Original Article

Thyroid autoimmunity and early pregnancy loss in Jos, Nigeria

Joseph T Samson, Jonathan A Karshima, Victor C Pam, Lucius C Imoh[1], Elizabeth A Ande, Patrick H Daru

Departments of Obstetrics and Gynaecology and [1]Chemical Pathology, Jos University Teaching Hospital, Jos, Nigeria

ABSTRACT

Background: Early pregnancy loss is a challenging experience for both the patient and the physician; it is unfortunately a common complication of human gestation. Early pregnancy loss is defined as the termination of pregnancy before 20 weeks of gestation or with a fetal weight of <500 g. Immunological disorders have been attributed to early pregnancy loss in addition to chromosomal abnormalities. Thyroid autoimmunity is one of the immunological causes of early pregnancy loss that has been poorly studied in sub-Saharan Africa.

Objective: This study was aimed at determining the relationship between early pregnancy loss and thyroid autoimmunity in Jos, North-Central Nigeria.

Patients and Methods: This was a case-control study involving 44 women with a current history of miscarriage at an average gestational age of 11.57 ± 4.3 weeks (cases) and 44 pregnant women with previous history of delivery with no history of miscarriage(s) at a mean gestational age of 17.9 ± 4.9 weeks (controls). Serum thyroglobulin antibody (TgAb) and thyroid peroxidase antibody (TPOAb) were assayed by Electro-chemiluminescence immunoassay (ECLIA) using Cobas e411 auto analyzer (by Roche). The data obtained were analyzed using SPSS version 16.0.

Results: TgAb was neither present in the cases nor in the control group. The prevalence for TPOAb was 11.4% for the cases and 4.5% for the controls. The difference in proportion was not statistically significant ($P = 0.434$).

Conclusion: There was no statistically significant relationship between thyroid autoimmunity and early pregnancy loss.

Key words: Autoimmunity; pregnancy loss; thyroid.

Introduction

Early pregnancy loss is a difficult situation for both the patient and physician; unfortunately, it is a common complication of human gestation. Up to three-quarters of fertilized ova and about 15% of clinically recognized pregnancies end as miscarriages.[1,2] Majority of spontaneous pregnancy losses occur early, with approximately half occurring before or just after a missed period[3] whereas the rest occur before 10 completed weeks of gestation; in both situations, chromosomal abnormalities are the most common causes.[2]

Early pregnancy loss is defined as the termination of pregnancy before 20 weeks of gestation or with a fetal weight of <500 g.[4] This definition excludes ectopic and molar pregnancies. Considering the fact that the exact cause (s) of early pregnancy loss is not known in over half of the cases,[5] this has become a topic of consideration by researchers.

Apart from idiopathic early pregnancy loss, several etiological reasons have been proposed. Immunological disorders are a known cause of early pregnancy loss. These include rheumatoid arthritis, systemic lupus erythematosus, type-1

Address for correspondence: Dr. Joseph T Samson, Department of Obstetrics and Gynaecology, Jos University Teaching Hospital, Jos, Nigeria.
E-mail: drsamjoe@yahoo.com

Access this article online	
Website: www.tjogonline.com	Quick Response Code
DOI: 10.4103/TJOG.TJOG_64_17	

How to cite this article: Samson JT, Karshima JA, Pam VC, Imoh LC, Ande EA, Daru PH. Thyroid autoimmunity and early pregnancy loss in Jos, Nigeria. Trop J Obstet Gynaecol 2018;35:44-8.

diabetes mellitus, antiphospholipid antibody syndrome (APS), and thyroid disorders among others. Thyroid autoimmunity in pregnancy is associated with increased rates of miscarriage, preeclampsia, placental abruption, growth restriction, prematurity, and stillbirths.[6] The presence of thyroid autoantibodies is relatively common in women of reproductive age.[7] In an "unselected" population of women, the prevalence ranges from 6% to 20%,[8] and it is higher in women with a history of recurrent pregnancy loss from 17 to 33%,[9-11] and in women with a history of sub-fertility from 10 to 31%.[12–14]

In industrialized nations, thyroid autoimmunity is the main cause of hypothyroidism, which itself results in poor obstetric outcomes. Even in women with biochemically normal thyroid function, the studies have reported an association between the presence of thyroid autoantibodies, particularly thyroid peroxidase antibodies, and adverse pregnancy outcomes, including miscarriage, preterm birth, and adverse neurodevelopmental sequele in children.[15–18]

In Nigeria, hypothyroidism is relatively common mainly in Plateau state, north-central Nigeria.[19,20] Although most of the cases of hypothyroidism have been attributed to iodine deficiency, little is known about the role of thyroid antibodies in thyroid dysfunction and pregnancy outcomes in Nigerian women.[21–23] Considering that thyroid antibody testing is not routinely available in developing countries and only a few studies have measured thyroid antibodies in Africans,[21,24,25] this study was designed to examine the association between thyroid antibodies and pregnancy loss in Nigerian women.

Materials and Methods

This study was carried out between March 2015 and September 2015. The study population comprised all consenting pregnant women presenting with a history of spontaneous early pregnancy loss (≤20 weeks). The control group comprised consenting pregnant women (≤24 weeks) with at least one successful pregnancy and no history of miscarriages who presented for routine antenatal care (ANC).

The study recruited 44 cases and 44 controls. A structured questionnaire was administered and blood sample was collected for thyroid antibody screening for both cases and controls. A sample of 5 ml of blood was collected into a plain vacutainer tube. The collected sera were stored at −20°C before analysis.

Thyroglobulin antibody (TgAb) and thyroid peroxidase antibody (TPOAb) were assayed by Electro-Chemiluminescence Immuno Assay (ECLIA) using Cobas e411 auto analyzer (by Roche). Significant antibody titre for TPOAb and TgAb were derived from the kits manufacturers' reference values for pregnant women in the second trimester.[26]

Quality control was assured by proper calibration of the auto-analyzer and running commercial controls at two levels (supplied by kits manufacturers). The control values were within the prescribed limits.

All statistical analyses were performed using SPSS software (version 16.0). Frequencies and percentages were computed for sociodemographic characteristics of the cases and controls. The relationship between presence of thyroid autoantibodies and early pregnancy loss was tested using Chi-square and odds-ratio. A P value of <0.05 was considered as statistically significant.

Ethical clearance was obtained from the appropriate Ethical Committee and consent was also obtained from the participants before they were enrolled in the study.

Results

A total of 88 participants (44 cases and 44 controls) were involved in this study. The sociodemographic characteristics of women that participated in the study are shown in Table 1. The cases and control groups were comparable in terms of maternal age. The mean age of women that comprised the cases was 29.3 ± 5.0 years and the control group was 29.1 ± 5.2 years. The overall mean age was 29.2 ± 5.1 years. A total of 52% of cases and 57% of controls were below age 30 years.

The mean gestational age of presentation was 11.6 ± 4.3 weeks for the cases whereas the controls presented at an average gestational age of 17.9 ± 4.9 weeks. The combined average gestational age at presentation for both the cases and the controls was 14.7 ± 4.5 weeks.

The mean parity was 1.9 ± 1.6 and 1.9 ± 1.2 for the cases and the controls, respectively, with an overall mean parity of 1.9 ± 1.4 for both groups. Both maternal age and parity in both cases and the control groups were comparable.

Anthropometric and clinical characteristics as summarized in Table 2 showed that the average maternal weight was 63.5 ± 16.2 kg for the cases and 69.1 ± 8.1 kg for the controls. The controls significantly had higher mean weight than the cases ($P = 0.043$). The mean weight for both groups was 66.3 ± 13.0 kg.

From Table 2, the height and systolic and diastolic blood pressures were comparable in both cases and controls. The

mean height was 1.61 ± 0.06 m for the cases, 1.58 ± 0.06 m for the control with an overall mean height of 1.6 ± 0.05 m for both groups. Blood pressure pattern was within normal range for all participants, as shown in Table 2 below.

In Table 3, overall average of TgAb and TPOAb were higher among the controls than cases; however, the observed differences were not significant ($P = 0.673$ and $P = 0.450$ for TgAb and TPOAb, respectively).

Two different cutoff values were used to determine significant titer of TgAb as shown in Table 4. The kit manufacturer[26] proposed a cutoff value of 116 IU/mL for pregnant population (second trimester), whereas the study-derived reference interval using the control in this study was 43 IU/mL (corresponding to the 95th percentile). Using the cutoff value of 116 IU/mL, none of the cases and controls were found to have a significant antibody titer. However, using the cutoff value of 43 IU/mL, none of the cases had a significant titer, but in 2 (4.5%) of the controls, not withstanding, this was not statistically significant ($P = 0.494$).

Table 1: Demographic characteristics of subjects

Variable	Cases *n*=44(%)	Control *n*=44(%)	Total *n*=88(%)
Age group (years)			
<30	23 (52.3)	25 (56.8)	48 (54.5)
30+	21 (47.7)	19 (43.2)	40 (45.5)
Mean±SD	29.3±5.0	29.1±5.2	29.2±5.1
Parity			
0	8 (18.1)	0 (0.0)	8 (9.1)
1	16 (36.4)	21 (47.7)	37 (42.0)
2-4	16 (36.4)	21 (47.7)	37 (42.0)
5+	4 (9.1)	2 (4.5)	6 (6.8)
Mean±SD	1.9±1.6	1.9±1.2	1.9±1.4
Gestation age (weeks)			
≤10	23 (52.3)	4 (9.1)	27 (30.7)
11-20	20 (45.5)	28 (63.6)	48 (54.5)
>20	1 (2.3)	12 (27.3)	13 (14.8)
Mean±SD	11.6±4.3	17.9±4.9	14.7±4.5

Table 2: Anthropometric and clinical characteristics

Variable	Cases	Control	Overall	*t*-test	*P*
Weight (kg)	63.5±16.2	69.1±8.1	66.3±13.0	2.054	0.043
Height (m)	1.61±0.06	1.58±0.06	1.6±0.05	2.928	0.004
SBP (mmHg)	115.6±12.4	111.7±14.9	113.6±13.8	1.330	0.187
DBP (mmHg)	73.8±9.9	68.8±11.5	71.3±10.9	2.181	0.032

Table 3: Chemical characteristics

Variable	Cases IU/mL	Control IU/mL	Overall IU/mL	*t*-test	*P*
TgAb	20.4±6.8	21.2±8.7	20.8±7.7	0.423	0.673
TPOAb	38. 1±9.6	39.4±6.5	38.7±8.2	0.759	0.450

Also, two different cutoff values were used to determine significant titer of TPOAb as shown in Table 5. The kit manufacturer[26] has a value of 51 IU/mL, whereas the study-derived reference interval using the control in this study was 54 IU/mL (corresponding to the 95th percentile). Using both cutoff values of 51 IU/mL[26] and 54 IU/mL, 5 (11.4%) of the cases and 2 (4.5%) of the controls had significant antibody titer. However, this disparity in TPOAb is not statistically significant ($P = 0.434$).

Discussion

For now, there is no agreed cutoff value for thyroid autoantibodies; this could be the basis for differences in the studies on the subject matter.[21] In this study, two different cutoff values were used to determine significant levels of TgAb and TPOAb. Cutoff values for TgAb were 116 IU/ml from the manufacturer's manual[26] and 43 IU/ml as the derived upper reference limit from the control group of the study population (corresponding to the 95th percentile).

The study-derived cutoff value was much lower than the quoted values from the manufacturer, which was derived from largely Caucasian population. Although there was no significant difference between the prevalence of autoimmunity among cases and controls at the different cutoff values, no significant autoimmunity was found among cases and controls with the manufacturer's cutoff, whereas 4.5% of controls had significant TgAb titre with the study-derived cutoff values; this was found not to be statistically significant ($P = 0.494$).

For TPOAb, cutoff values of 51 IU/ml from the manufacturer's manual[26] and 54 IU/ml as derived reference interval were comparable. In this study, using both the kit manufacturer's

Table 4: Thyroid autoimmunity based on different cutoffs of TgAb

Cut-off IU/mL	Cases		Control		Total		χ^2, *P*
	Autoimmunity		Autoimmunity		Autoimmunity		
	Yes	No	Yes	No	Yes	No	
116	0 (0.0)	44 (100.0)	0 (0.0)	44 (100.0)	0 (0.0)	88 (100.0)	0.494*
43	0 (0.0)	44 (100.0)	2 (4.5)	42 (95.5)	2 (2.3)	86 (97.7)	

Table 5: Thyroid autoimmunity based on different cutoffs of ATPO

Cut-off IU/mL	Cases *n*=44		Control *n*=44		Total *n*=88		χ^2, *P*
	Autoimmunity		Autoimmunity		Autoimmunity		
	Yes	No	Yes	No	Yes	No	
51	5 (11.4)	39 (88.6)	2 (4.5)	42 (95.5)	7 (8.0)	81 (92.0)	0.434*
54	5 (11.4)	39 (88.6)	2 (4.5)	42 (95.5)	7 (8.0)	81 (92.0)	0.434*

and study-derived cutoff, TPOAb autoimmunity was present in 2 (4.5%) of the controls and in 5 (11.4%) of the cases. Though TgAb prevalence was higher among the control group and a higher prevalence of TPOAb in the cases, these were found not to be statistically significant ($P = 0.434$). This study utilized ECLIA to analyze TPOAb and TgAb levels as against ELISA, which was the method in similar studies.[21–23] ECLIA has a higher sensitivity and precision when compared to ELISA.

From related studies in Nigeria, Okosieme *et al.*[23] found TPOAb in 7% and TgAb in 4% of the patients in a general endocrine clinic. From a population of normal pregnant women, El-Bashir *et al.*[22] noted TPOAb in 9% of the population whereas Kayode *et al.*[21] reported a TPOAb prevalence of 25% from another group of pregnant women. TPOAb prevalence is comparatively higher in these studies as against 4.5% from this study.

The findings from our study concerning the association between TPOAb or TgAb and pregnancy loss is similar to the reports of some earlier studies.[27–29] Esplin *et al.*[27] studied 74 non-pregnant women with a history of recurrent pregnancy loss and from 75 healthy, fertile control subjects of similar gravidity for thyroglobulin and thyroid peroxidase antibodies by means of radioimmunoassay kits. It was found that women with a history of recurrent pregnancy loss are no more likely than the fertile control subjects to have circulating thyroid autoantibodies.

Furthermore, Russworth *et al.*[28] concluded that the future risk of pregnancy loss in women with unexplained recurrent miscarriages is not affected by their thyroid antibody status. Kusum *et al.*[29] found that the prevalence of thyroid autoimmunity was higher in pregnant women with a history of recurrent abortion compared with healthy pregnant control population. There was no difference in the prevalence of miscarriage or obstetric outcomes between recurrent miscarriage and healthy pregnant women group irrespective of TPO status.

However, some studies have shown significant relationship between pregnancy loss and both thyroid autoimmunity and hypothyroidism.[30–33] The exact mechanism of an association of thyroid autoimmunity with miscarriage remains largely unknown; it is still a postulate of theories.

Although thyroid hormones and thyroid stimulating hormones (TSH) were not analyzed in this study, the similar thyroid antibodies between the case and control groups would suggest that any differences in frequency of hypothyroidism in these groups is unlikely to be related to thyroid antibodies. One cannot, however, rule out the role of other effects of hypothyroidism, including subclinical hypothyroidism, in the etiology of early pregnancy loss in our environment. The finding from this study has probably helped by leaving one question less among the several questions that have been asked regarding the role of thyroid antibodies and thyroid abnormalities in early pregnancy losses in our environment.

Conclusion

This study suggests that routine testing for thyroid autoantibodies is unlikely to be cost-effective in the evaluation of patients with pregnancy loss in our environment. Notwithstanding, this study might have been limited by its small sample size, hence the need to study a larger population of women.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Boklage CE. Survival probability of human conceptions from fertilization to term. Int J Fertil 1990;35:75, 79–94.
2. Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, *et al*. Incidence of early loss of pregnancy. N Engl J Med 1988;319:189–94.
3. Edmonds DK, Lindsay KS, Miller JF, Williamson E, Wood PJ. Early embryonic mortality in women. Fertil Steril 1982;38:447–53.
4. Preimplantation genetic testing: A Practice Committee opinion. Fertil Steril. 2007;88:1497-504.
5. Matalon ST, Blank M, Ornoy A, Shoenfeld Y. The association between anti-thyroid antibodies and pregnancy loss. Am J Reprod Immunol 2001;45:72–7.
6. Stagnaro-Green A, Glinoer D. Thyroid autoimmunity and the risk of miscarriage. Best Pract Res Clin Endocrinol Metab 2004;18:167–81.
7. Gilad T, Avi S, Howard Al, Yehuda S. Pathogenesis of infertility and recurrent pregnancy loss in thyroid autoimmunity. J Autoimmun 2012;38:275–81.
8. Poppe K, Velkeniers B, Glinoer D. The role of thyroid autoimmunity in fertility and pregnancy. Nat Clin Pract Endocrinol Metab 2008;4:394–405.
9. Bussen S, Steck T. Thyroid autoantibodies in euthyroid non-pregnant women with recurrent spontaneous abortions. Hum Reprod 1995;10:2938–40.
10. Kutteh WH, Yetman DL, Carr AC, Beck LA, Scott RT Jr. Increased prevalence of antithyroid antibodies identified in women with recurrent pregnancy loss but not in women undergoing assisted reproduction. Fertil Steril 1999;71:843–8.
11. Pratt D, Novotny M, Kaberlein G, Dudkiewicz A, Gleicher N. Antithyroid antibodies and the association with non-organ-specific antibodies in recurrent pregnancy loss. Am J Obstet Gynecol 1993;168:837–41.
12. Kim CH, Chae HD, Kang BM, Chang YS. Influence of antithyroid antibodies in euthyroid women on *in vitro* fertilization-embryo transfer outcome. Am J Reprod Immunol 1998;40:2–8.

13. Muller AF, Verhoeff A, Mantel MJ, Berghout A. Thyroid autoimmunity and abortion: A prospective study in women undergoing *in vitro* fertilization. Fertil Steril 1999;71:30–4.
14. Negro R, Formoso G, Coppola L, Presicce G, Mangieri T, Pezzarossa A, *et al*. Euthyroid women with autoimmune disease undergoing assisted reproduction technologies: The role of autoimmunity and thyroid function. J Endocrinol Invest 2007;30:3–8.
15. Glinoer D, Soto MF, Bourdoux P, Lejeune B, Delange F, Lemone M, *et al*. Pregnancy in patients with mild thyroid abnormalities: Maternal and neonatal repercussions. J Clin Endocrinol Metab 1991;73:421–7.
16. Glinoer D, Delange F. The potential repercussions of maternal, fetal, and neonatal hypothyroxinemia on the progeny. Thyroid 2000;10:871–7.
17. Andrea TB, Stanley MN, Carl LK, Eric MG. The implications of autoimmunity and pregnancy. J Autoimmun 2010;34:287–99.
18. Anthony PW. Immunity, thyroid function and pregnancy: Molecular mechanisms. Nat Rev Endocrinol 2010;6:311–8.
19. Das SC, Isichei UP. The fetomaternal thyroid function interrelationships in an iodine deficient region in Africa- the role of T3 in possible fetal defence. Acta Endocrinol 1993;128:116–9.
20. Das SC, Isichei UP, Egbuta J C, Banwo A I. Cations and anions in drinking water as putative contributory factors to endemic goiter in Plateau State, Nigeria. Trop Geogr Med 1989;4:346–52.
21. Kayode OO, Odeniyi IA, Iwuala S, Olopade OB, Fasanmade OA, Ohwovoriole AE. Thyroid autoimmunity in pregnant Nigerians. Indian J Endocr Metab 2015;19:620–4
22. El-Bashir JM, Abbiyesuku FM, Aliyu IS, Randawa AJ, Adamu R, Adamu S, *et al*. Prevalence of gestational thyroid disorders in Zaria, north-western Nigeria. Ann Nigerian Med 2015;9:51–5
23. Okosieme OE, Taylor RC, Ohwovoriole AC, Parkes AB, Lazarus JH. Prevalence of thyroid antibodies in Nigerian patients. Q J Med 2007;100:107–12.
24. Hawa MI, Picardi A, Costanza F, D'Avola D, Beretta Anguissola G, Guglielmi C, *et al*. Frequency of diabetes and thyroid autoantibodies in patients with autoimmune endocrine disease from Cameroon. Clin Immunol 2006;118:229–32.
25. Njemini R, Meyers I, Demanet C, Smitz J, Sosso M, Mets T. The prevalence of autoantibodies in an elderly sub-Saharan African population. Clin Exp Immunol 2002;127:99–106.
26. Hollowell JG, Staehling NW, Hannon WH, Flanders WD, Gunter EW, Spencer CA, *et al*. Serum thyrotropin, thyroxine and thyroid antibodies in the United States population (1988 to 1994): NHANES III. J Clin Endocrinol Metab 2002;87:489-99.
27. Esplin MS, Branch DW, Silver R, Stagnaro-Green A. Thyroid autoantibodies are not associated with recurrent pregnancy loss. Am J Obstet Gynecol 1998;179:1583–6.
28. Rushworth FH, Backos M, Rai R, Chilcott IT, Baxter N, Regan L. Prospective pregnancy outcome in untreated recurrent miscarriers with thyroid autoantibodies. Hum Reprod 2000;15:1637–9.
29. Lata K, Dutta P, Sridhar S, Rohilla M, Srinivasan A, Prashad GRV, *et al*. Thyroid autoimmunity and obstetric outcomes in women with recurrent miscarriage: A case–control study. Endocr Connect 2013;2:118–24.
30. Stagnaro-Green A, Roman SH, Cobin RH, el-Hazary E, Alvarez-Marfany M, Davies TF. Detection of at-risk pregnancy by means of highly sensitive assays for thyroid autoantibodies. JAMA 1990;264:1422–5.
31. Lejeune B, Grun JP, de Nayer P, Servais G, Glinoer D. Antithyroid antibodies underlying thyroid abnormalities and miscarriage or pregnancy induced hypertension. Br J Obstet Gynaecol 1993;100:669–72.
32. Glinoer D, Soto MF, Bourdoux P, Lejeune B, Delange F, Lemone M, *et al*. Pregnancy in patients with mild thyroid abnormalities: Maternal and neonatal repercussions. J Clin Endocrinol Metab 1991;73:421–7.
33. Pratt DE, Kaberlein G, Dudkiewicz A, Karande V, Gleincher N. The association of antithyroid antibodies in euthyroid nonpregnant women with recurrent first trimester abortions in the next pregnancy. Fertil Steril 1993;60:1001–5.