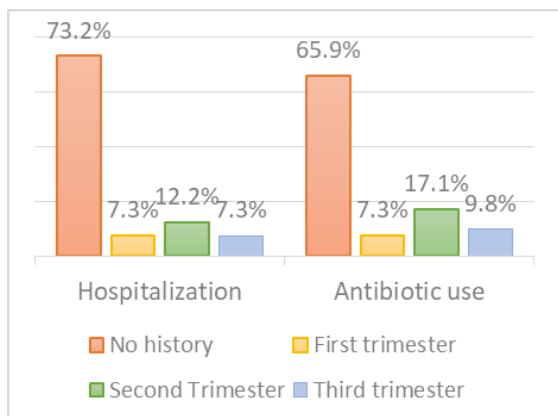
As for the condition of delivery (Tabe 2); elective Caesarean section (CS) compromised 41.4% of all labour and deliver conditions, followed by Preterm delivery at 21.1%, then emergency CS 18.6%, and 4.8% had Forceps use to assist in delivery.

### TABLE 2
#### DELIVERY CONDITIONS

| Labour and Delivery | F | % |
|---|---|---|
| Preterm | 26 | 21.1 |
| PROM/Spontaneous | 6 | 4.8 |
| Forceps use | 6 | 4.8 |
| Vacuum use | 0 | 0 |
| Elective CS | 51 | 41.4 |
| Emergency CS | 23 | 18.6 |
| Breech | 0 | 0 |
| **Total** | **112** | **90.7%** |

## 6 DISCUSSION

The aim of this study was to describe some of the maternal infection and other characteristics dur-ing pregnancy and labour, The aim of this study was to describe some of the maternal infection and other characteristics dur-ing pregnancy and labour, maternal diabetes was most abundant, in the study participants, almost half of the study participants mothers suffered from diabetes, and although the degree of control during pregnancy was not explored in tis study, studies suggested the connection between maternal diabetes and ASD [46], It was also suggested that exposure to maternal GDM was associated with risk of ASD for the child [47].

Preeclampsia has been examined as a risk factor for ASD in multiple investigations with mixed results for example a meta-analysis [48] of 17 studies suggested substantial unexplained het-

erogeneity of effect estimates and also population-based, case-control studies [49],[50],[51] reported statistically significant increased adjusted odds of ASD after pregnancies complicated by preeclampsia. However in this study the percentage of maternal hypertension was low which is more likely due to coincidence

Findings also suggest that other maternal conditions in pregnancy such as asthma is not likely associated with increased risk of ASD agreeing with another study [52].

In this study infections; both bacterial and viral were not prevalent in pregnancy nor was hospital admission, in a previous study also no overall association between diagnoses of any maternal infection during pregnancy whether viral or bacterial was associated with ASD However, women with infections diagnosed during a hospital admission, mainly bacterial infections were at increased risk of delivering a child with ASD. And multiple infections during pregnancy were associated with ASD [53], our results do not suggest that use of antibiotics during pregnancy is strong risk factors for ASD similar to another study [54].

Delivery conditions were not momentous  except for CS, which risk is agreed upon with previous findings that stated children born by CS (elective or emergency) are approximately 20% more likely to be diagnosed as having ASD, considering the reason behind choosing this mode of delivery is probably the actual risk factor [55],[56].

## 7 CONCLUSION

Our results suggests that DM and CS are risk factors for ASD, also it suggesst that bacterial infections, viral infections, or use of antibiotics during pregnancy are strong risk factors for ASD. The few positive findings are possible concidence findings.

## 8 RECOMMENDATIONS

The recommendations from this study is to carry out educational campaigns for the community about the risk of developing ASD. And to conduct further research exploring these factors in a larger population in various regions of the country, and comparing the risk factors in pregnant ladies who give birth to healthy children.

### END SECTIONS

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