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Interferon gamma Release Assay of Latent Tuberculosis infection amongst Prisoners in Anambra State

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Abstract
Background: *In populations subject to conferment, such as those in nursing homes, psychiatric hospitals and prisons, Tuberculosis constitutes a major public health problem. In Nigeria there is striking paucity of data on the prevalence of LTBI amongst the general populace especially prisoners. The essence of the screening is to achieve intensified case finding (ICT) and to treat. The treatment of latent tuberculosis infection (LTBI) is essential in controlling and eliminating TB by reducing the risk that TB infection will progress to disease. This is one step toward fulfilling TB partnership objectives which is to halt and reverse the increasing incidence of tuberculosis (TB) and halve the 1990 prevalence and mortality rates as soon as possible. While comparing the diagnostic values of the putative Tuberculin Skin Test (TST) and the new Interferon Gamma Release Assay (IGRA) in the diagnosis of latent tuberculosis amongst prisoner in Anambra state, the goal of this present study also determine if prolonged incarceration of these prisoners increases their chances of acquiring latent tuberculosis infection.*
Materials and Methods*: The new Interferon Gamma Release Assay(Tspot TB) and the putative Tuberculin Skin Test (Mantoux)were performed simultaneously on prisoners and non prisoners who agreed to participate in the study. A total of 240 prisoners were selected for inclusion in this study while 120 individuals from the general population (within the prison environment) were randomly selected to serve as control. Human Immuno-deficiency Virus(HIV) screening and Fasting Blood Sugar (FBS) were also done for all the participants to rule out HIV infection and Diabetes.*
Results: *Latent Tuberculosis Infection (LTBI) was high amongst the prisoners using both TST and IGRA in comparison to the control group and there was a discordance between the results of IGRA and TST ($p<0.05$). Age and longer duration of incarceration were significantly associated with LTBI in prisoners ($p<0.05$). There was no predisposition of either sex in acquiring LTBI($p>0.05$) .*
Conclusion*: There was a high prevalence of latent tuberculosis infection amongst prisoners in Anambra State which linearly increases with longer duration in prison. IGRA and TST diagnostic results were not concordant with each other but IGRA appears to be more specific than TST in diagnosing LTBI.*
Key words*: Prisoners, IGRA, TST, Latent Tuberculosis, Anambra State*

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I. Introduction

Tuberculosis constitutes a major public health problem. In prisons located in developing countries, Tuberculosis has been reported as the most common cause of death [1]. High levels of TB in prison population are likely to be attributed to the fact that a disproportionate number of prisoners are from population groups already at high risk of TB disease (for example, alcohol or drug users, homeless people, mentally ill individuals, former prisoners and illegal immigrants from area characterized by high prevalence [2]. Furthermore, the prison setting where segregation criteria are based on crime characteristic rather than on possible health concerns may facilitate transmission. In addition, overcrowding, late detection, inadequate treatment for infectious cases, high turnover of prisoners and poor implementation of TB infection control measures are all known factors contributing to transmission of Mycobacterium tuberculosis [3].

Primary infection with *Mycobacterium tuberculosis* leads to clinical disease only in a few individuals. In the remaining cases, the ensuring immune response arrest further growth of *Mycobacterium tuberculosis*. However, the pathogen is completely eradicated in only about 10% of the infected population, while the

remaining 90% only succeeds in containment of infection as some bacilli escape killing by blunting the microbicidal mechanism of immune cells and remain in non-replicating (dormant or latent) stage in old lessons [4]. The bulk of this disease burden resides in sub-saharan Africa and the majorities of these infections are asymptomatic and may reactivate later in life. Of these latently infected individuals, 5-10% will develop acute disease during their life time, while the rest will contributes an important source of infection and a continuous source of transmission [5].

Currently, a golden standard for the diagnosis of the LTBI is lacking. A test with greater accuracy and convenience would greatly enhance tuberculosis control efforts [6]. Tests with high sensitivity and specificity characteristics for detecting *Mycobacterium tuberculosis* infection could facilitate tuberculosis control on both fronts. A sensitive test would facilitate screening of people who would benefit from closer evaluation for infectious disease or treatment to prevent it from developing. Due to the small amount of *Mycobacterium tuberculosis* in LTBI patients, diagnosis of LTBI mainly depends on the immune reaction of the host rather than the bacteria itself. There are two currently available screening tests for LTBI: the long established tuberculin skin test (TST) and the newly released interferon gamma release assays (IGRAs) which include the QuantiFERON-TB Gold and the T-SPOT TB test.

These new blood assays to detect M. tuberculosis infection are based on the response of antigen-specific memory T-cells releasing interferon-gamma (IFN-γ) in response to previously encountered mycobacterial antigens. Interferon-gamma release assays (IGRAs) measure the cellular immune responses to *Mycobacterium tuberculosis*-specific antigens, including early-secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10), antigens encoded in the region of difference (RD1) of the *Mycobacterium tuberculosis* genome. These proteins are absent from all strains of *Mycobacterium bovis* BCG and the vast majority of non-tuberculous mycobacteria (with the exception of *Mycobacterium kansasii, Mycobacterium szulgai*, and *Mycobacterium marinum*) but present in isolates of *Mycobacterium tuberculosis*. In comparison, the TST uses the mixed, nonspecific PPD, a culture filtrate of tubercle bacilli containing over 200 antigens, which results in its low specificity [7].

Two IGRA systems using RD1-encoded antigens are currently commercially available for TB detection. One system includes Quanti-FERON-TB Gold and its variant Quanti-FERON-TB Gold In-Tube (uses tubes pre-filled with antigens) (Cellestis, Victoria, Australia), which uses whole blood specimens, with an unknown number of leukocytes, to measure IFN-γ released by antigen-activated T lymphocytes. The other system is the T-SPOT.TB (Oxford Immunotec, Oxford, England). It uses the ELISPOT method, wherein the number of peripheral blood mononuclear cells (PBMC) in the assay is quantified, in order to measure IFN-γ-secreting T cell counts ("spots") on stimulation by *Mycobacterium tuberculosis*-specific antigens in microplate wells. The read out of the two tests is different: These new blood tests have an internal positive control, i.e., a sample well stimulated with a potent non-specific stimulator of IFN-γ production by T- cells. This controls the results of the test for technical errors, such as failure to add viable, functioning cells to the well. The failure of the positive control in the tests provides information that the test's results cannot be reliably interpreted since it may reflect an underlying in vivo immune suppression, negatively affecting T-cell function in the in vitro stimulation.

This study was undertaken to determine the prevalence and the factors associated with latent tuberculosis infection (LTBI) in Anambra State prisons. The essence of the screening is to achieve intensified case finding (ICT) and to treat. The treatment of latent tuberculosis infection (LTBI) is important in controlling and eliminating TB by reducing the risk that TB infection will progress to fulminant tuberculosis.

II. Materials and Methods

This is a controlled, epidemiological, diagnostic study of Latent Tuberculosis Infection (LTBI) amongst Prisoners in Anambra state of Nigeria using the new Interferon Gamma Release Assay (IGRA) in conjunction with the putative Tuberculin Skin Test (TST). This study conducted from February 2016 to April 2018 involved three correctional facilities chosen from the three senatorial zones in the state. A total of 360 adult individuals (both male and females) of aged ≥ 18 years were used for this study.

Study Design: This was a diagnostic cross sectional ,multi-prison study covering three prisons in each senatorial zones of Anambra State involving 240 prisoners and 120 non prisoners as the control.

Ethical considerations: Samples were collected from only participants who voluntarily gave informed consent and were able to submit themselves to blood sample collection for Interferon Gamma Release Assay(IGRA) and Tuberculin Skin Test (TST). This research was approved by the university ethical committee of Chukwuemeka Odumegwu Ojukwu University, Uli, Anambra state. Also the various prisons ethical committees gave their written approvals.

Study Location: This was a multi-prison study covering three prisons in each senatorial zones of Anambra State. Anambra State is situated within longitude 6^{o} 30′ E to longitude 7^{o} 10′ and latitude 6^{o} 15′ to 7^{o} 07′. It has a land mass of 4,416 sq.km spread across 21 local government areas. The State is bordered by Delta State to the

west, Imo State to the south, Enugu State to the east and Kogi State to the north. The State has a total estimated population of 4million people (2004 estimate). This was a multicenter study covering three general hospitals in Anambra State. The prisons were chosen from the three senatorial zones in the state. They were Onitsha prison representing Anambra North, Awka prison representing Anambra Central and Aguata prison which represented Anambra South. Each of these prisons has its own health centre and they are all integrated with the National Tuberculosis and Leprosy Control Program in provision of DOTs services.

Duration of study: February 2018 to November 2019

Sample size: 240 prisoners and 120 non prisoners

Sample size calculation: The target population from which we randomly selected our sample was considered 3500. We assumed that the confidence interval of 10% and confidence level of 95%. The sample size actually obtained for this study was 240 prisoners from all the prisons and 120 control participants. There was 3% drop out rate especially from the control participants.

Subjects & selection method: Interferon Gamma Release Assay(Tspot TB) and the putative Tuberculin skin test (Mantoux)were performed simultaneously on prisoners who agreed to participate in the study. A total of 240 prisoners were selected for inclusion in the study while 120 individuals from the general population (within the prison environment) were randomly selected to serve as control. Human Immuno-deficiency Virus (HIV) screening and Fasting Blood Sugar (FBS) were also done for all the participants to rule out HIV infection and Diabetes.

Inclusion criteria:

1. There must be informed consent by the participants which was obtained by filling a questionnaire containing vital information**.**
2 Participants must be from the correctional facilities used.
3 The controls must also be from the environment within the correctional facility.
4 Either sex.
5 Participants must be 18 years and above.

Exclusion criteria:

1. Pregnant women.
2. Patients with genetic disorders.
3. Patients with diabetes or HIV.
4. Participants who have evidence of active TB.
5. Those who had received chemoprophylaxis or TST within the last six months

5 Participants from the above risk groups that have a compounding risk factor (s) were also excluded

Procedure methodology

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited participants (inmates and non inmates). The questionnaire included socio-demographic characteristics such as age, gender, nationality, height, weight, physical activity and lifestyle habits like smoking and alcohol. Samples were collected from only participants who voluntarily gave informed consent and were able to submit themselves to blood sample collection for Interferon Gamma Release Assay(IGRA) and willing to present themselves twice for Tuberculin Skin Test (TST). This research was approved by the university ethical committee of Chukwuemeka Odumegwu Ojukwu University, Uli, Anambra state. Also the various prisons ethical committees gave their written approvals.

Specimen Analysis

HIV Screening: Each patient was screened for HIV 1/II according to the national algorithm [8].

Diabetes Screening; Point of Care Glucose Meter (Accu Chek Active) was used to screen the participants for diabetes. It was used according to manufacturers instruction [9].

Interferon Gamma Release Assay (T-Spot TB): The T-SPOT TB is the interferon gamma release assay used in this research work [10]

Step 1: Cell Isolation: Whole blood sample was collected into a lithium heparin tube and mixed thoroughly by inventing the tube 5 – to times. The tubes were centrifuged at 1800 relative centrifugal force (RCF) for 30 minutes at room temperature to isolate polymorph nuclear blood cells (PMBC).

Step 2: Washing and counting of cells: Cells were washed using a standard culture medium (AIM-V). The white cloudy band of PMBC was collected using a pipette and transferred to a 15 ml conical centrifuge tube. The volume was made up to 10 ml with cell culture medium and centrifuged at 600 RCF for 7 minutes. The supernatant was poured off and the pellets re-suspended in the medium. Centrifugation was repeated at 350 RCF for another 7 minutes after which the pellets were re-suspended in 0.7 ml cell culture medium. An

appropriate aliquot was placed unto a haemocytometer and the cells in the grid counted. After counting, the cells were diluted to 250,000 cells/100µl.

Step 3: Adding of antigens and controls: The T-SPOT-TB test requires 4 wells to be used for each patient's sample. A nil control and a positive control which were run with each individual sample. The samples were arranged vertically on the plate.

Nil control (AIM-V)
Panel A (ESAT -6)
Panel B (CFP- 10)
Positive control (PHA)

50 µl of AIM-V cell culture medium was added to each nil control well. 50 µl of positive control solution, 50 µl of ESAT-6 and 50 µl of CFP-10 were also added to the required wells. To each of the 4 wells used for a patient's sample, 100 µl of the patient's final cell suspension (containing 250, 000 cells) was added and the plate incubated in a humidified incubator at 37^0c with 5% co_2 for 18 hours.

Step 4: Adding of secondary antibody conjugate: The plates were removed from the incubator and the cell culture medium discarded by flicking the content into an appropriate container. 200 µl phosphate buffered saline (PBS) solution added to each well. The PBS was later discarded and the washing repeated 3 times. 50 µl working strength conjugate reagent solution added to each well and incubated at $2\text{-}8^{0c}$ for 1 hour.

Step 5: Adding of substrate solution: The conjugate was discarded and the wells washed four times with PBS solution. 50 µl substrate solution was added to each well and incubated at room temperature for 7 minutes. The plates were washed with distilled water to stop the reaction. The plates were allowed to dry by standing then in a well ventilated area.

Step 6: Reading of wells; The number of distinct, dark blue spots on the membrane of each well were counted and recorded.

Result interpretation and assay criteria; The test is positive if (panel A-Nil) and/ or (panel B-Nil) $\geq$ 8 spots. The test is negative if both (panel A-Nil) and (panel B-Nil) $\leq$ 4 spots.

Tuberculin Skin Test (TST): A tuberculin skin test was administered by the Mantoux method [10]. 0.1 ml of Purified Protein Derivative (PPD) was injected intra-cutaneously in the volar area of the fore arm. A water proof ink mark was drawn around the injection site so as to avoid difficulty especially when the level of induration was small. The reaction was read after 48-72 hours. The size of the reaction was determined by measurement of the induration (palpable, raised, hardened area or swelling).

The area of induration was measured transversely across the fore arm (left to right, not up and down) with a caliper and recorded to the nearest millimeter. A measurement equal to or more than 10 mm was considered positive for non HIV participants while measurement of 5mm or above was regarded as positive for HIV – positive participants.

Statistical analysis

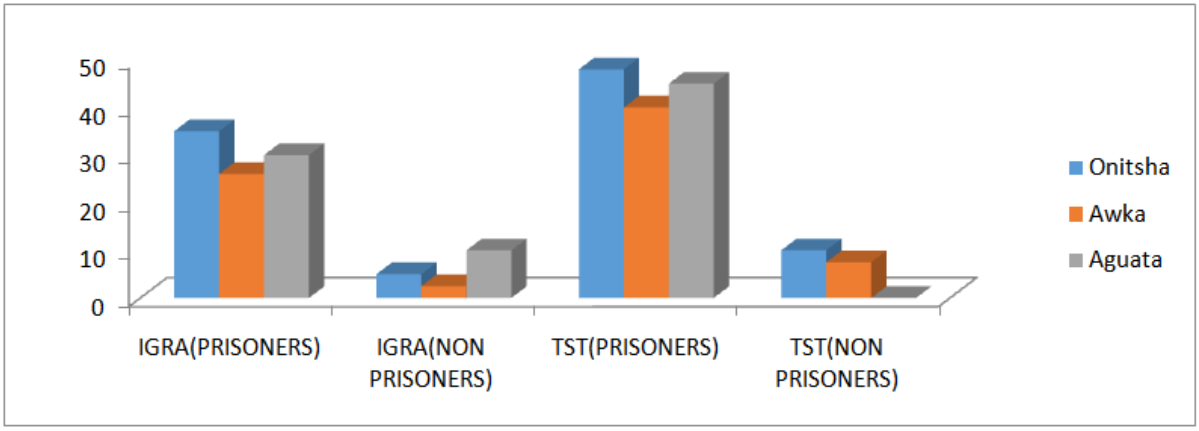
Epi Info version 6.1. was used to cross check the filing of the questionnaire, Data analysis was done with R Programming and SPSS version 22. Pearson chi – square was used to check for independence among study variables. Correlation between TST and IGRA was assessed with Spearman's correlation test. Statistical significance was accepted at $P<0.05$.

III. Result

The prevalence of Latent Tuberculosis Infection (LTBI) amongst the prisoners was 31% and 45% for IGRA and TST respectively and 5% and 7.5% for non inmates. There was a markedly significant difference between the results of both IGRA and TST from inmates and non inmates($p<0.05$). From table no 1 it can be seen that the highest number of positive LTBI was seen in Onitsha prison with 35% and 48% for IGRA and TST respectively, while non inmates had 5% and 10% also for IGRA and TST respectively. In the same above format Aguata Prison had the second highest prevalence with 30%: 45%, while its control had 10%: 0%. Awka prison had the lowest LTBI with 26%:40% for the inmates and 2.5%:7.5% for the non inmates (controls).

Table no1: Results obtained from the various prisons

Study site	Number Examined		% IGRA Positive(prisoners)	% IGRA Positive(control)	%TST Positive(prisoners)	%TST Positive (control)
	Prisoners	Control				
Onitsha prison	120	60	42(35)	3(5)	58(48)	6(10)
Awka prison	80	40	21(26)	1(2.5)	32(40)	3(7.5)
Aguata prison	40	20	12(30)	2(10)	18(45)	0(0)
Total	240	120	75(31)	6(5)	108(45)	9(7.5)



The records seen in table no2 shows that various categories of adult ages were incorporated in the study with prisoners > 61 years of age having the highest prevalence of 78% and 90% for IGRA and TST respectively while the control group in the same age category had 30% each for both IGRA and TST. Using the same above format, 51 – 60 age range came second with 36.5%:80%, its control group had 6.5%:8%. In decreasing order of prevalence there were 41 – 50 years with 32%:46%, its control had 4%:4%, 31 – 40 (28% : 39%, and 3.3%: 6.6% for the controls), 18 – 30 years (17.6%:38% and 0%:3% for its control). There was a statistically difference ($p<0.05$) in LTBI prevalence for ages > 50 years for both prisoners and non prisoners compared to ages <50 years for both cohorts. This means that risk of acquiring LTBI increases with age.

Table no 2 LTBI among the various age ranges

Age Group	Number Examined		% IGRA Positive(prisoners)	% IGRA Positive(control)	%TST Positive(prisoners)	%TST Positive (control)
	Prisoners	Control				
18- 30	34	30	6(17.6)	0(0)	13(38)	1(3.3)
31-40	75	30	21(28)	1(3.3)	29(39)	2(6.6)
41-50	81	25	26(32)	1(4)	37(46)	1(4)
51-60	41	25	15(36.5)	1(4)	20(80)	2(8)
>61	9	10	7(78)	3(30)	9(90)	3(30)
TOTAL	240	120	75 (31)	6(5)	108(45)	9(7.5)

P-value ≤ 0.05 is significant

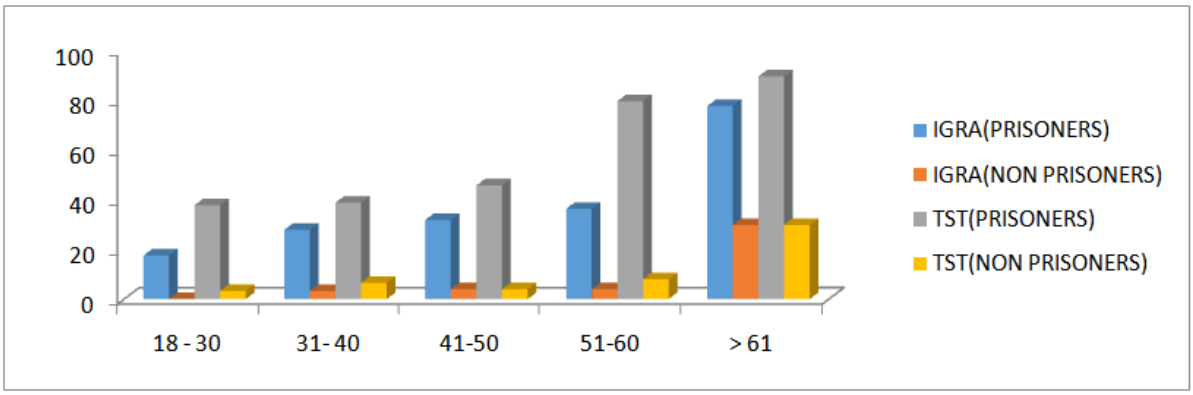
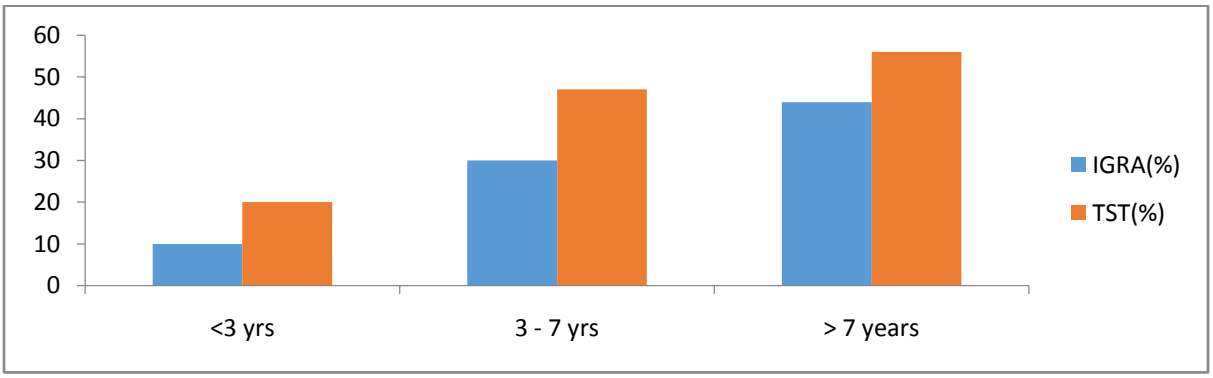


Table no3 depicts the prevalence of LTBI according to duration of incarceration. In 240 inmates tested, IGRA was positive in 31% while 45% were positive to TST. Those that stayed < 3 years had 10%:20% to IGRA:TST respectively. 3 – 7 years was 30%:47% using the above format. Greater tan 7 years of incarceration had the highest prevalence of 44%:56% to IGRA:TST proportion. The difference between the various groups of the incarcerated prisoners were statistically significant ($p<0.05$) to each other.

Table no 3 LTBI according to duration of stay in prison

Duration of stay(yrs)	Number Examined	% IGRA Positive	%TST Positive
< 3 years	60	6(10)	15(20)
3 – 7 years	78	24(30)	36(47)
>7 years	102	45(44)	57(56)
TOTAL	240	75(31)	108(45)

P-value ≤ 0.05 is significant



Participation rates were higher in males than females. Out of 240, males were 190 and female 50, (table no 5). Also the prevalence was more in males (32% and 45%) than females (28% and 44%) for both IGRA and TST, though the difference between the two sexes was not statistically significant($p>0.05$).

Table no 4 Gender Related Prevalence of LTI

Sex	Number Examined	% IGRA Positive	%TST Positive
Male	190	61(32)	86(45)
Female	50	14(28)	22(44)
TOTAL	240	75(31)	108(45)

P-value ≤ 0.05 is significant

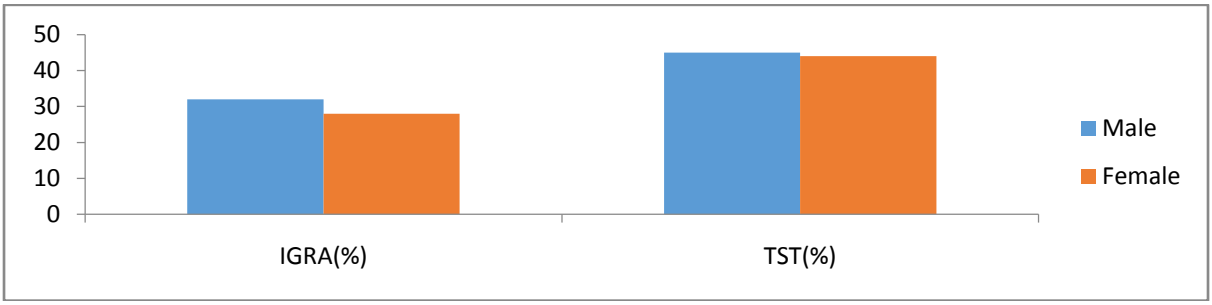


Table no 5: Discordant variables amongst the prisoners and non prisoners

Groups		Concordant	Discordant		Total Positive	
	Number Examined	IGRA/TST	IGRA alone(%)	TST alone(%)	TST	IGRA
Prisoners	240	67(69)	8(3.3)	41(17)	108(45)	75(31)
Non Prisoners	120	5(67)	1(0.8)	4(3.3)	9(7.5)	6(5)
TOTAL	360	72(69)	9(2.5)	45(12.5)	117(32.5)	81(22.5)

Table no. 5 shows the concordant/discordant variables between the two test methods. Concordance here is defined as when a test subject is simultaneously positive to both IGRA and TST, while discordant is when a test subject is positive to only one of the test methods. By this definition 67(28%) prisoners and 5(4%) of non prisoners were concordant. IGRA and TST respective results were 3.3% and 17% discordant results for the prisoners, while 0.8% and 3.3% for non prisoners.In summary, out of 320 participants studied, 20% results were concordant while 2.5% and 12.5% showed discordant results for IGRA and TST respectively. Using the already established TST results, in comparison IGRA was 69% concordant to TST results for the prisoners and 67 % for non prisoners. Out of all 360 participants used for the study, there was 69% concordance fpr IGRA.

IV. Discussion

The findings of this study revealed high prevalence of LTBI among prison inmates in Anambra state. The finding conforms to the results obtained by several other researchers regarding the estimated prevalence of LTBI in prison facilities being higher than that found in the general population. It also conforms to the work of Husain *et al* (2013) who reported a prevalence of 48% using TST in Pakistan [11]. Sole *et al* (2015) recorded a prevalence of 49.3% in Spain [12]. Riffer *et al* (2013) discovered a prevalence rate of 46.9%[13]. However, in a result by Margoles et al (2015), a higher prevalence of 88% was seen in Malaysia prison [14]. Carlos *et al* (2001) found a prevalence of 61.5% in Bahia Brazil [15].

Basically, there are three reasons for the high prevalence rates of LTBI observed in prisons. First, prisoners have higher risks of being infected with TB than the general population. They are predominantly young male adults who come from less privileged social classes and have low educational level [16, 17]. Secondly, prisoners have higher rate of risk factors or a lifestyle that predisposes them to develop active TB, once infected. Also a study found out that prisoners have a higher prevalence of HIV infection and use of injectable drugs than that reported in the general population [18]. Finally, the conditions of the prison environment, such as over crowding, inadequate ventilation, poor hygienic and nutritional conditions, as well as limited access to health care facilities [17]. These are factors that contribute to increase the probability of TB-/HIV co-infection and to progression from latent to active TB.. This is practically true in setting without TB screening upon prison entry and thereafter. In a recent review of global screening practices in prisons, TB prevalence was found to be significantly higher in prisons without routine TB screening compared to prisons with regular screening practices [19].

From our questionnaires, we discovered that majority of the inmates were smokers or previous smokers of tobacco/ cigarettes and consumed a lot of alcohol before incarceration. Scientific research has shown that mucocillary clearance is crucial as a primary innate defense in the airways [20]. Smoking therefore leads to impaired mucocillary clearance that impedes the ability of the lungs to combat attacks against Mycobacteria and other infections. There was a significant predisposition to LTBI as the duration of incarceration increases. This is because inmates that have stayed longer than 7 years had the highest prevalence rate which was statistically significant compared to those serving lower years

The least prevalence of LTBI was seen in participants within the age range of 18 – 30. There was a linear increase in LTBI as the age range increases with the highest prevalence seen in the age group >50 years. It's a long established fact that ageing, though a natural process, results in decline of T cell immunity that hampers the ability to combat Tuberculosis infection effectively. Also, researchers discovered that the waning effect of BCG vaccination with age could be a factor in the increased incidence of LTBI with age [21, 22].

The knowledge that airborne transmission of TB is promoted by close and prolonged contact with an infectious case has been used with the preposition that if a test is a good marker of LTBI, it should correlate closely with the level of exposure. There was discordance in the overall results between the two diagnostic methods with TST having a significant higher values in LTBI diagnosis than IGRA. The causes of this discrepancy are multifaceted which some of them being; the diagnostic principles of both tests, IGRA which is more specific requires a single patient visit, and being an in-*vitro* test, does not boost anamnestic immune responses and the interpretation is less subjective than the TST, and also less affected by prior BCG vaccination and reactivity to non-tuberculous mycobacteria than the TST. Also the instance of false positive might be high in TST group as a result of BCG vaccination at birth of all the participants. Unforeseen technical glitches were factors that could also lead to discrepancy in the results obtained. These discordant results indicated that dual sequential testing with TST and IGRA, may be the optimal approach for LTBI screening on prisoners and also implies that neither test can be used in place of the other thus, these methodologies should be used to complement each other.

Inteferon Gamma Release Assays have been shown to correlate well with TB exposure in low- and medium burden region in both well-defined outbreaks and community based contact investigations [23] , but IGRA are labor intensive, and there is a time limit from blood draw to receipt in a qualified laboratory and incubation with test antigens. Also the cost to-benefit ratio favors TST over IGRA in Nigeria and other most third world countries.

The concordance value obtained here (62%) was low in comparison to the results of Mazurek, *et al*. (2001) who showed 83% agreement of IGRA in comparison to TST in persons with varying risk for MTB infection, It was less affected by BCG vaccination, discriminated responses due to Non Tuberculous Mycobacteria (NTM), and avoided the variability and subjectivity associated with placing and reading the TST [24]. Based on the above discordant results, IGRAs will be preferred for testing prisoners who have received BCG and generally for testing groups that have low rates of returning to have their TSTs read. But from literature, An IGRA or a TST may be used without preference for testing recent contacts to persons with infectious pulmonary TB with considerations for follow-up testing. An IGRA or a TST may also be used without preference for periodic screening of persons who might have occupational exposure to *Mycobacterium tuberculosis* with considerations for conversions and reversions [25].

V. Conclusion

There was a high prevalence of latent tuberculosis infection amongst prisoners in all the prisons tested in Anambra State. IGRA and TST diagnostic results were not concordant with each other but IGRA appears to be more specific than TST in diagnosing LTBI. Currently there is no diagnostic accuracy for LTBI of any test and is a major challenge because there is no available gold standard. Use of those tests is highly recommended for prisoners considering their different limitations. Though cost is a limiting factor especially with IGRA, but the end result is justifiable in end TB policies which its main objective is to eradicate TB IN which treatment of prisoners with latent TB is a right step.

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