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Comparative Analysis of the Effects of Drugs on the Treatment of Tuberculosis.

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ABSTRACT.
This work focused on the comparative analysis of the effects of certain drugs in the treatment of tuberculosis. It primarily compared the efficiency of these following drugs: isoniazids, Rifampin, pyrazinamide and Ethambutol so as to make proper recommendations. The sample data collected from mile four hospital Abakaliki was analyzed using analysis of variance (ANOVA) which gave the following results: Fcal under treatment =0.39 while F_{tab} =3.49 and Fcal under block =0.59 and F_{tab} =3.26 which led to the acceptance of H_0 since Fcal< $F_{tab,}$. The comparison was favourable and results showed that the four drugs used for treating the tuberculosis patients at the Hospital are the same that is to say there are no significant differences among them.

I. INTRODUCTION

So many scientific investigations that are quantitative help researchers sought for some objective criteria for presenting, concluding and analyzing numerical observations or data. Many people who had not survived primary infections were infected by acute pulmonary tuberculosis.

Roughly, one third of the world's population has been infected with Mycobacterium tuberculosis, and new infections occur at a rate of one per second. However, not all infections with Mycobacterium tuberculosis cause tuberculosis disease and many infections are asymptomatic.

Tuberculosis diseases are diseases caused by a germ called Mycobacterium tuberculosis that is spread from one person to another through the air. Tuberculosis usually affect the lungs but it can also affect other parts of the body such as the brain, the kidneys or the spine.

In the last three decades, the emergence of HIV/AIDS as well as the appearance and spread of drug-resistant forms of tuberculosis have been associated with an increase in the tuberculosis rates in several low, middle and high income countries, Together with HIV /AIDS and Malaria. TB is one of the most significant causes of death worldwide, most frequently affecting men in their economically productive age groups with a TB incidence rate considerably below 10 cases per 100, 000 inhabitants over the last 10 years, Nigeria can be considered as a low burden country of TB. Nevertheless, Tuberculosis has increasingly become an illness affecting specific population subgroups; approximately 40% of reported TB causes in Nigeria involve foreign patients resident in Nigeria.

According to the latest estimates by Adolphe (2001-2005), there were 8.6 million new cases of TB and 1.3 million TB deaths in 2012(EFFA, 2007), several discoveries from the global context indicate that a population's knowledge of TB is crucial to facilitate the seeking of early medical care and avoidance of further M. tuberculosis transmission and the development of multidrug resistant TB across the world.

Isoniazid is one of the drugs of choice for the treatment of tuberculosis diseases as it contains some germs resisted power in the body. In the whole world today, the major hinderance to the effective cure of tuberculosis is the drug resistant strain which will require several drugs at once. The problem of antibiotics resistance creates an important public health problem that may be related to therapeutic failure since bacteria sensitive to antibiotics become resistant in order to survive (John and Raphael, 2013). The infection is usually spread from one person to another through air. The diseases are common in the East Asia, Africa, Central, South America and other regions. Symptoms include nausea or vomiting, loss of appetite, jaundice or yellow color to ones skin and dark urine.

There are two types of tuberculosis diseases which include: (1) Latent TB infections which do not have any symptoms and do not make the person feel sick. They are infected with

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Mycobacterium tuberculosis but do not have TB disease. (2) Active TB infection: This type of TB infection subjects the patients to feel sick and shows symptoms like vomiting, jaundice etc. If one has latent tuberculosis, the person need to take just one type of drug while if one has active tuberculosis particularly if it is a drug resistant strain, it will require several drugs at once. For some years now, if one has a drug resistant TB, a combination of antibiotics called fluoroquinolenes and injectable medications such as Amikacin, kanamycin or capreomycin are generally used for 20 to 30 months. Antibiotics like Isoniazid, Rifampin and Ethambutol were used for the treatment of tuberculosis diseases. This research aims to compare the efficacy of isoniazid, rifampin, ethambutol and pyrazinamide in the treatment of tuberculosis diseases.

1. The aim of this work is to compare the efficacy of Isoniazid, Rifampin, Ethambutol and Pyrazinamide tuberculosis drugs prior to the treatment of tuberculosis diseases using two way Analysis of Variance .

II. METHODS OF DATA COLLECTION/MATERIALS.

Data collection is a very vital stage in any statistical investigation. Data can be collected through the following processes: Direct observation, mail questionnaires, personal interview or interview which are all primary sources of data. Also, by registration, census e.t.c. which are secondary sources of data. Since our study is based on "Estimating drugs effect for the treatment of tuberculosis in mile four hospitals", the method of data collection here will be by registration which implies that we are using data collected by keeping records of events either before or after its occurrence.

2.1 .The model for randomized complete block design or two ways analysis of variance is given as:$Y_{ij} = \mu+\alpha_i +\beta_j+ E_{ij}$ For all i=1,2,……,t and j=1,2,…..,n……..…(3.1)

Where Y_{ij} is the jth observation from the ith treatment.

μ is the grand mean.

αi is the ith treatment effect.

βj is the jth column effect or block effect.

Eij is the random error and is NID(0, σ^2_e).

2.2 THE TEST HYPOTHESIS

The appropriate test hypothesis to be tested under two ways analysis of variance are:

1. The effect of treatment (Tuberculosis drugs)

H_0: αi =0 for all i (The efficacy of the tuberculosis drugs in treating tuberculosis are not significantly different). VS

H_1: αi ≠ 0 For all i (The efficacy of the tuberculosis drugs in treating tuberculosis are significantly different).

2. The effect of the blocks(Hospitals)

H_0: βj =0 for all j (The block effect is not significantly different) VS

H_1: βj ≠0 for all j (The block effect is significantly different).

Also, the appropriate hypothesis to be tested will be tested using F- distribution at 5% significance level. If the calculated test statistic is greater than the critical value or the tabulated value, then the null hypothesis (H_0) should be accepted.

2.3 PARTITIONING INTO SUM OF SQUARE.

1. The sum of square Total (SS_{TOTAL}) is estimated as :

$$SS_{TOTAL} = \sum_{i=1}^{t}\sum_{j=1}^{n} y_{ij}^2 - \frac{y_{..}^2}{N}$$

2. The sum of square treatment ($SS_{TREATMENT}$) is estimated as :

$$SS_{trt} = \sum_{i=1}^{t} \frac{y_{i.}^2}{ni} - \frac{y_{..}^2}{N}$$

3. Sum of square block (SS_{BLOCK}) is estimated as :

$$SS_{blk} = \sum_{j=1}^{n} \frac{y_{j}^2}{nj} - \frac{y_{..}^2}{N}$$

4. The sum of square error (SS_{error}) is calculated as:

$SS_{error} = SS_{TOTAL} - SS_{TRT} - SS_{BLK.}$

2.4 THE MEAN SUM OF SQUARE (VARIANCE)

1. Variance between groups.

(a) Mean square of treatment (MS_{TRT}) $MS_{trt} = \frac{SS_{trt}}{t-1}$

(b) Mean square of block (MS_{BLK})

$$MS_{blk} = \frac{SS_{blk}}{b-1}$$

2. Variance within groups, MSE is estimated as

$$MS_{Error} = \frac{SS_{Error}}{(t-1)(b-1)}$$

2.5 ANOVA TABLE OF RANDOMIZED COMPLETE BLOCK DESIGN.

Source of variation	Degree of freedom	Sum of square	Mean square (MS)	FCal	Ftab

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Treatment	(t-1)	SS_{trt}	SS_{trt}/t-1	MSS_{TRT}/MSS E	$F_{(t-1),(t-1)(b-1)\alpha}$%
Block	(b-1)	SS_{blk}	SS_{blk}/b-1	MSS_{blk}/MSS E	$F_{(b-1),(t-1)(b-1)}$ α%
Error	(t-1)(b-1)	SS_{error}	SS_e/(t-1)(b-1)	MSS_{Blk}/MSS E	
Total	N-1	SS_{TOTAL}			

THE CRITICAL VALUE: THE CRITICAL Value is obtained by;

$$Ftab = F_{\alpha,\%\,(t-1),(t-1)(b-1)} \text{ for treatment effect}$$

And

$$Ftab = F_{\alpha\%,(b-1),(t-1)(b-1)} \quad \text{.....(*)}$$

Decision Rule: The null hypothesis is rejected if the Fcal > Ftab while if otherwise the null hypothesis is accepted.

Conclusion Rule: if H_o is rejected, then it means that the alternative (H_1) has been accepted. Therefore, there is significant difference in the efficacy of tuberculosis drugs in treating tuberculosis but if otherwise, there is no significant difference in the efficacy of the tuberculosis drugs.

2.6 DATA

The analysis of this research will be carried out sequentially starting from the application of analysis of variance in the determination of the efficacy of the drugs used for the treatment of tuberculosis using the data collected on the efficacy of drugs in five different wards at mile four hospitals, Abakaliki.

2.7 PRESENTATION OF DATA.

TABLE 2.7.1: TREATED CASES OF TUBERCULOSIS.

BLOCKS (Wards)	ISONIAZIDS	ETHAMBUTOL	PYRAZINAMIDE	RIFAMPIN	TOTAL NO OF TREATED CASES.
Ward	Respond non-respond	Respond non-respond	Respond non-respond	Respond non-respond	

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Ward I total	10 25	15	30 12 42	40 45 85	07 05 12	164
Ward II Total	20 28	08	22 28 50	15 10 25	14 16 30	133
Ward III Total	6 08	02	03 01 04	24 12 36	18 13 31	79
Ward IV Total	16 20	04	10 15 25	19 11 30	25 09 34	109
Ward V Total	40 50	10	30 15 45	16 12 28	11 06 17	140

Let W_1 Denote ward 1
Let W_2 Denote wards 2
W_3 Denote wards 3
W_4 Denote wards 4
W_5 Denote wards 5
AND Let T_1 Denote Isoniazids
T_2 Denote Ethambutol
T_3 Denote Pyrazinamide
T_4 Denote Rifampin.

Table 2.7.2: SUMMARIZED DATA OF TREATED AND RESPONDED CASES OF TUBERCULOSIS.

BLOCKS	T_1	T_2	T_3	T_4
W_1	10	30	40	07
W_2	20	22	15	14
W_3	6	03	24	18
W_4	16	10	19	25
W_5	40	30	16	11

Table 2.7.3: ANALYSIS TABLE FOR TREATED AND RESPONDED CASES

HOSPITAL (DRUGS)
DRUGS.

BLOCKS	T_1	T_2	T_3	T_4	TOTALS
W_1	10	30	40	07	87
W_2	20	22	15	14	71
W_3	06	03	24	18	51
W_4	16	10	19	25	70
W_5	40	30	16	11	97
TOTALS	92	95	114	75	376

2.8 ANALYSIS OF VARIANCE OF THE TREATED AND RESPONDED CASES

TABLE 2.7.4: ANOVA TABLE FOR TREATED/ RESPONDED CASES.

Sources of variation	Degree of freedom	Sum of Square	Mean of Square	F_{Cal}	F_{tab}

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Treatment	3	153.2	51.07	0.39	F^3_{12} (0.05)=3.49
Blocks	4	311.2	77.8	0.59	F^4_{12}(0.05)=3.26
Error	12	1584.8	132.07		
Total	19	2049.2			

2.8 HYPOTHESIS TESTING.

(1) H_O: $t_i = 0$ VS H_1 : $t_i \neq 0$ for all i

(2) H_0 : $b_j = 0$ VS H_1: $b_j \neq 0$ for all j

(1**) DECISION RULE:** Since $F_{Cal} < F_{tab}$, We accept H_0

CONCLUSION: The efficacy of the drugs are not significantly different in the treatment of tuberculosis disease.

(2) **DECISION RULE:** Since $F_{Cal} < F_{tab}$, We accept H_0

CONCLUSION: The efficacy of the drugs are not significantly different in the block effect.

TABLE 2.7.5: SUMMARIZED DATA OF TREATED AND NON-RESPONDED CASES OF TUBERCULOSIS.

DRUGS

BLOCKS	T_1	T_2	T_3	T_4
W_1	15	12	45	05
W_2	08	28	10	16
W_3	02	01	12	13
W_4	04	15	11	09
W_5	10	15	12	06

TABLE 2.7.6: ANALYSIS TABLE FOR TREATED AND NON- RESPONDED CASES.

BLOCKS	T_1	T_2	T_3	T_4	TOTALS
W_1	15	12	45	05	77
W_2	08	28	10	16	62
W_3	02	01	12	13	28
W_4	04	15	11	09	39
W_5	10	15	12	06	43
TOTALS	39	71	90	49	249

TABLE 2.7.7: ANOVA TABLE FOR NON-RESPONDED CASES.

S.V	D.F	SS	MS	F_{CAL}	F_{TAB}
TREATMENT	3	312.55	104.18	1.14	3.4902
BLOCKS	4	381.7	95.43	1.05	3.2592
ERROR	12	1094.7	91.23		
TOTAL	19	1788.95			

HYPOTHESIS TESTING :

(1) H_0 : $t_i = 0$ vs H_1: $t_i \neq$ for all i

DECISION RULE: Since $F_{CAL} < F_{TAB}$, We accept H_0

CONCLUSION : Treatment effects are not significantly different

(2) H_0:bj =0 vs H_1:bj≠0 for all j

Decision Rule: Since $F_{CAL} < F_{TAB,}$ We accept H_0

Conclusion Rule: Block effects are not significantly different.

III. CONCLUSION

In this research work, we collected data of patients treated of tuberculosis using the following drugs: Isoniazids, Ethambutol, Pyrazinamide, and Rifampin at mile four hospital, Abakaliki. The statistical tools used in this research work are two way analysis of variance .

On comparing the results obtained from the statistical tool used, it was observed that there is no difference among the drugs irrespective of their names which implies that the efficacy of the drugs are the same when applied on the tuberculosis infected patients.

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