African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)
www.abjournals.org

LATENT DEMOGRAPHIC AND CLINICAL CORRELATES OF DRUG-RESISTANT TUBERCULOSIS AMONG TREATED PATIENTS

Nwankwo Chike H.[1] and Mbanuzuru Victor Ahoma[2]

[1]Department of Statistics, Faculty of Physical Sciences, Nnamdi Azikiwe University Awka.

[2]Department of Community Medicine & Primary Health Care, Nnamdi Azikiwe University Nnewi Campus.

Cite this article:

Nwankwo C. H., Mbanuzuru V. A. (2024), Latent Demographic and Clinical Correlates of Drug Resistant Tuberculosis Among Treated Patients. African Journal of Mathematics and Statistics Studies 7(2), 144-161. DOI: 10.52589/AJMSS-QLTC9AWL

Manuscript History

Received: 24 Jan 2024

Accepted: 23 Apr 2024

Published: 14 May 2024

ABSTRACT: *Demographic and Clinical variables (data) collected from tuberculosis patients whose cases were drug resistant were analysed. The tuberculosis patients studied were those treated in the 11 Local Governments Areas and a treatment centre of Anambra State, Nigeria, for six years (2017 – 2022). Data from 197 Drug Resistant Tuberculosis (DR-TB) patients were analysed. The pair of data collected, being multivariate in nature, were analysed using the Canonical Correlation Analysis (CCA) and the Canonical loadings (structure coefficients) between the Demographic and Clinical Variables were extracted. Data obtained showed that mean age of the study participants was 40.2 ± 18.9 years (95% Confidence Interval). Males were 60.9%. Participants with HIV co-infection was 22.3%. The CCA showed that the first canonical variate was significant with 79% contribution, extracting 28.5% of the variance from demographic variables and 6.7% variance from the clinical variables. The variables that significantly contributed to the relationship include Age, Location and Body Mass Index (BMI). Human Immuno-Deficiency Virus (HIV) negative was protective in the relationship but not statistically significant.*

KEYWORDS: Canonical Correlation Analysis, Drug-Resistant Tuberculosis, Demographic, Clinical, Correlates, Structural coefficient.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

www.abjournals.org

INTRODUCTION

In canonical correlation, some sets of multivariate data where the variables divide naturally into two groups, are analysed to investigate the relationship between the two groups, extracting the nature (modalities) of the relationship (Manly, 2005; Onyeagu, 2003). Canonical Correlation Analysis (CCA) has been noted as one of the powerful multivariate tools to jointly investigate the relationships among multiple data sets, and also uncover the joint multivariate relationships among different modalities (Zhuang et al., 2020). It was described as a top level of the generalized linear model (GLM) and can be rather easily conceptualized as a method closely linked with the more widely understood Pearson ρ correlation coefficient (Sherry & Henson, 2005). Canonical correlation analysis (CCA) answers the question, what relationships, if any, exist between the two sets of variables (Manly, 2005). It was developed by Hotelling in 1936, as a means of assessing the relationship between two sets of variables.

Multidrug-resistant TB (MDR-TB)

Tuberculosis as a disease, poses a public health challenge and multi-drug resistant type poses higher, both in treatment outcome and cost of treatment. Multidrug resistant tuberculosis is listed as one of the emerging and re-emerging diseases of public health importance worldwide (Kidenya et al., 2014). It is noted as a global health threat with high risk of morbidity and mortality, posing a challenge at the national and international level. It is estimated that 3.5% of the new cases of TB and 18% of the previously treated cases of TB have multi-drug resistant or rifampicin-resistant TB (MDR/RR-TB), (WHO, 2017). This translated to estimated global 558,000 new cases and 230,000 deaths. On the global scale, Nigeria is ranked 6th among 30 high-burden TB countries and among the 14 countries for Drug-resistant TB based on estimated incidence of MDR/RR TB, with the national MDR/RR TB burden estimated to be 21,000 annually [National Tuberculosis, Leprosy Control Programme (NTBLCP), 2021]. Nigeria is reported as one of the high MDR-TB burden countries with an estimated proportion of 4.3% of the new cases of TB and 15% of the previously treated TB cases presenting as MDR/RR-TB (Bakare et al., 2021). The cost of treatment of TB has been noted to be enormous, putting pressure on those infected and affected by the disease. According to the Centre for Disease Control and Prevention (CDC), the average cost of treating a person with drug susceptible TB is about $20,000 while that of drug resistant TB is about $568,000 outside indirect costs like loss of income (CDC, 2022).

Tuberculosis (TB) is a disease caused by acid-alcohol resistant bacilli (bacteria) known as *Mycobacterium tuberculosis Complex,* which comprises: *M. tuberculosis, M. bovis, M. africanum, M. microti, M. caneti, M. pinnipedii, M. caprae,* which generally spreads from person to person through the air, affecting mainly the lungs, but can also affect other parts of the body, such as the brain, the kidneys, intestine, ovaries or the spine. The commonest symptom of pulmonary TB being productive cough for 2 weeks or more which may be accompanied by other respiratory symptoms like shortness of breath, chest pain and coughing up blood (haemoptysis), loss of appetite, fever, weight loss, night sweats, and tiredness. (NTBLCP, 2021)

Multidrug-resistant TB (MDR-TB) emerges as a result of spontaneous gene mutations in the Mycobacterium tuberculosis that renders the organism resistant to the drugs used in treating TB, at least isoniazid and rifampin (the two most potent anti-TB drugs). Resistance to anti-TB drugs can occur when these drugs are misused or mismanaged, such as when patients do not

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

complete their full course of treatment; when health-care providers prescribe the wrong treatment, the wrong dose, or length of time for taking the drugs; when the supply of drugs is not always available; or when the drugs are of poor quality, hence drug-resistance is generally seen as man-made. Broadly, drug-resistant TB is divided into two: individuals who have not been previously treated for TB or who received anti TB treatment for less than one month (new patients or primary resistance) and people who have previously been treated for TB for one or more months (previously treated patients or acquired resistance). The drug treatment of MDR-TB is divided into conventional regimen (CR), shorter regimen (SR) and individualized regimen (IR), and throughout the duration of treatment, drug intake must be observed daily, and documented daily in the patient treatment card and appointment card, i.e. Directly Observed Therapy (DOT). The conventional regimen lasted over long period of about 20 months and it is currently phased out. Following development of more potent drugs, the shorter regimen last for a period of between 6 – 11 months.

Drug Regimen for DR-TB:

As noted in the National Tuberculosis Guidelines, (NTBLCP, 2021), the treatment regimen of multi-drug resistant TB is as follows:-

❖ **Shorter all-oral bedaquiline-containing regimen:**

4-6 Bdq-Mfx-Cfz-Pto-Z-E-Hh / 5 Mfx-Cfz-E-Z.

(meaning an intensive phase of 4 months that may be extended to 6 months, and a continuation phase of 5 months, giving a total duration of 9–11 months).

❖ **Modified Bedaquilline-based all oral shorter MDR-TB treatment regimens for MDR-TB:** 6Bdq-Pa-Lzd-Mfx

(meaning 6 months of bedaquilline, pretomanid, linezolid and moxifloxacin)

❖ **Individualized Regimen** - used for patients who are Pre XDR-TB or XDR-TB (depending on pattern of resistance) 6Bdq-Cfz-Lzd-Cs/ 12Cfz-Lzd-Cs

6Bdq-Mfx*-Cfz -Lzd/ 12Mfx-Cfz-Lzd

6Bdq-Cfz-Dlm-Cs/ 12Cfz-Dlm-Cs

6Dlm-Cfz-Lzd-Cs/ 12Cfz-Lzd-Cs

Explanatory Notes for DR-TB Regimen*:* Bdq = Bedaquilline, Cs = Cycloserine, Cfz = Clofazimine, Dlm = Delamanid, E = Ethambutol, Hh = Isoniazid – high dose, Lzd = Linezolid, Mfx = Moxifloxacin, Pa = Pretomanid, Z = Pyrazinamide.

Drug-resistant TB as disease of public health importance, requires all hands to be on deck (Healthcare providers, patients and patient-relatives) in helping to control it by quick diagnosis of cases, applying recommended treatment guidelines, monitoring patients' response to treatment, and making sure therapy is completed as well as infection control. (CDC, 2022).

This study aimed to extract the relationships of the demographic and clinical correlates of MDR-TB patients treated within Anambra State between 2017-2022 using canonical correlation analysis (CCA).

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

www.abjournals.org

MATERIALS and METHODS

Source (Scope) of Data

Data for this study were collected from all the Local Government Areas (LGAs) of Anambra State with records of Multi-Drug Resistant Tuberculosis (MDR-TB) treatment (see Appendix). Data are secondary in nature and were collected using LGA TB and Leprosy Supervisors (TBLS's) as research assistants. The population for this study includes all that were treated for MDR-TB in the State from 2017 to 2022 irrespective of age and gender. The proforma for collection of the data that was used for the analysis is as shown in Table A (in appendix). The data collected are: Date of diagnosis, Identification Number, Gender, Age, Body Mass Index (BMI), Site of the disease, type of treatment, registration group (diagnosis group), retroviral status (RVS), and outcome of the treatment. Some data like marital status, educational level, occupation, and level of income were not available.

Ethical Consideration: Ethical clearance was sought and obtained from the State Ministry of Health Anambra State before commencement of the study, with ref number MH/AWK/M/321/416 dated 27th January 2023.

Structure of MDR-TB Treatment in Anambra State

The treatment of MDR-TB can be Community-based or Facility (hospital)-based or mixed approach. For community model, the patient generally receives treatment from the home, while for the facility approach, treatment is from the hospital or treatment site. The treatment is coordinated by the National TB and leprosy control programme (NTBLCP) at the various Outpatient Department (OPD) Care sites or treatment facility in all Local Government Areas (LGAs), with reports through the services of Tuberculosis and Leprosy Supervisors (TBLS'es) of each attending LGA. Anambra State has two major Tertiary Health Institutions and many Secondary Health Facilities (Public and Private) offering care for the MDRTB among other ailments.

The Tertiary Institutions include Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, and Chukwuemeka Odimegwu Ojukwu University Teaching Hospital (COOUTH), Amaku Awka. Recently, General Hospital Onitsha in the State was upgraded to a Federal Medical Centre (FMC) making the tertiary institutions to be three. On monthly basis, the MDR-TB patients attend out-patient general assessment at NAUTH in Nnewi LGA, COOUTH in Awka South LGA, FMC Onitsha in Onitsha South LGA or Iyienu Hospital in Idemili North LGA, based on where the patient resides, until the treatment is completed.

Anambra as one of the States in South-Eastern Nigeria with the capital and seat of government at Awka has 21 Local Government Areas (LGAs) distributed in 3 Senatorial Zones (Anambra East, Anambra Central and Anambra South Zones). The State derived its name from the Omambala River (Anambra River) which is a tributary of River Niger, and covers an area of 4,416 km^2 and with projected population of 4,005,048 people based on 2006 census (NPC, 2009; NPC, 2010; SMOI, 2015). The major ethnic group of the State is the Igbos (98% of the population), while the rest 2% are Igala speaking mainly in the North-Western part of the State. The MDR-TB treatment structure caters for the entire population of the State.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

www.abjournals.org

Method of Data Analysis

Descriptive analysis was used to describe characteristics of the MDR-TB cases according to age, gender, location, BMI, HIV status and disease category and the distribution of treatment outcomes such as cured, treatment completed, died, treatment failure, loss to follow up, broadly grouped into successful and non-successful treatment outcome. Statistical Package for the Social Science version 25 was used for the statistical analysis in this study. Chi-square test of association used for bivariate analysis of categorical variables as well as Canonical Correlation Analysis for the demographic and clinical variables. The demographic (DEM) variables set include age/age category, gender and location (site) of treatment, while the clinical (CLIN) variables set used in this CCA include body mass index (BMI), retroviral status (RVS) and treatment or registration group of the patients. The results were presented in Table with further graphical representation of the canonical loadings presented as Figure 4.2.

The fundamental principle behind canonical correlation analysis is creation of a number of canonical solutions, each consisting of a linear combination of one set of variable which has the form: $U_i = a_1(DEM_1) + a_2(DEM_2) + \ldots + a_m(DEM_m)$

and a linear combination of the other set of variables which has the form:

$$V_i = b_1(CLIN_1) + b_2(CLIN_2) + \ldots + b_n(CLIN_n)$$

RESULTS

Descriptive statistics

The study participants were age-ranged 14 – 86 years with mean of 40.2 years and standard deviation of 18.9 years, with mean BMI of 18.2 ± 4.3. Majority (60.9%) were males. All the study participants (100%) had pulmonary disease site, with almost all (99.5%) had shorter regimen (SR) of treatment. The result further shows that 22.3% of the participants were HIV positive. New cases ranked the highest (65%) among the participants, followed by treatment after failure (12.2%).

Table 4.1: Demographic and some clinical characteristics of the study subjects

Variables			Frequency	Percent	Cumulative Percent
Age Category (in years)	< 19	(Children/Adolescents)	9	4.6	4.6
	20-40	(Young Adult)	103	52.8	57.4
	41-60	(Adults)	61	31.3	88.7
	>60	(Older Person)	22	11.3	100.0
	Total		195	100	
Age (± S.D.) in years		40.2 ± 14.9 (95% C.I.)		Min = 14	Max= 86
Gender		Female	77	39.1	39.1
		Male	120	60.9	100.0
		Total	197	100.0	

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

Treatment type	0 (Individualized)	1	.5	.5
	1 (Shorter regimen)	196	99.5	100.0
	Total	197	100.0	
Disease site	0 (Extra-pulmonary)	0	0.0	0.0
	1 (pulmonary)	197	100.0	100.0
Patient Registration Group	1 (New case)	128	65.0	65.0
	2 (Failure)	24	12.2	77.2
	3 (Loss to follow-up)	23	11.7	88.8
	4 (Previously treated)	18	9.1	98.0
	5 (Unknown history)	1	.5	98.5
	6 (Transfer in)	2	1.0	99.5
	NA	1	.5	100.0
	Total	197	100.0	
Retroviral status (RVS)	0 (Negative)	143	72.6	72.6
	1 (Positive)	44	22.3	22.3
	NA	10	5.1	5.1
	Total	197	100.0	100.0
Outcome of treatment	1 (Cured)	32	16.2	16.2
	2 (Treatment completed)	31	15.7	32.0
	3 (Died)	24	12.2	44.2
	4 (Treatment failure)	3	1.5	45.7
	5 (Loss to follow up)	19	9.6	55.3
	6 (Not evaluated)	88	44.7	100.0
	Total	197	100.0	
Success status	NE	86	43.7	43.7
	Successful	63	32.0	75.6
	Unsuccessful	48	24.4	100.0
	Total	197	100.0	

***S.D**. = Standard Deviation; **C.I**. = Confidence Interval; **NA** = not available; **NE** = not evaluated*

Majority of the participants (52.8%) were among the young adults aged 20 – 40 years. Also, though TB can affect any part of the body, but all the subjects in this study had pulmonary type of TB, with greater number (65%) registered as ‘new cases’.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

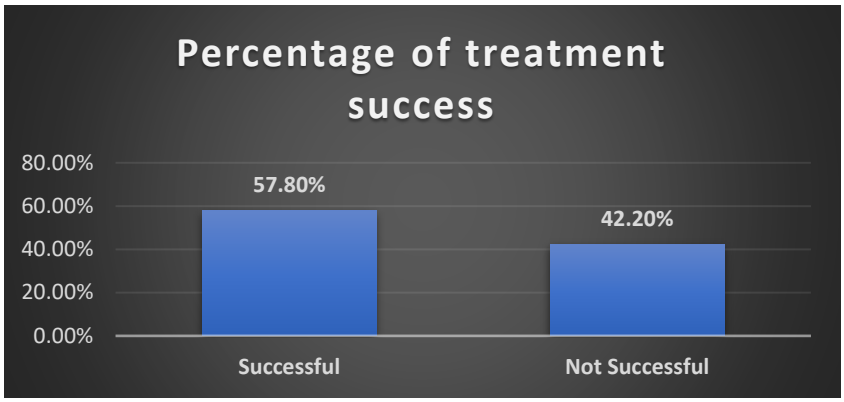


Figure 4.1: Distribution of the success status of MDR-TB treated

The proportion of successful outcome of treatment from this study was 57.8%. The proportion of unsuccessful outcome from this study was 42.2%.

Association Between Demographic/Clinical Variables and Treatment Outcome: Cross-tabulation of the treatment outcome and some demographic and clinical variables was done with chi-square test of association. The results were presented in Table 4.2 and 4.3.

Table 4.2 Association Some Demographic Variables and Treatment Outcome

Variable		Treatment Outcome (%)		Total (%)	χ^2 - value	P-value
		No Success	Success			
Age Category (in years)	**≤19** (Children/adolescents)	0 (0.0)	2 (100.0)	2 (100)	1.337	0.650
	20 - 40 (Young adults)	27 (46.6)	31 (53.4)	58 (100)		
	41 – 60 (Adults)	13 (38.2)	21 (61.8)	34 (100)		
	>60 (Older persons)	5 (38.5)	8 (61.5)	13 (100)		
Gender	Female	11 (28.9)	27 (71.1)	38 (100)	4.202	0.045
	Male	35 (49.3)	36 (50.7)	71 (100)		
Year of Treatment	2017	4 (33.3)	8 (66.7)	12 (100)	12.588	0.026
	2018	6 (30.0)	14 (70.0)	20 (100)		
	2019	9 (36.0)	16 (64.0)	25 (100)		
	2020	3 (25.0)	9 (75.0)	12 (100)		

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

	2021	12 (48.0)	13 (52.0)	25 (100)
	2022	12 (80.0)	3 (20.0)	15 (100)

There was statistically significant association between gender and outcome of treatment with females having higher percentage of successful outcome (71.1%) compared to males (50.7%), [$\chi^2 = 4.202$, $p = 0.045$]. The relationship between age category and treatment outcome was not statistically significant.

Table 4.3 Association between some clinical characteristics and treatment outcome

Variable		**Treatment Outcome (%)**		**Total (%)**	**χ^2 - value**	**P-value**
		No Success	Success			
Treatment Group (Registration Group)	Group 1	34 (41.5)	48 (58.5)	82 (100)	3.780	0.627
	Group 2	6 (50.0)	6 (50.0)	12 (100)		
	Group 3	2 (33.3)	4 (66.7)	6 (100)		
	Group 4	4 (66.7)	2 (33.3)	6 (100)		
	Group 5	0 (0.0)	1 (100.0)	1 (100)		
	Group 6	0 (0.0)	2 (100.0)	2 (100)		
HIV Status	Positive	36 (42.9)	48 (57.1)	84 (100)	0.000	1.000
	Negative	9 (42.9)	12 (57.1)	21 (100)		
Body Mass Index (BMI) ± SD		19.4 ± 5.9	19.0 ± 4,2		t-test 0.312	0.756

Registration Groups: ***1*** *= New case.* ***2*** *= Treatment after failure.* ***3*** *= Treatment after loss to follow up.* ***4*** *= Other previously treated TB patients.* ***5*** *= Unknown previous TB treatment history.* ***6*** *= Transfer in (from another DR-TB treatment site).* ***SD*** means Standard deviation. ***Type of treatment*** *was not applicable as almost all the cases were shorter regimen*

There was no statistically significant association between treatment outcome and HIV status, BMI and registration group.

Table 4.4: Correlation of the variables

	Age	**Age Category**	**Gender**	**RVS**	**BMI**	**Reg Grp**	**Outcome**
Age	1						
Age Category	0.931	1					
Gender	0.245**	0.229**	1				
RVS	0.091	0.040	-0.015	1			

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

BMI	0.217*	0.244**	-0.103	-0.083	1		
Reg Grp	0.067	0.065	0.058	0.117	-0.094	1	
Outcome	-0.089	-0.059	-0.025	0.047	-0.117	0.126	1

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed). RVS = Retroviral status; BMI = Body Mass Index

The bivariate correlation shows that there was statistically significant positive correlation between gender and age/age-category, as well as BMI and age/age-category.

Table 4.5: Canonical Correlations Roots/Solutions of the Canonical Variates

Root Number	Eigen Value (λ)	Percentage	Canonical Correlation	Square Correlation (R^2)
1	0.23528	79.7	0.43642	0.19046
2	0.05872	19.9	0.23550	0.03516
3	0.00108	0.4	0.03289	0.0018

The above table (4.5) shows the corresponding eigen values of the canonical variates which are square of the corresponding canonical correlation. The percentage contribution from 1st canonical variate was 79.7%, while that of 2nd and 3rd canonical variates were 19.9% and 0.4% respectively.

Table 4.6: Dimension Reduction Analysis of the Canonical Variates

Roots	Wilks-Lamda	F	Hypothesis DF	Error DF	P-value (sig)
1 to 3	0.763	4.117	9.00	316.54	< 0.001
2 to 3	0.943	1.932	4.00	262.00	0.105
3 to 3	0.998	0.142	1.00	132.00	0.706

The dimension reduction analysis shows that only 1st canonical variate was statistically significant with overall Wilks-Lamda value as 0.76 (p-value of < 0.001) signifying significant relationship between the two sets of variables (demographic and clinical) among DRTB patients treated in Anambra State.

Table 4.7: Canonical Correlation Analysis Result for second Canonical variate

Variables	**1st Canonical Variate (CV)**		**2nd Canonical Variate (CV)**		**3rd Canonical Variate (CV)**	
	Correlation	Coefficient	Correlation	Coefficient	Correlation	Coefficient
SET 1 (Demographic)						
Age Category	0.40187	0.49241	0.89643	0.90517	0.18686	- 0.04980
Gender	-0.31716	-0.54474	0.22324	0.06017	0.92172	0.88291
Location	0.77087	0.81641	-0.39171	-0.44713	0.50231	0.38922
Percent of variance	28.5		33.5		37.8	

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)
www.abjournals.org

SET (Clinical)	**2**						
BMI		0.87338	0.83965	0.46162	0.54961	0.15532	0.08347
RVS		0.00879	0.14409	0.13701	0.06367	-0.99053	-0.99947
TG		-0.54574	-0.48633	0.83757	0.88060	-0.02532	0.11749
Percent variance	of	6.7		1.7		0.03	
Canonical Correlations		0.43642		0.23550		0.03289	

BMI *= body mass index,* ***RVS*** *= Retro-viral disease (HIV Status),* ***TG*** *= Treatment group (also called Registration group).*

The Table 4.7 showed that significant 1st canonical variate pair extracted 28.5% of the variance from the demographic (DEM) variables and 6.7% of the variance from the clinical (CLIN) variables, with 0.43 as correlation and the linear combination from the pair will be:

$U_1 = 0.492\ (Age) - 0.544\ (Gender) + 0.816\ (Location)$

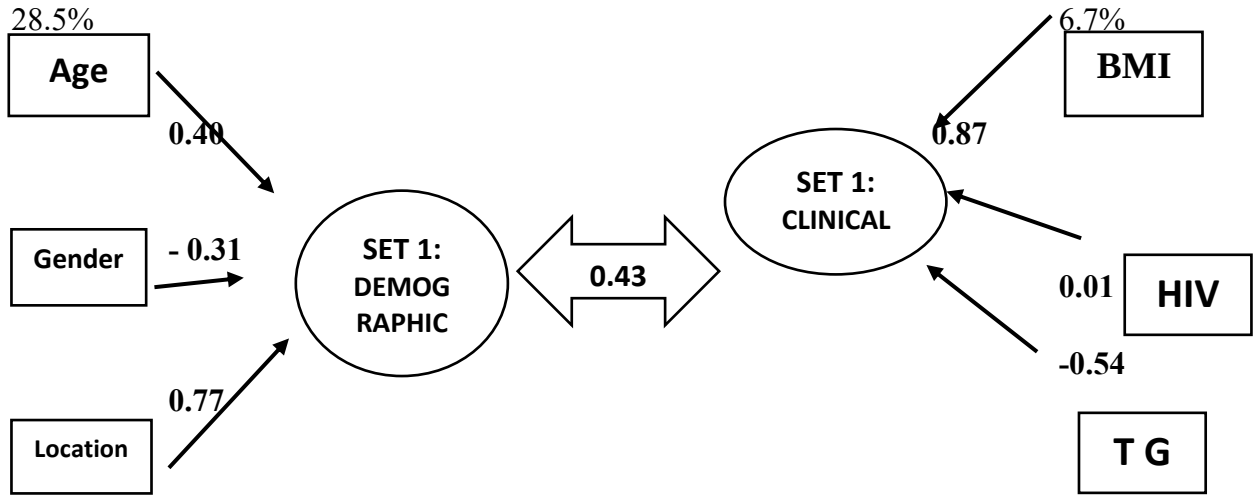
$V_1 = 0.839\ (BMI) + 0.144\ (RVS) - 0.486\ (TG)$

The 2nd canonical correlation was 0.23, though not statistically significant, and from the canonical coefficients (Table 4.9), the linear combination from 2nd canonical variate pair will be: $U_2 = 0.905\ (Age) + 0.060\ (Gender) - 0.447\ (Location)$

$V_2 = 0.549\ (BMI) + 0.063\ (RVS) + 0.880\ (TG)$

The 3rd canonical correlation was 0.03, though not statistically significant, and from the canonical coefficients (Table 4.10), the linear combination from 3rd canonical variate pair will be: $U_3 = -0.049\ (Age) + 0.882\ (Gender) + 0.389\ (Location)$

$V_3 = 0.083\ (BMI) - 0.999\ (RVS) + 0.117\ (TG)$



Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

Figure 4.2 Canonical loadings of the first Canonical Variate.

The variables with absolute value of correlation (loadings) greater than 0.3 include age, gender and location for set demographic variables, and BMI and treatment group (TG) for set clinical variables.

DISCUSSION

The mean age of the participants in this study was 40 ± 18 years, indicating middle age population. Majority of the persons studied (60.9%) were males, while all the patients (100%) had pulmonary type of DRTB. There was no case of extra-pulmonary tuberculosis. among whom 22% were HIV positive, 99.5% of the participants were on shorter regimen of treatment. New cases accounted for 65% of the participants. Within the study period, 57.8% had successful outcome of treatment among those evaluated.

There was significant relationship between gender and treatment outcome, [χ^2 (1) = 4.202, p = 0.045], as well as the location and the outcome, while other hand relationship between clinical correlates and outcome of treatment were not statistically significant. The proportion of successful outcome of treatment (57.8%) was below the 75% expectation set by World Health Organization, closer to 63.3% reported globally for pre-extensive DR-TB by Pedersen et al. (2023). The proportion of unsuccessful outcome from this study (42.2%) was far higher than what obtained in a low incidence TB country like Netherlands with 5% (Pradipta et al., 2019). While mortality was only 1% in Netherlands, this study reported 12.2% death, and 9.6% loss to follow-up. On the bivariate correlation, there was significant correlation between age and gender, and between age and body mass index (BMI).

The result of the canonical correlation analysis (CCA) shows that the overall Wilks-Lamda value was 0.76 with p-value of < 0.001 signifying significant relationship between the two sets of variables (demographic and clinical) among DRTB patients treated in Anambra State between 2017 and 2022. The canonical correlation analysis revealed three canonical variates (CVs) with three roots, but only the first root with eigen value of 0.23, percentage contribution of 79% and canonical correlation of 0.43 was statistically significant (p-value < 0.001). This is in consonance with the report by Manly (2005) as well as Sherry & Henson (2005) which states that each pairs of canonical variables (U_1, V_1), (U_2, V_2), …, (U_r, V_r) represents an independent dimension in the relationship between the two sets of variables (X_1, X_2,…..,X_p) and (Y_1, Y_2,…..,Y_q), with r representing the smaller of p and q and the first pair (U_1, V_1), having the highest possible correlation and therefore the most important, and the second pair (U_2, V_2), the second highest correlation and therefore the second most important, and so on. The second CV and third CV were not statistically significant (p = 0.105 and p = 0.706 respectively). Following the significant result of the 1st canonical variate, the interpretation of the results of this study was based mainly on the first CV. The significant first canonical variate (CV) pair extracted 28.5% of the variance from the demographic (DEM) variables and 6.7% of the variance from the clinical (CLIN) variables. The 1st and 2nd CVs cumulatively accounted for 99% of the relationship. The results were in keeping with some previous works on CCA

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

(Adarkwah & Hirsh, 2020; Enginyurt et al., 2016; Mohammed-Abbas, 2015; Ojurongbe et al., 2018; Liu et al., 2023)

The first canonical variate of this study showed that variables age, gender and location for demographic set were significant. Also the variables, body mass index (BMI) and treatment group (TG) for clinical set were significant. This is based on absolute value of correlation (or loadings) greater than 0.3, according to Razavi et al. (2005). Retroviral status (RVS) or simply Human immune-deficiency virus (HIV) was not statistically significant with loading of 0.01, though HIV negative seems protective. This is similar to reports by Kidenya et al. (2014) and Okemba-Okombi et al. (2020). The clinical variable set mainly reflects the body mass index (BMI).

In conclusion, this study investigated the proportion of MDR-TB patients in Anambra State treated between 2017 and 2022 according to demographic and clinical correlates, while determining the relationship between these correlates and outcome of treatment, as well as establishing canonical relationship between demographic variables (age, gender, location) set and clinical variables set (BMI, HIV, treatment group, disease site, type of treatment). We therefore recommend that further studies be carried out in MDR-TB in other States of the Federation and the whole of Sub-Saharan Africa, and possibly extending the period of the study beyond 2022 for more insight into the inter-relationship between demographic and clinical correlates. This will increase the power and generalizability.

Limitation of the Study: The study involved patients with multi-drug resistant tuberculosis (MDR-TB) confirmed through GeneXpert machine and treated in the various Local Government Areas (LGAs) of Anambra State as well as Treatment Centre in Anaocha LGA between 2017 and 2022. This work is limited to the available data within the respective LGAs where the treatment for multi-drug resistant tuberculosis took place. Data could not be obtained from most LGAs. In places where reasonable data exist, they were from year 2017, hence time period for this study (2017-2022). It may be necessary to note that because of the nature and structure of MDR-TB programme, where the LGA Tuberculosis and Leprosy Supervisors (TBLS) record the patients details, some clinical variables like blood pressure, pulse rate, respiratory rate, and oxygen saturation as well as educational level, occupation and economic status could not be captured.

Acknowledgement: Our gratitude goes to different persons that helped towards success of this work. Special mention is the Honourable Commissioner of Health Anambra State, Dr Afam Obidike, and Director of Medical Services, Dr Ugochukwu Chukwulobe, for the support during this work and guidance. The thanks also go to Mrs Amaka, Monitoring and Evaluation Officer as well as all the Tuberculosis & Leprosy Supervisors (TBLS's) from the Local Government Areas of Anambra where DRTB cases are managed.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

REFERENCE

Adarkwah, C. C. and Oliver H. (2020). The association of work-satisfaction and burnout risk in endoscopy nursing staff—A cross-sectional study using canonical correlation analysis. *International Journal of Environmental Research and Public Health.* 17 (8), 2964. https://doi.org/10.3390/ijerph17082964.

Bakare, A.M., Udunze, O.C., Bamidele, J.O., Omoniyi, A., Osman, E., Olusoji, J.D. (2021). Outcome of Community-initiated treatment of drug resistant tuberculosis patients in Lagos, Nigeria. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 115 (9), 1061-1065.

CDC, Center for Disease Control and Prevention (2022). Drug-resistant TB. CDC. Available online at https://www.cdc.gov/tb/topics/drtb (Accessed on 23rd Oct, 2023).

Enginyurt O., Cankaya S., Aksay K., Tunc T., Koc B., Bas O., Ozer E. (2016). Relationship between organisational commitment and burnout syndrome: a canonical correlation approach. *Australian Health Review* 40, 181-187. https://doi.org/10.1071/AH14177.

Hotelling, H. (1936). Relations between two sets of variates. *Biometrika*, 28, 321 – 377.

Kidenya, B.R., Webster, L.E., Behan, S., Kabangila, R., Peck, R.N., Mshana, S.E., et al. (2014). Epidemiology and genetic diversity of multidrug-resistant tuberculosis in East Africa. *Tuberculosis*, 94 (1), 1-7.

Liu, H., Gan, Q., Tan, J., Sun, X., Liu, Y., Wan, C. (2023). The association between quality of life and subjective wellbeing among older adults based on canonical correlation analysis. *Front Public Health*. Sep 19;11:1235276. doi: 10.3389/fpubh.2023.1235276. PMID: 37799159; PMCID: PMC10548456. (Accessed on 09th Jan, 2024).

Manly, B. F.J. (2005). Multivariate statistical methods: A primer. *3rd Ed. Chapman & Hall/CRC. United States of America.* Pp.143-161.

Muhammed-Abbas, A. (2015). A study of the prevalence of HIV/AIDS using canonical correlation analysis (a case study of General Hospital Minna). *UDUS Open Educational Resources.* Available at http://hdl.handle.net/123456789/671. (Accessed 28/12/2023)

National Population Commission. 2006 population and housing census of the Federal Republic of Nigeria. Official Gazette Federal Rep. Nig. 2009: 96 (2):1

National Tuberculosis, Leprosy and Buruli Ulcer Control Programme, NTBLCP (2021). National Tuberculosis, Leprosy and Buruli Ulcer Management and Control Guidelines. 7th Edition. *NTBLCP, Department of Public Health, Federal Ministry of Health. Abuja.* 2021:28-149.

National Population Commission. (2010). Population Distribution by Sex, State, LGA & Senatorial District. 2006 Popul Hous Census. 2010; III: 1-64. Available from http://population.gov.ng/images/Vol 03Tables DSx LGA....pdf.

Ojurongbe, T.A., Oseni, B.S., Bashiru, K.A. (2018). Evaluation of maternal factors on infant's birth size using Canonical Correlation Analysis in Osogbo, Osun State. *NOUN Journal of Physical & Life Sciences.* 2 (1), 67-83.

Okemba-Okombi, F.H., Essango, E.N., Kayomo, M.K., Ossale-Abacka, B.K., Bopaka, R.G., Atipo-Ibara, B.I. (2020). Multi-resistant tuberculosis in Brazzaville: Epidemiological, clinical, radiographic and progressive aspects. *J Func Vent Pulm*. 33 (10), 1-xx. Available online at www.jfvpulm.com (Accessed on 10th March, 2024).

Onyeagu, S. I. (2003). A first course in multivariate analysis. *Mega-Concept. Awka.* Pp.187-201.

Pradipta, I.S., van't Boveneind-Vrubleuskaya, N., Akkerman, O.W., Alffenaar, J.C., Hak, E.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

(2019). Treatment outcomes of drug-resistant tuberculosis in the Netherlnds, 2005-2015. *Antimicrob Resist Infect Control*. 8, 115. https://doi.org/10.1186/s13756-019-0561-z. (Accessed on 12th March, 2024).

Razavi, A.R., Gill, H., Stal, O., Sundquist, M., Thorstenson, S., Ahlfeldt, H., Shahsavar, N. (2005). Exploring cancer register data to find risk factors for recurrence of breast cancer – application of Canonical Correlation Analysis. *BMC Medical Informatics and Decision Making*. 5, 29. doi:10.1186/1472-6947-5-29.

Sherry, A. and Henson, R.K. (2005). Conducting and interpreting Canonical Correlation Analysis in Personality Research – A user-friendly primer. *Journal of Personality Assessment.* 84 (1), 37-48.

State Ministry of Information (2015). Executive Diary. Government of Anambra State. *SMOI* Awka.

World Health Organization (2017). Multidrug Resistant tuberculosis. Available at https://www.who.int/ (Accessed on 23rd Oct 2023)

Zhuang, X., Yang Z., Cordes, D. (2020). A technical review of canonical correlation analysis for neuroscience applications. *Hum Brain Mapp.* 41, 3807-3833.

APPENDIX

DATA & SUMMARY OF ANALYSIS

Table A: Proforma for Data Collection on MDR-TB Patients in Anambra State Treated Between 2017 and 2022.

S/N	LGA/Site	Date	Year	Patient ID	Sex	Age	BMI (Kg/m2)	Treatment Type	Site of Disease	Registration Group	RVS

The Body Mass Index (BMI) is measured as weight in kilogramme (or pounds) divided by the square of height in meters (or feet). $\text{BMI} = \frac{Weight(Kg)}{Height^2\,(m^2)}$

Disease site: **0** = Extra-pulmonary (EP)

1 = Pulmonary (P)

Treatment Type: **0** = Individualized regimen (IR)

1 = Shorter regimen (SR)

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

Registration Group: **1** = New case.

2 = Treatment after failure.

3 = Treatment after loss to follow up.

4 = Other previously treated TB patients.

5 = Unknown previous TB treatment history.

6 = Transfer in (from another DR-TB treatment site)

Retroviral Status (RVS/HIV Status): **0** = Negative

1 = Positive

Outcome: **1** = Cured (C)

2 = Treatment completed (TC)

3 = Died (D)

4 = Treatment failure (F)

5 = Loss to follow up (LF)

6 = Not evaluated.

Treatment Outcome Status: **0** = Not Successful (eg died, failure, loss to follow-up)

1 = Successful (Cured and Treatment completed)

Table B: Local Government Area (LGA) Site of the Study Subjects

Variable	Frequency	Percent	Cumulative Percent
Anaocha (Treatment Centre)	69	35.0	35.0
Awka North	1	.5	35.5
Awka South	17	8.6	44.1
Idemili North	17	8.6	52.7
Ihiala	11	5.6	58.3
Nnewi North	26	13.2	71.5
Ogbaru	10	5.1	76.6
Onitsha North	29	14.7	91.3
Onitsha South	5	2.5	93.8
Orumba North	3	1.5	95.3
Orumba South	4	2.0	97.3
Oyi	5	2.5	100.0
Total	197	100.0	

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

African Journal of Mathematics and Statistics Studies
ISSN: 2689-5323
Volume 7, Issue 2, 2024 (pp. 144-161)

www.abjournals.org

Table C: Year of Treatment of the study subjects

Variable	Frequency	Percent	Cumulative Percent
2017	13	6.6	6.6
2018	33	16.8	23.4
2019	39	19.8	43.1
2020	28	14.2	57.4
2021	39	19.8	77.2
2022	45	22.8	100.0
Total	197	100.0	

Some Programmatic Definitions Within Tuberculosis Management (NTBLCP, 2021)

Co-morbidities: Other ailments suffered by patients other than the case of study (in this context, other ailments other than drug-resistant TB).

Presumptive TB case: A person who presents with symptoms or signs suggestive of TB.

Pulmonary tuberculosis (PTB): This is a form of tuberculosis that involves the lung parenchyma (tissues) and tracheobronchial tree.

Extra-pulmonary tuberculosis (EPTB): This is a form of TB that involves one or more organs other than the lung parenchyma. Eg the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, meninges, etc.

Classification of TB based on history of previous treatment:

New patients: These are TB patients who have never had treatment for TB, or who have taken anti-TB drugs for less than 4 weeks.

Relapse patients: Previously treated TB patients with documented outcome of cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB.

Treatment after failure patients: Previously treated TB patients whose treatment failed (bacteriological positive at month 5 or later) in the most recent course of treatment.

Treatment after loss to follow up: Previously treated TB patients who were declared loss to follow up (treated for more than 4 weeks, and interrupted treatment for at least 8 consecutive weeks) at the end of their most recent course of treatment, and now diagnosed with TB.

Other previously treated patients: Previously treated TB patients whose outcomes after their most recent course of treatment are unknown or undocumented and are now diagnosed to have TB.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

Transfer-in patients: These are TB patients diagnosed and commenced on treatment in a facility in one LGA, and now transferred to another facility in another LGA (within or outside the State) to continue treatment.

Classification of TB based on HIV status

*HIV-positive TB patients***:** These are TB patients (bacteriologically or clinically diagnosed) who have documented HIV-positive result or with documented evidence of enrolment in HIV care.

*HIV-negative TB patients***:** These are TB patients (bacteriologically or clinically diagnosed) who have documented HIV-negative result from a test conducted at the time of diagnosis.

*HIV status unknown TB patients***:** Patients with TB who do not have a documented HIV test result.

Classification of TB based on Drug Resistance

*Mono-resistance***:** resistance to one first line anti-TB drugs (Rifampicin, Isoniazid, Pyrazinamide, or Ethambutol) only.

Poly-resistance: resistance to more than one anti-TB drugs (other than both Isoniazid & Rifampicin).

Multi-drug resistance (MDR): resistance to at least both Isoniazid and Rifampicin.

Rifampicin-resistance (RR): resistance to Rifampicin (mono-resistance, multi-drug resistance, poly-resistance and extensive drug resistance).

Extensive drug resistance: This is MDR-TB or RR-TB and also resistance to any fluoroquinolone, and at least one additional Group A drug.

Pan-resistance: this is resistance to all clinically available drugs.

Treatment Outcomes for TB

*Cured***:** A pulmonary TB patient with bacteriologically conformed (Xpert MTB/RIF, smear or culture positive) tuberculosis at the beginning of treatment and who completed treatment, and was smear negative in the last month of treatment (and on at least one previous occasion).

*Treatment completed***:** This is TB patient who completed treatment without evidence of failure but with no record to show that smear/culture results in the last month of treatment and on at least on one previous occasion were negative, either because it was not done, or not available or not indicated (as in EPTB).

*Treatment failure***:** A TB patient whose sputum smear or culture is positive at month 5 or later during treatment, or a TB patient whose treatment regimen needed to be terminated or permanently changed to a new regimen or treatment strategy.

Lost to follow-up: A TB patient who did not start treatment or TB patient whose treatment was interrupted for 8 consecutive weeks or more.

Died: A TB patient who died for any reason before starting or during the course of treatment.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL

Not evaluated: A TB patient for whom no treatment outcome was assigned, including cases transferred out to another treatment unit, and where the treatment outcome is unknown to the reporting unit.

Treatment success: The sum of cured and treatment completed.

Article DOI: 10.52589/AJMSS-QLTC9AWL
DOI URL: https://doi.org/10.52589/AJMSS-QLTC9AWL