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Research Paper

FOETAL AND MATERNAL SERUM IMMUNOGLOBULINS LEVELS: A COMPARATIVE STUDY BETWEEN MOTHERS WITH GESTATIONAL DIABETES AND HEALTHY MOTHERS

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Abstract

Immunoglobulins are protective substances produced in the body to fight infections. Diabetes is a condition that poses several complications to mother and foetus. This study seeks to determine and compare the serum levels of Immunoglobulin G (IgG), Immunoglobulin M (IgM) and Immunoglobulin A (IgA) levels in mothers and foetuses in both mothers with gestational diabetes and healthy mothers. 16 women were recruited from the antenatal clinic and with their consent, the research was carried out using both primary and secondary data. The primary data was gotten by invasively collecting their blood samples while the secondary data was gotten through their antenatal case notes. Six pregnant women with gestational diabetes who were classified using American Diabetes Association (ADA) criteria for 75g, 2h- OGTT were included in the study and ten healthy pregnant women were also used as control. Results showed that maternal IgA and IgM were higher than foetal IgA and IgM in both diabetic and healthy mothers. Foetal IgG was higher than maternal IgG in both cases. IgG levels in fetuses of diabetic mothers was higher than that of healthy mothers. This study therefore suggests that IgG is transported across the placenta from mother to fetuses while the other immunoglobulins are not and that hyperglycemia may increase IgG transport.

Key words: Immunoglobulin G, Immunoglobulin A, Immunoglobulin M, Gestational Diabetes, foetal, maternal.

INTRODUCTION

Immunoglobulins are gamma globulins called antibodies produced by B-lymphocytes and plasma cells which have a primary function of protecting the body against infectious agents.

There are five antibody types which are known as IgA, IgD, IgE, IgG and Ig M.[1] Antibodies are transferred across the placenta from mother to foetus during pregnancy. Immunogobulin G is the only antibody that is transferred across the placental barrier to the foetus. This process of transfer begins during the second trimester of pregnancy and is maximal during the third trimester of pregnancy.[2][3] Fetal IgG serum concentrations has been found to be equal to the maternal values by the thirty-third week of gestation while IgA and IgM were infrequently found in fetal serum[4]. The maternal contribution of IgG to the human infant depends upon several factor, topmost of which are placental function, length of gestation, birth weight, and serum IgG concentration in the mother [5] Diabetes is a chronic disease of impaired blood sugar regulation occurring either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces leading to hyperglycemia when uncontrolled and many complications can arise . A pregnant woman may be diabetic before pregnancy or the onset of diabetes may be first noticed during pregnancy in which case it is referred to as gestational diabetes [6]. Gestational diabetes has been said to develop in over 10% of non-diabetic pregnant women and occurs late in second and third trimesters of pregnancy [7]. There are some complications that accompany diabetes mellitus such as increased cases of miscarriages, macrosomia, congenital malformations and even perinatal death [8]. In uncontrolled diabetes, there is hyperglycemia , a state of elevated blood sugar and this hyperglycemia has been said to alter IgG transfer from mother to foetus and decrease immunoglobulin levels in maternal blood[9].This study seeks to determine and compare the levels of IgG, IgM and IgA in mothers and foetuses in both gestational diabetic and healthy mothers.

MATERIALS AND METHODS

The research design for this study is experimental prospective research design. The research was conducted at the University of Port-Harcourt Teaching Hospital. Approval for the study was gotten from the University Human Anatomy department and the

Department of Obstetrics and Gynaecology, University of Port-Harcourt Teaching Hospital.

16 women were recruited from the antenatal clinic and with their consent, the research was carried out using both primary and secondary data. The primary data was gotten by invasively collecting their blood samples while the secondary data was gotten through their antenatal case notes. Six pregnant women with gestational diabetes who were classified using American Diabetes Association (ADA) criteria for 75g, 2h- OGTT were were included in the study while Patients with comorbidities and other diseases like human immune viruses (HIV), pre-eclampsia, hypertension and cardiovascular diseases were excluded from the study. Ten pregnant women who had no history of diabetes were taken as control.

Blood Collection

About 5ml of blood was collected from the antecubital vein of the women seated comfortably on a bed or chair. The blood collected was transferred to an anticoagulant bottle appropriately labelled. The same volume of blood was collected from the umbilical cord with a 5ml syringe and needle. The blood sampled were centrifuged to get the sample for each of the sera. The sera obtained were stored at -20 degree centigrade until they were ready for immunoglobulin assay. All assays were done within two weeks of blood collection.

Assay of immunoglobulin level

Serum levels of immunoglobulin A (IgA) immunoglobulin G (IgG) and immunoglobulin M were determined on the withdrawn sample by the immunoturbidimetric assay method using a fully smart automated clinical chemistry analyzer, cromatest IgA, IgG and IgM kits.

Immunoturbidimetric method

Immunoturbidimetric method involves using photometric measurement of immune complexes between immunoglobulin of the antibodies and immunoglobulins present in the samples for determination of immunoglobulin concentration. Preparation of reagent was done using the standard start method: which involved dilution of a standard powder of reagent (SP-NORMOTROL-a lyophilized human based control serum) with

5ml of distilled water and the vial was allowed to stand for 30 minutes, and it was swirled occasionally. A calibration graph which estimates the different concentration of immunoglobulin levels is plotted. The concentration which was deduced by the multiplication of the standard factor of each immunoglobulin reagent by the standard concentration of each reagent is plotted against absorbance (produced from 6 constituted samples made of standard reagent which was diluted with NaCl in different ratios). Then, 0.5ul of the serum samples were pipetted into appropriately labelled test tubes and 350ul of the IgA and IgG reagent. For IgM testing 0.5ul of blood serum was pipetted into a test tube and 500ul are mixed. The mixtures which are done in different test tubes are prewarmed for 2 minutes in the well-calibrated analyzer. With each individual reagent specifications used for the production of absorbance that is corresponding absorbance was read with the use of the appropriate calibration formed for each reagent. Diluent bottles were filled with distilled water.

The assay procedure was programmed fully on the smart chemistry analyzer using multi-standard programs method and test identification was entered for IgA, IgG, and IgM. Assay conditions were set accordingly: 340nm for IgM and IgA, and 540nm for IgG, 37^0C temperature, cuvette light path of 1.0cm and absorbance range of 0-0.25A. Calibrations were made at manufacturer's specifications for automated chemistry analyzer.

Data analysis

Statistical Package of Social Sciences (SPSS) was used to analyze the data. The results are expressed as mean and standard deviation. T-test is used here to determine the statistical significant differences in the immunoglobulin levels in the diabetic pregnant and healthy pregnant women. Analysis are conducted here at 95% confidence level.

III RESULTS

Table 3.1: Comparison of mean difference in measured parameters of healthy (H-M) and diabetic mothers (D-M)

Variable	Healthy Mothers (H-M; N=10) Mean±S.D	Gestational Diabetic Mothers (GD-M; N=6) Mean±S.D
Maternal IgA	101.40±39.44	182.00±14.81
Foetal Ig A	28.20 ± 34.92	10.67±3.72
Maternal IgG	825.00±106.91	949.00±132.45
Foetal IgG	963±132.33	1071±170.69
Maternal IgM	63.90±22.27	82.17±21.41
Foetal IgM	22.14±8.02	15.00±5.44

Note: Ig=Immunoglobulin

S.D= Standard Deviation, N= Distribution,

Table 3.2: Comparison of mean difference in measured parameters of healthy and gestational diabetic mothers

Variable	M.D *(HM – GD-M)*	t-value	p-value	Inf.
Maternal IgA	-80.600	-5.815	<0.001	S
Maternal IgG	-124.000	1.938	0.073	NS
Maternal IgM	-18.267	-1.610	0.130	NS
Foetal IgA	17.533	1.573	0.149	NS
Foetal IgG	-108.667	-1.430	0.175	NS
Foetal IgM	7.140	1.919	0.076	NS

Note: Ig= Immunoglobulin, BW= Birth weight

M.D= Mean difference, S.D= Standard Deviation, N= Distribution, Min= Minimum, Max= Maximum, Inf=Inference (S=Significant, NS=Not Significant), M.D (HM – D-M) = Mean difference between healthy and diabetic mothers

HBP-M= Hypertensive mothers, H-W=Healthy mothers, S.D=Standard deviation, N=Distribution

DISCUSSION

The result of the study showed that levels of IgG, IgA and IgM were higher in gestational diabetic pregnant women than in healthy pregnant women. Increased levels of IgG in mothers with gestational diabetes is in keeping with a study carried out by Guo et al, adults with diabetes showed higher levels of IgA than healthy adults however their study showed lower levels of IgG and IgM [10]. A study carried out by Mazer et al has also shown impaired humoral immune response with lowered levels of IgG, IgA nd IgM in diabetics which is not in keeping with our study [11].This may be because the study participants were cases of gestational diabetes with onset of diabetes being within the pregnancy. This implies that the picture of immunoglobulins is not the same as in chronic cases of diabetes seen in the study of Mazer and Guo.

The mean difference in immunoglobulin levels in gestational diabetic and healthy mothers was not significant except that of immunoglobulin A which was significantly higher in gestational diabetic than non diabetic mothers.

Maternal IgA and IgM were higher than foetal IgA and IgM suggesting that IgA and IgM were not transported across the placenta during pregnancy. However, foetal IgG was higher than maternal IgG suggesting that IgG was transported across the placenta from mother to foetus during pregnancy. This is in keeping with a study where when human placenta was studied for the binding of IgG, IgE and IgM to the cell membrane of the trophoblast, IgG was the only immunoglobulin observed on the syncytial cytotrophoblastic cell membrane and basement membrane, and in the cytoplasm and the nucleus in all stages of gestation [12].

Immunoglobulin G levels in foetuses of diabetic mothers was higher than that of non diabetic mothers . This suggest that IgG transport across the placenta is higher in gestational diabetic mothers than in pregnancies of healthy mothers.This may also be due to the explanation given from the study by Eduardo et al (2012) in which immunoglobulin G levels were higher in cord blood than in maternal blood for hyperglycaemic mothers and suggests that hyperglycemia may increase IgG transport .

CONCLUSION

This study suggests that Ig G is transported across the placenta from mother to foetus and that IgA and Ig M are not transported across the placenta from mother to foetus and that gestational diabetes may increase Ig G transport across the placenta. This study was limited as it did not take into consideration mothers who had chronic Type 2 diabetes before the pregnancy. Further studies should consider the effect of long standing diabetes on Immunoglobulin levels.

REFERENCE

1. Naik, P., 2012. Plasma proteins and Immunoglobulins. Essentials of Biochemistry. Jaypee brothers Medical Publishers, pp 62-69
2. Simister,N. E., 2003, Plancental Transport of immunoglobulin G, *vaccine,* 21(24), pp 3365-3369.
3. Costa, B. T., Carneiro-Sampaio, M. M., Sole, D., Naspitz, L. E. and Sorensen, R. U.,1999,Transplacental Transmission of Serotype-Specific Pneumococcal Antibodies in a Brazilian Population, *Clinical and Diagnostic Laboratory Immunology,* 6(1): 50-54**.**
4. Gusdon, J.P., 2016, Foetal and maternal Immunoglobulin levels during pregnancy, American Journal of Obstetrics and Gynaecology, 103(7), pp 895-900
5. Chandra, R.K., 1976, Levels of IgG subclasses, IgA, IgM and Tetanus antitoxin in paired maternal and foetal sera: findings in healthy pregnancy and placental insufficiency Materno-foetal Transmission of Immunoglobulins, The proceedings of a symposium on Transmission of Immunoglobulins from mother to young. W.A. Hemmings, Cambridge University Press, pp 77-85.
6. World Health Organization, 2020. https://www.who.int/news-room/fact-sheets/detail/diabetes. Accessed on 9/05/2020
7. Balsells, M., Garcia-Patterson, G. I. and Corcoy, R., 2009, Maternal and fetal outcome in woman with type 2 versus type 1 diabetes mellitus: A systematic review and meta-analysis. *Journal of clinical Endocrinology and Metabolism,* 94, pp 4284-4291**.**
8. Evers I.M., de Valk H.W and Visser G.H., 2004, Risk of complications of pregnancy in women with Type 1 diabetes: Nationwide prospective study in Netherlands, British Medical Journal, 328(7445), pp 915

9. Eduardo, L.F., Iracema de Mattos, Paranhos C., Elisa L.V. and Glilciane M., 2012, Transfer of Maternal Immunity to Newborns of Diabetic Mothers, Journal of Immunology Research, 928187.
10. Guo X et al.,2016, Serum levels of Immunoglobulin in an adult population and their relationship with Type 2 Diabetes, Diabetes Res Clin Pract, 115, pp 76-82
11. Mazer N.A, Welbourn D., Bernstein R.K. and Rubinstein A., 2011, Immunoglobulin Deficiency in Patients with Diabetes Mellitus, The Journal of Allergy and Clinical Immunology, 127(2)
12. Dimmette J.E., 1976, Studies of human pregnancy I, Immunoglobulins attatched to the trophoblast, Obstetrics and Gynecology,47(6), pp 730-732