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Full Length Research Paper

Prevalence of Immune Antibodies against red cell among TB Patients in Sokoto, North Western Nigeria

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Abstract

Background: Tuberculosis (TB) poses significant challenges to developing economies as it primarily affects people during their most productive years. This study is intended to find out the prevalence of immune (IgG) antibodies against red cells among TB patients.
Materials and Method: Ninety tuberculosis patients were screened for the presence of IgG autoantibodies against red cells in their plasma. The age range was 18 to 80 years with mean age of 36.80±13.074 years. IgG autoantibodies presence was screened by Ortho Biovue system cassettes (AHG/Coombs) technique.
Results: The prevalence of IgG autoantibodies among TB patients was 11.1%; (10.0% for those on anti-TB drugs and 1.1% for those not on anti-TB drugs). The Odd Ratio for cohort IgG autoantibodies positive was 0.556. There was no statistical significant difference (*P* = 0.549) between anti-TB drugs and the prevalence of IgG autoantibodies. Age groups 21-30 and 31-40 years were found to have the highest prevalence of IgG autoantibodies among TB patients. There was however, no statistical significant difference between age groups and the formation of IgG autoantibodies (*P* = 0.753). The sociodemographic factor also indicates no statistical significant differences (*p*-values> 0.05). All TB patients with IgG autoantibodies were Hausa tribe. Married, business and illiterates had the highest prevalence (6.7% each), the males were most affected (8.9%) in this study.
Conclusion: The study revealed a high prevalence of IgG autoantibodies among tuberculosis patients with 90% of the prevalence among patients on anti-TB drugs.

Key words: Immune antibodies, red cell, Tuberculosis, Sokoto, Nigeria.

INTRODUCTION

The World Health Organization (WHO) declared Tuberculosis (TB) a global emergency in 1993 and it remains one of the world's major causes of illness and death (Nigeria TB Fact Sheet, 2012).It was estimated that one third of the world's population, two billion people, carry the TB bacteria and more than nine million of these Population become sick each year with active TB that can be spread to others (Nigeria TB Fact Sheet, 2012). TB poses significant challenges to developing economies as it primarily affects people during their most productive years especially in the developing countries with more than 90% of new TB cases and deaths (Nigeria TB Fact Sheet, 2012). Nigeria ranks 10th among the 22 high-burden TB countries in the world (Nigeria TB Fact Sheet, 2012),

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WHO estimates that 210,000 new cases of all forms of TB occurred in the country in 2010, equivalent to 133/100,000 Population, with 90,447 TB cases notified and 41, 416 (58%) cases as new smear positives, and a case detection rate of 40% (Nigeria TB Fact Sheet, 2012). There were an estimated 320,000 prevalent cases of TB in 2010, equivalent to 199/100,000 cases.

The introduction of the directly observed treatment short course (DOTs) for the treatment of tuberculosis by the World Health Organization (WHO) was adopted by Nigeria and guidelines for tuberculosis treatment regimens was developed and standardized by the federal ministry of health in 2008 (Guidelines for clinical management of TB and HIV/AIDS, 2008 Guidelines for clinical management of TB and HIV/AIDS, 2008). The treatment regimen consists of two phases; the initial intensive phase of fully supervised daily administration of drugs of 2 months for new cases (Category 1) and 3 months for re-treatment cases (Category 2) also called the short course. And the continuation phase of treatment for new cases of 6 months of monthly drug collection by the patient, and is usually self-administered. For retreatment cases, the continuation phase is 5 months which is supervised daily or thrice weekly (Guidelines for clinical management of TB and HIV/AIDS, 2008). The short course regimen includes two months intensive phase of four drugs namely rifampicin, isoniazid, pyrazinamide and ethambutol and six months continuation phase of two drugs namely Thiacetazone and Isoniazid for newly diagnosed smear positive tuberculosis patients (Jindani, Nunn and Enarson, 2004).

Although the therapeutic regimens are extremely effective, studies have shown that undesirable drug interactions can occur, so also can adverse reactions of varying degrees of severity occur (Blumberg,*et al.,* 2003). Many factors are reported to be responsible for the adverse reactions to anti-tuberculosis drugs, and the principal determinants of such reactions are said to be the dose and time of day at which the medication is administered, as well as patient age and nutritional status, together with the presence of preexisting diseases or dysfunctions, such as alcoholism, impaired liver function, impaired kidney function, and HIV coinfection (FUNASA/CRPHF/SBPT; 2002). Reports have indicated that if the adverse reactions are severe, the therapeutic regimen may change and may lead to the use of drugs that are less active and occasionally more toxic (Schaberg, *et al.,* (1996) and Javadi, *et al.,* 2007),substantially increasing treatment costs, as well as the number of home visits, outpatient visits, and hospitalizations (Yee, *et al.,* 2003). These reactions can lead patients to interrupt or abandon treatment (Olusoji, *et al.,* (2015) and Breen, *et al.,* 2006), resulting in higher rates of treatment failure and acquired resistance, as well as an increase in the number of tuberculosis cases (Shin, *et al.,* 2007) and, more rarely, in the number of deaths (Gholami, *et al.,* 2006).No information is available on the prevalence of IgG autoantibodies among TB patients, this study therefore, was aimed at determining the prevalence of IgG autoantibodies among TB patients in Sokoto, Nigeria.

Selection criteria

Ethical clearance was obtained from the ethical committee of the Specialist hospitals, Sokoto. While written informed consent was sought from all participants in this study. All consenting women in whom a red cell transfusion was indicated were eligible for recruitment into the study. And all non- consenting women and women in whom red cell transfusion was not indicated and male patients were excluded in the study.

MATERIALS AND METHOD

Three (3ml) milliliters of whole blood was collected from each patient into an EDTA anticoagulated tubes. The plasma was collected after centrifugation of the blood specimen and was used to screen for the presence IgG autoantibodies by Ortho Biovue system cassettes (AHG/Coombs) and screening cells technique. The manufacturer's instructions were strictly followed.

Data analysis

The data obtained were presented in tabular forms and in proportions and hypothesis was tested with statistical software (SPSS version 20) at 0.05 significant levels and 95% confidence using the Person Chi-square test.

RESULTS

Table 1 shows the prevalence of IgG autoantibodies among TB patients as11.1%; the prevalence of IgG autoantibodies for those on anti-TB drugs (rifampicin, isoniazid, pyrazinamide which is usually for the initial 2 or 3 months and ethambutol and thiacetazone taking for 6 or 5 months for newly diagnosed and relapse patients respectively) was 10.0% and for those not on anti-TB drugs was 1.1% giving a ratio of 9:1, while the ratio of patients on anti-TB drug to patients not on anti-TB drugs was 5:1. The Odd Ratio for cohort IgG autoantibodies positive was 0.556. The effect of anti-TB drugs on the formation of IgG autoantibodies however, showed no statistical significant difference (P = 0.549). Age groups 21-30 and 31-40 years appeared to have the highest prevalence of IgG autoantibodies among the TB patients. There was no statistical significant difference between age groups and the formation of IgG autoantibodies (P = 0.753) as can be seen in table 2. Table 3 is table for sociodemographic factors for gender, marital status,

Table 1. Medication status and the prevalence of IgG autoantibodies among TB patients

	IgG antibody (%)					
Medication Status	**Negative**	**Positive**	**Total (%)**	**X^2**	**df**	**p-value**
Not on TB Drugs	15.6	1.1	16.7	0.360	1	0.549
On TB Drugs	73.3	10.0	83.3			
Total	88.9	11.1	100.0			

The above table shows the prevalence of IgG autoantibodies among TB patients as11.1%. the prevalence of IgG autoantibodies for those on anti-TB drugs was 10.0% and for those not on anti-TB drugs was 1.1% giving a ratio of 9:1, while the ratio of patients on anti-TB drug to patients not on anti-TB drugs was 5:1. The effect of anti-TB drugs on the formation of IgG autoantibodies shows no statistical significant difference (P = 0.549). X^2 = critical value for Chi-square, df = degree of freedom.

Table 2. Prevalence of IgG autoantibodies status and age groups among TB patients

	IgG antibody (%)					
Age group	**Negative**	**Positive**	**Total (%)**	**X^2**	**df**	**p-value**
≤20 years	5.6	0.0	5.6	2.656	5	0.753
21-30 years	35.6	4.4	4.0			
41-50 years	15.6	1.1	16.7			
51-60 years	5.6	1.1	6.7			
≥61 years	5.6	0.0	5.6			
Total	88.9	11.1	100.0			

Age groups 21-30 and 31-40 years appeared to have the highest prevalence of IgG autoantibodies among the TB patients. There was no statistical significant difference between age groups and the formation of IgG autoantibodies (P = 0.753). X^2 = critical value for Chi-square, df = degree of freedom.

ethnicity, educational status and occupational status. It indicates *p*-value of 0.0380, 0.763, 0.296, 0.912 and 0.659 respectively. All the variances show no statistical significant differences. However, 100% of the TB patients that developed the IgG autoantibodies were of the Hausa ethnicity with the prevalence of 11.1%. The married, business and those with no formal education having the highest prevalence (6.7% each), the male folks being affected the worst (8.9%).

Discussion:

This study revealed the prevalence of IgG autoantibodies against red cell among TB patients to be 11.1%; those on anti-TB drugs as 10.0% and those not on anti-TB drugs as 1.1%. The effect of anti-TB drugs on the formation of IgG autoantibodies was however, found to have no statistical significant difference (P = 0.549). Drug administration has been reported to causes from 16 to 18 per cent of cases of acquired immune hemolytic anaemia (Blumberg,*et al.,* 2003). It was reported that Methyldopa therapy results in the formation of red cell autoantibodies in 10-20% of patients taking the drug for longer than 4 months (Petri, 2006); and they said that the red cell antibodies were true autoantibodies that are directed against an autoantigen on the red blood cell membrane and not against the drug or against a drug-altered antigen.

It was observed that the ratio of the prevalence of IgG autoantibodies against red cell among patients on anti-TB drugs (rifampicin, isoniazid, pyrazinamide and ethambutol for short course regimen and six months continuation phase of Thiacetazone and Isoniazid (Jindani, Nunn and Enarson, 2004) to patients not on anti-TB drugs as 9:1, while the ratio of patients on anti-TB drug to patients not on anti-TB drugs was 5:1. The Odd Ratio for cohort IgG autoantibodies positive was calculated as 0.556. The hematological and immunological symptoms like eosinophilia, neutropenia, thrombocytopenia, hemolytic anemia, increased serum levels of bilirubin, Fatigue, dizziness, headache, dyspnea and red colored urine which was reported to occur after anti-TB drugs administration (WHO; (2010),Marcos, *et al.,*(2010)Noor, *et al.,*(2006)and Boudhrea, et al., 2009), may not be unrelated to the IgG autoantibodies produced against red cell as a result of the anti-TB drugs. A report indicated that 72.1% of TB patients on anti-TB drugs developed dark urine as side effects while yellowish eyes accounted for 0.7% (Bello and Itiola, 2010). IgG autoantibodies can potentially destroy owns red cells to cause autoimmune haemolytic anaemia (AIHA). These autoantibodies can cause haemolytic disease of the foetus and newborn (HDFN) in a pregnant woman. According to a report,

Table 3. chi-square test for sociodemographic factors and the development of IgG autoantibody

	IgG antibody (%)					
	Negative	**Positive**	**Total (%)**	**X^2**	**df**	**p-value**
Gender						
Female	30	2.2	32.2			
Male	58.9	8.9	67.8			
Total	88.9	11.11	0.0	0.770	1	0.380
Marital Status						
Single	24.4	4.4	28.9			
Married	58.9	6.7	65.6			
Divorced	2.2	0.0	2.2			
Widowed	3.3	0.0	3.3			
Total	88.9	11.1	100.0	1159	3	0.763
Ethnicity						
Hausa	71.1	11.1	82.2			
Fulani	15.6	0.0	15.6			
Others	2.2	0.0	2.2			
Total	8.9	11.1	100.0	2432	2	0.296
Educational Status						
Non	57.8	6.7	61.4			
Primary	6.7	1.1	7.8			
Secondary	20.0	2.2	22.2			
Tertiary	4.4	1.1	5.6			
Total	88.9	11.1	100.0	0.531	3	0.912
Occupation						
Unemployed	23.3	1,1	24.4			
Farmer	17.8	3.3	21.1			
Business	46.7	6.7	53.3			
Civil Servant	1.1	0.0	1.1			
Total	88.9	11.1	100.0	1600	3	0.659

Table above is Chi square table for sociodemographic factors for gender, marital status, ethnicity, educational status and occupational status. It indicates *p*-value of 0.0380, 0.763, 0.296, 0.912 and 0.659 respectively. All the variances shows no statistical significant differences. However, 100% of the TB patients that developed the IgG autoantibodies were of the Hausa ethnicity with the prevalence of 11.1%. The married, business and those with no formal education having the highest prevalence (6.7% each), the male folks being affected the worst (8.9%). critical value for Chi-square, df = degree of freedom.

minor or mild adverse reactions in patients treated with DOTS did not result in immediate change in the standard regimen (Vieira and Gomes, 2008), however, major or severe adverse reactions was reported to led to the discontinuation or alteration of the treatment the report said.

The study also revealed that age groups 21-30 and 31-40 years had the highest prevalence of IgG autoantibodies among the TB patients. These age groups was reported to have the highest ant-TB drug adherence rate (Bello and Itiola, 2010), with no statistical significant difference though, may have accounted for the high prevalence of IgG autoantibodies in these groups. It was also reported that tuberculosis primarily affects people during their most productive years especially in the developing countries with more than 90% of new TB cases and deaths (Nigeria TB Fact Sheet, 2012).

The sociodemographic factors of gender, marital status, ethnicity, educational status and occupational status, had *p*-values of 0.380, 0.763, 0.296, 0.912 and 0.659 respectively, and they all showed no statistical significant differences. However, 100% of the TB patients

that developed the IgG autoantibodies were the Hausa tribe with prevalence of 11.1%. The married, business and those with no formal education having the highest prevalence (6.7% each) and the males among them were affected the worst (8.9%).

CONCLUSION

The study revealed a high prevalence of IgG autoantibodies among tuberculosis patients with 90% of the prevalence among the patients on anti-TB drugs, even though; there was no statistical significant difference.

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