Suhana Singh; Neonate Outcome from Mothers with Brain-Reactive Antibodies; Biomedical Health and Sciences

a. **RATIONALE**:

The possibility that autoimmune mechanisms are a contributing factor in Autism Spectrum Disorder (ASD) has been entertained for decades, ever since early studies proposed that autoimmune diseases are common in the family histories of individuals with ASD (Hughes, 2018). ASD is reported to affect 1 in 67 live births in the United States and there has been a dramatic increase in the prevalence of ASD; the Centers for Disease Control and Prevention report a 78% increase in ASD prevalence between 2002 and 2008 (Itzchak, 2011). Studies have found that antinuclear antibody (ANA) and anti-brain antibody (Ab) levels are elevated in mothers who have children with ASD (Brimberg, 2013). This is consistent with the hypothesis that autoimmunity predisposes mothers to having brain-reactive antibodies and give birth to children with ASD (Brimberg, 2013). Anti-brain antibodies affecting the developing brain have been suggested to be the cause in a subset of Autism Spectrum Disorders. Maternal autoantibodies cross the placenta and enter the fetal brain, leading to alterations (Fox-Edmiston, 2015). Previous studies show autoreactivity presence in mothers who have rheumatoid arthritis and celiac disease. This gives the possibility of a relationship between maternal autoreactivity, autoantibody prevalence, and ASD (Brimberg, 2013). Due to the stark increase in the number of childbearing women with autoimmune diseases, there is a growing interest to study the relationship between maternal disease, pregnancy, and the development of offspring (Itzchak, 2012). Since mothers who have autoimmune diseases harbor autoimmune mechanisms such as ANA and ABA, there is a strong reason to study the effects of maternal autoreactivity on neonate outcome.

If there is a significant difference in the gestational characteristics – such as head circumference, birth weight and gestational age- of the offspring of mothers who have high antibody levels, then there is a link between maternal autoreactivity and neonatal outcome. If these characteristics align with the common characteristics of children with ASD, then future studies should focus on the degree to which maternal autoreactivity influences autistic-like characteristics in a neonate and if/ the measure that these autistic-like characteristics correlate with the onset of ASD.

b. **RESEARCH QUESTION(S), HYPOTHESIS(ES), ENGINEERING GOAL(S), EXPECTED OUTCOMES**:

I. Research Question: Does the presence of maternal anti-nuclear antibodies and anti-brain antibodies affect a offspring's gestational age, birth weight and head circumference?

II. Hypothesis: I hypothesize that autoreactive mothers, mothers who test positive for harboring antinuclear and anti-brain antibodies, have offspring with significantly lower head circumference, birth weight and gestational age measures.

III. Engineering Goals: Not Applicable

IV. Expected Outcomes: I expect to accurately compare, using statistical techniques, head circumference, birth weight, and prematurity of the offspring of mothers with autoreactivity (with maternal anti-brain antibodies and/or anti-nuclear antibodies (ANA) exposed) to those mothers who do not have autoreactivity (unexposed). I expect to successfully conduct the student two-tailed (unpaired) t-test and analysis of variance (ANOVA) assay and get a quantitative value that alludes to significance in order to successfully fulfill my objective.

V. This is based on the rationale above because if there are significant differences found in the characteristics of offspring of mothers with and without the presence of antibodies, and the autoreactive mothers had offspring with lower values for their neonatal

characteristics, then this aligns with the possibility of a relationship between maternal autoreactivity, autoantibody prevalence, and ASD. Additionally, this would align with the hypothesis that maternal autoreactivity poses an effect on neonate outcome.

c. Procedures**:**

I will conduct both descriptive and statistical analyses. Data will be transferred from REDCap, the informational technology data source that Generation ECHO used to store their data, to Microsoft Excel and then SPSS software to perform necessary data analyses. Descriptive statistics will be performed to describe the maternal and neonatal cohort. The neonatal cohort's demographics, prematurity, NICU stay and Apgar score will be described. The maternal cohort's ANA and ABA prevalence will be described. ANA and ABA values will be coded into discrete levels representing their presence in a mother's blood based on the Ab value and then separated into just 2 discrete values (+ or -) for statistical analysis. The Student unpaired t-test will be performed to determine whether there was a significant difference between the 1 minute and 5 minute postpartum health of the neonate, which is depicted by their Apgar score. Mean and sd values for each neonatal outcome will also be determined with respect to the sex of the neonate.

Statistic analyses will also be conducted. The Mann–Whitney test will be performed to establish the level of significance between sex of the neonate and each of the respective neonatal outcomes. The sd and mean of the four neonatal outcomes per ANA and per ABA exposure will be measured. Analysis of variance (ANOVA) will then be performed to determine whether there is a significant difference between the offspring of mothers harboring either the ANA or the ABA. All tests will be two- tailed and values ≤ 0.05 will be considered statistically significant.

Risk and Safety: Not Applicable

Data analysis: Refer to project "procedures"

Bibliography:

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1. Humans participants research: not applicable
2. Vertebrate animal research: not applicable
3. Potentially hazardous biological agents research: not applicable
4. Hazardous chemicals, activities and devices: not applicable

Post Research Summary: No changes made