

The Effects of Anti-tuberculosis Drugs Side Effects On Treatment Adherence Among Tuberculosis Patients At Kenyatta National Hospital

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ABSTRACT

Side effects are one of the major causes that result to poor adherence of tuberculosis treatment. Poor adherence could lead to prolonged treatment, drug resistance, treatment failure, increased morbidity and mortality of disease. The main objective of this study was to determine the effect of anti-tuberculosis drugs side effects on treatment adherence among Tuberculosis patients at Kenyatta National Hospital. The study design was a descriptive cross sectional design. A total of 169 patients were sampled for this study using purposive method of sampling. Quantitative data was collected using a structured questionnaire and analyzed using Statistical Package of Social Sciences Version 24.0. Data was summarized in form of bar graphs and pie charts. Qualitative data was collected using interviews as per the objectives and then analyzed using N-Vivo software 11 where themes and sub- themes that constituted narrative based on research objectives were generated. The level of adherence among Tuberculosis patients at Kenyatta National Hospital was poor 34.9% (n=51). Both minor and major side effects of anti-tuberculosis drugs resulted to poor adherence. (p< 0.05). Health care workers should emphasize the importance of adherence to anti-tuberculosis drugs regardless of side effects. Patients need to be educated on possible side effects and how to handle them. The side effects should be well managed to ensure adherence.

Key words: Non-adherence, Anti-tuberculosis drugs, Major side effects, Minor side effects, drug resistant Tuberculosis

1. BACKGROUND

Tuberculosis(TB) is an infection that is caused by a bacteria known as mycobacterium tuberculosis(WHO, 2014).According to World Health Organization(WHO)report, tuberculosis is a huge disease burden. Tuberculosis is at number nine in causing deaths globally. In the year 2016, 10.4 million people got infected with TB. About 16% of those died throughout the world. Tuberculosis infection is more common in resource-limited countries with high Human immune deficiency (HIV) infection rates co-existing with low social economic status (WHO, 2017)

Africa contributes a high percentage of the global TB burden. Among the 30 high burden countries (HBCs), 15 of them are in Africa and Kenya is among them with an infection rate of 300 per 100,000 population (WHO, 2017).The World Health Organization recommends that newly diagnosed TB patients should be treated for six months with a multi drug regimen treatment. This should start with a two month intensive treatment phase followed by a continuation phase of four months. The Multi drug regimen treatment causes many side effects to TB patients. (WHO, 2010).

These side effects are classified as minor or major. Minor side effects are common and include loss of appetite, abdominal pain, joint pain, nausea, discoloration of body fluids and skin rashes. A patient can continue with drug therapy due to minor side effects. Major side effects are rare but lethal and they often lead to drug discontinuation. They include jaundice, ototoxicity, peripheral neuritis and arthralgia.(Gadkowski, 2014). Poor adherence to medication is the inability to follow prescribed treatment and is a multidimensional health problem. The causes of poor adherence may be related to the patient, treatment, and/or health care provider.(Hugtenburg *et al.*, 2013).

A study done in Ethiopia indicated that side effects of anti-tuberculosis drugs are a major cause of poor adherence among Tuberculosis Patients (Adane *et al.*, 2013).Lack of proper adherence to treatment is a big problem for TB patients taking medication. This leads to complications such as drug resistance resulting to Multi drug resistant Tuberculosis which could complicate further to extensive drug resistant tuberculosis (Kiplangat et al, 2017). A study done in Nakuru County in Kenya indicated that side effects due to anti-tuberculosis drugs contributed to non-adherence. 23% of the respondents indicated that side effects led them to terminate their treatment. (Oyugi *et al.*, 2017)

A study done by Wahome *et al.*, 2013 found out that about 300 TB cases are diagnosed at Kenyatta National Hospital (KNH) each month. Among those treated and followed up in KNH, only75% of them were treated successfully. Little research has been done on the effect of (anti tuberculosis drugs) Anti-Tbs side effects on treatment adherence in Kenyatta national hospital. My study proposed to address the effects of Anti-tuberculosis drugs side effects on treatment adherence among TB patients at KNH.

2. MATERIALS AND METHODS

The study adopted a descriptive cross sectional design. Qualitative study was also preferred for the ability of the approach to incorporate respondents' perceptions that may not be quantified. Triangulation technique was used where there was inquiry through quantitative approach and validation through qualitative approach. Phenomenological method under qualitative approach was employed. An in-depth experience of TB patients who experienced side effects was recorded.

This study was conducted at Kenyatta National hospital (KNH) at 10 study areas. A sample size of 169 respondents were to fill the self-administered semi-structured questionnaires. For the qualitative component, 7 Tuberculosis patients were selected per study area. Interviews were used to collect qualitative data. Purposive sampling was used for both quantitative and qualitative studies. Data from the completed questionnaires was entered using SPSS version 24 and the password protected. Confidentiality was maintained for information given on questionnaires as no names or personal identifications were used. The tape recordings were transcribed into a Microsoft office word document before being transferred into NVIVO software version 11.

The quantitative data generated from the questionnaires were coded and keyed into MS Access database. The Access database was imported into SPSS v 24 for descriptive analysis to generate frequencies, percentages and tabulations. Demographic data was analyzed using descriptive statistics. Categorical data was presented as frequencies and percentages. Adherence was measured using visual analogue scale and pill count. Multiple regression was done to find out the statistical significance of the association between the independent and dependent variables were interpreted using Chi Square test where P values of 0.05 or less were considered to be significant. Verbatim transcription of in-depth interview notes was done in Microsoft office word. The transcripts were imported into N-Vivo software program version 11 for axial coding and categorization on pre- identified thematic areas. Coding was performed manually and inductively, in stages, then analyzed in form of main themes, subthemes and narratives. The data collected was stored in a computer and secured it with a unique password. The data was retrieved during the analysis process and later kept in the same safe environment until the study was completed. Once the researcher completed the use of the raw data; it was professionally disposed to reduce unethical usage of the data. Approval to conduct the study was sought from Kenyatta National Hospital –University of Nairobi Ethics Research Committee, medical department at Kenyatta National Hospital administration and consent sought from TB patients.

3.0 RESULTS

3.1 Level of Adherence

The study reported a response rate of 87%, (n=147) (Table 1).

Adherence to anti tbs

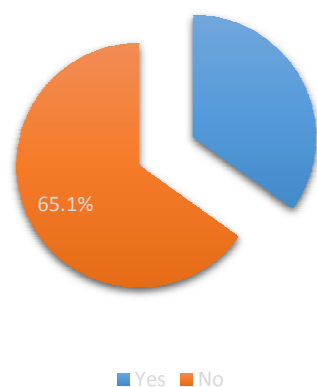


Figure 1: Adherence to Anti tbs.

Table 1: Adherence according to Visual analogue scale

Number of respondents	Adherence according to Visual analogue scale
9	90%
43	60%
95	55%

66% (n=97) of the respondents had more pills than the expected. 34% (n=50) of them had the actual number of the expected remaining pills (Table 2).

Table 2: Number of remaining pills being more than the expected

Yes	No
97	50

3.2 Side effects of Anti-TB drugs

Majority of the respondents 77.9% (n=115) on anti-TB drugs reported that they have ever experienced side effects while 22.1% (n=32) had never experienced anti TBs side effects (Figure 2).

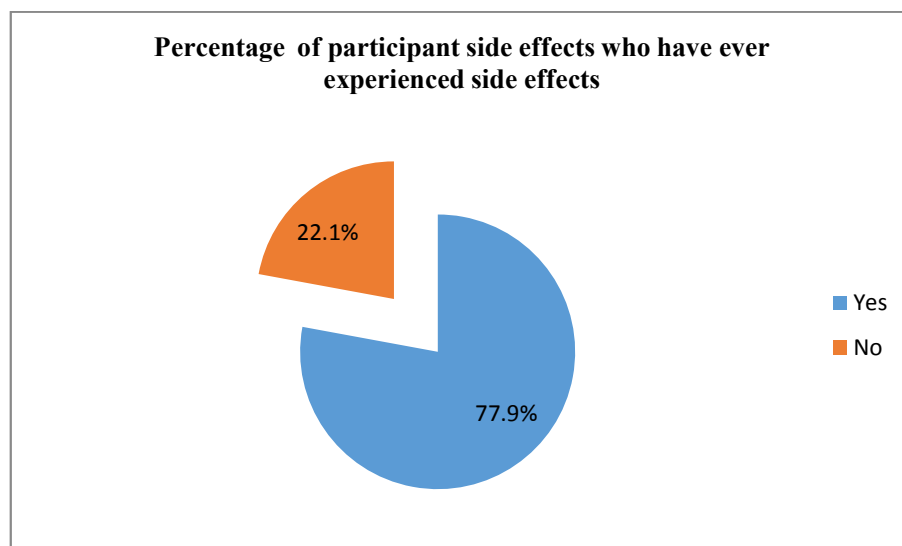


Figure 2: percentage of participants who have ever experienced side effects

Table 3: Minor side effects experienced by patients on anti tbs.

Minor side effects experienced	Frequency	Percentage
Nausea and Vomiting	69	37.7
Headache/dizziness	36	19.7
Discoloration of body fluids	34	18.6
Diarrhea	20	10.9
Skin rash	16	8.7
Loss of color vision	8	4.4
Total	183	100.0

Table 4: Association between minor side effects and adherence to anti-TB medication

Minor side effects experienced	Adherence	Non adherence	χ^2	P-value
Diarrhoea	18 (89.5%)	2 (10.5%)	2.415	0.067
Nausea & Vomiting	18 (26.7%)	52 (73.3%)	9.874	0.034
Skin rash	4 (22.7%)	12 (77.3%)	14.516	0.003
Headache/dizziness	23 (64.3%)	13 (35.7%)	2.578	0.312
Loss of color vision	3 (40.6%)	5 (59.4%)	17.214	0.015
Discoloration of body fluids	13 (37.9%)	21 (62.1%)	11.658	0.001

Table 5: Major side effects experienced on anti-TB drugs

Major side effects experienced	Frequency	Percentage
Jaundice	31	56.4
Joint pain	12	21.8
Numbness	7	12.7
Ankle swelling	5	9.1
Total	55	100.0

Table 6: Association between major side effects and adherence to anti-TB medication

Major side effects experienced	Adherence	Non adherence	χ^2	P-value
Jaundice	11 (34.5%)	20 (65.5%)	8.432	0.014
Numbness	5 (67.2%)	2 (32.8%)	2.589	0.072
Joint pain	4 (34.5%)	8 (65.4%)	7.654	0.003
Ankle swelling	2 (41.9%)	3 (59.1%)	7.521	0.001

3.3 Non adherence due to side effects

62% (n=71) of the respondents who experienced side effects stopped taking medication while 38% (n=44) of them did not stop taking medication. This indicates that side effects influenced adherence among a significant proportion of the study participants (Figure 9).

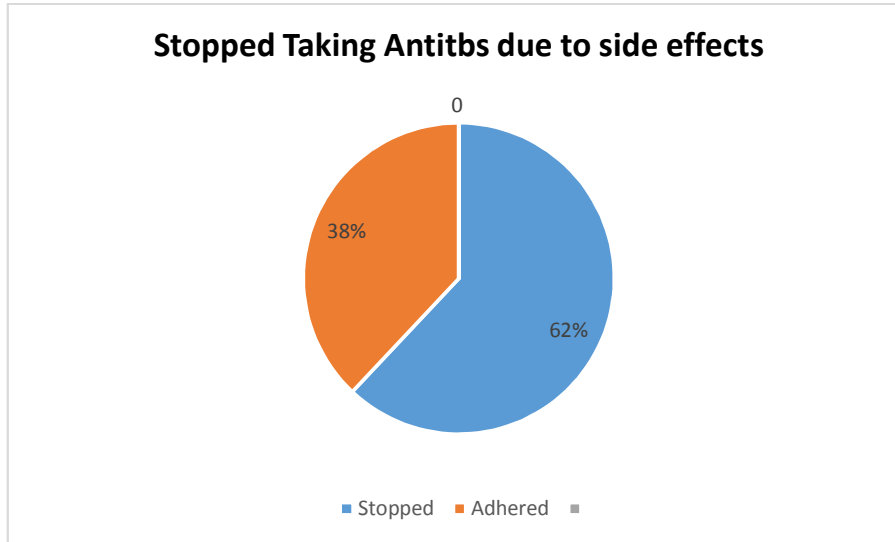


Figure 3: Non adherence to Anti-Tbs due to side effects.

3.4 Qualitative Data Analysis

In order to determine patient’s experiences regarding side effects and adherence, this study adopted a qualitative approach using in-depth semi structured interviews where the participants consented and participated in this study. All interviews were recorded on a tape recorder. The interviewees were all coded with numbers such as. Code 020, code 015. Several questions were asked and responded to. NVIVO software 11 was used to analyze the qualitative data. Three themes emerged from the analysis. They were: expectations to experience a side effect, patients’ reaction after experiencing the side effect and health care workers contribution to non-adherence. These three themes were supported by a number of sub-themes.

Table 7: Expectation to experience a side effect.

THEME 1	EXPECTATION TO EXPERIENCE SIDE EFFECTS	
	NO	YES
SUBTHEMES	50	20

Majority of the respondents 70% (n=50) interviewed answered that they did not expect to experience side effects. The others 30% (n=20) did expect to experience side effects. This is because when being started on anti tbs, they were never told that they would experience side effects (Table 8).

“The only thing that was mentioned to us is that if we fail to take our drugs, we would restart treatment again. We were never informed that we could experience vomiting and joint pains.”- Code 30

Table 8: Reaction after experiencing a side effect

Theme 2	Reaction to Side effects
Stopped adherence	63%(n=44)
Side effects subsided	11% (n= 8)
Reported to the health facility	26% (n=18)

The respondents reported that they went to the health facility to report, others waited for the symptoms to subside on their own while others stopped taking medication (Table 9)

Subtheme 1: Stopped taking medication

Approximately two thirds of the respondents 63% (n=44) reported that they stopped taking medication after experiencing a side effect. This was similar to the number of patients stopped adhering to treatment when they experienced side effects as they indicated in the questionnaire (Table 9).

“I had not been told that my urine would turn red in color, so once I experienced it, I thought it was blood, I got worried and stopped treatment”- code 20

“My husband informed me that my eyes had turned yellow in color so I stopped treatment”- code 22.

Sub theme 2: Side effects subsided on their own

Some of the respondents 11% (n= 8) reported to have waited for the side effects to subside on their own (Table 9).

“I experienced headache in the afternoon that was not too severe, so I continued taking the drugs as usual”- code 15

“I experienced diarrhea, however, it was not that bad, I went ahead taking my medication as prescribed”.- code 17

Sub theme 3: Reported to the health facility.

Some respondents 26% (n=18) went to the health facility to report so that they could be treated (Table 9).

“Once I experienced a skin rash, I went to the hospital to report. They gave me drugs to go and take at home. After three weeks, the rash resolved” - code 19

Table 9: Health care workers contribution to non-adherence

Theme 3	Contribution of non- adherence
Lack of Education on TB	28% (n= 20)
Lack of Education on side effects	43% (n= 30)
No contribution by health care workers	29% (n = 20)

Most of the respondents 71% (n= 50) felt that healthcare workers contributed to non-adherence by not giving them health education concerning TB and side effects. The others 29% (n=20) felt that health care workers had not contributed to non-adherence (Table 10).

Subtheme 1: Failure to educate on TB

Some respondents 28% (n= 20) reported that they have never been educated on TB (Table 10).

“We have never been educated on how TB affects us. I have never known why TB causes me a lot of back pain. It’s important for health care workers to explain to us the effect of TB in our body”. – code 40

Subtheme 2: Failure to educate on side effects

Some respondents 43% (n= 30) expressed that they have never been educated about side effects and they felt it is important for the side effects to be explained to patients before starting treatment (Table 10).

“Health care workers do not inform us of the side effects to expect. When they occur, we stop treatment. All the side effects should be to us. This will prepare us so that we are not too worried when we experience some of them”. – code 23.

4. DISCUSSION

This study found out that the rate of adherence to anti tbs was still poor at KNH. More than half of the respondents in this study had ever missed their medication in at least one occasion. More than two thirds of the respondents had more pills remaining than the actual expected number. This was similar to a study by Oyugi *et al.*, (2017) that found out that side effects led to 60% of TB patients on anti tbs to default treatment in Nakuru Kenya. This variation may be attributable to the fact that the study findings represent result from a single hospital. This indicated that health care workers should come up with better strategies and proper follow up methods in order to enhance adherence.

In this study, there was a significant association between nausea/vomiting and adherence as many of the respondents who experienced nausea/vomiting stopped treatment. Similar results were found in Ethiopia that 33.4% of patients on anti- tuberculosis drugs who experienced nausea and vomiting resulted to defaulting (Gube *et al.*, 2018). In order to reduce GIT side effects, it’s necessary for health care workers to advise TB patients to always take their drugs with meals.

Approximately a third of the respondents experienced headaches. About two thirds of them continued taking medication. According to this study, there was no significant association between headache/dizziness and adherence. This contradicted the findings of a study conducted in Northwest Ethiopia that found out that 37% of research participants complained of headache or dizziness hence leading to default of treatment (Adane *et al.*, 2013). This means presence or absence of headache or dizziness did not affect adherence to treatment in our study. Headache could be controlled with the use of analgesics hence ensuring adherence.

Some study participants reported to have experienced discoloration of body fluids. There was a significant statistical association between discoloration of body fluids and adherence. This findings were similar to a study conducted in Ethiopia that found out that 75.2% of research participants on Anti-tuberculosis drugs reported urine discolorations as a cause of non-adherence (Adane *et al.*, 2013). This indicates that proper reassurance of patients is important when starting treatment, explanations that this side effect is common and is normal will help in enhancing adherence.

There was a significant association between skin rash and adherence. Similarly, a study in Britain found out that 8% of the patients who experienced skin rash interrupted their medication (Breen *et al.*, 2006). The overall incidence of severe skin rash in our study was low but played a role in causing non-adherence. This means that patients who experience skin rash fear to adhere. This means that patients who experience skin rash fear to adhere. It is therefore important to treat skin rash as a side effect using antihistamines (chlorpheniramine) to enhance adherence among those patients who experience it.

The least of the respondents on anti tbs developed ocular toxicity. Loss of color vision was the reported symptom. Over half of them stopped taking their anti tbs due to side effects. There was a statistical significance between ocular toxicity and adherence. This study had similar findings with another conducted in Pakistan that found out that 18% of patients receiving more than 30 mg/kg per day of ethambutol per day experienced ocular toxicity and this negatively affected their adherence (Shah *et al.*, 2014). Loss of color vision is a rare yet important side-effect that affects adherence. It should be carefully monitored and controlled to enhance adherence among TB patients.

There was no statistical significance between numbness and adherence. This finding was similar to those of a study done in India found out that none of the patients who experienced by numbness continued their treatment. However, a study in Ethiopia found out that peripheral neuropathy experienced by 30% of the respondents made them to default treatment (Gube *et al.*, 2018). However, patients who experience numbness should be treated with pyridoxine 100 mg daily to control this side effect.

There was a statistical significance between joint pain/ankle swelling and adherence according to this study. This finding was similar to a study conducted in Kyrgystan prisons in Zurich on factors promoting adherence to TB medication, found out that hyperuricemia was responsible for termination of therapy in up to 23% of patients during the intensive phase of treatment. Proper monitoring has to be carried out during the whole treatment course, including clinical examination and laboratory tests of uric acid levels.

This study found out that there was an association between jaundice and adherence to medication. This finding was similar to that of a study done in Ethiopia that indicated that jaundice was a common side effect that caused patients to stop adhering to treatment (Medhin, Alemu and Desalegne, 2015). This indicates that it is necessary for TB researchers to develop hepato-protective drugs.

5. CONCLUSION

Overall there was poor level of adherence among the respondents. Minor side effects of anti-tuberculosis drugs contributed to poor adherence. Major side effects of anti-tuberculosis drugs also contributed to poor adherence. Therefore, i) Health care workers should emphasize the importance of adherence to TB patients on anti-tuberculosis drugs regardless of experiencing side effects. ii) The patients need to be educated on possible side effects of anti-tuberculosis drugs and how to handle them. iii) Health care workers should also manage the side effects of anti-tuberculosis drugs so as to ensure adherence. iv) Moreover, the directly observed therapy program at Kenyatta National Hospital should be strengthened.

6. COMPETING INTERESTS

The authors declare that they have no competing interests regarding the publication of this paper.

7. FUNDING

This research was not funded

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REFERENCES

- Adane, A. A., Alene, K. A., Koye, D. N., & Zeleke, B. M. (2013). Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in northwest Ethiopia. *PLoS ONE*, 8(11). <https://doi.org/10.1371/journal.pone.0078791>
- Breen, R. A. M., Miller, R. F., Gorsuch, T., Smith, C. J., Schwenk, A., Holmes, W., ... Lipman, M. C. I. (2006). Adverse events and treatment interruption in tuberculosis patients with and without HIV co-infection. *Thorax*, 61(9), 791–794. <https://doi.org/10.1136/thx.2006.058867>
- Gadkowski, L. B. (2014). TB Drugs: Side Effects, Adverse Events and Their Management. *Eastern Virginia Medical School - Division of Infectious Diseases*, 1–9.
- Gube, A. A., Debalkie, M., Seid, K., Bisete, K., Mengesha, A., Zeynu, A., ... Gebremeskel, F. (2018). Assessment of Anti-TB Drug Nonadherence and Associated Factors among TB Patients Attending TB Clinics in Arba Minch Governmental Health Institutions, Southern Ethiopia. *Tuberculosis Research and Treatment*, 2018, 1–7. <https://doi.org/10.1155/2018/3705812>
- Hugtenburg, J. G., Timmers, L., Elders, P. J. M., Vervloet, M., & van Dijk, L. (2013). Definitions, variants, and causes of nonadherence with medication: A challenge for tailored interventions. *Patient Preference and Adherence*, 7, 675–682. <https://doi.org/10.2147/PPA.S29549>
- Ibrahim, L. M., Hadejia, I. S., Nguku, P., Dankoli, R., Waziri, N. E., Akhimien, M. O., ... Nsubuga, P. (2014). Factors associated with interruption of treatment among pulmonary tuberculosis patients in plateau state, Nigeria. 2011. *Pan African Medical Journal*, 17, 1–8. <https://doi.org/10.11604/pamj.2014.17.78.3464>
- Kiplangat Arap Sang, R. (2017). Patient Factors Which Contribute to Non-adherence to TB Treatment in Kericho and Nakuru Counties of Kenya. *Science Journal of Public Health*, 5(4), 329. <https://doi.org/10.11648/j.sjph.20170504.18>
- Oyugi, S. O., Garama, C. M., Kweri, J. K., Malik, N. A., Bett, S. K., & Biego, S. C. (2017). Patient Factors Influencing Adherence To Anti-Tuberculosis Medication in Njoro Sub County Hospital , Nakuru County , 7(5), 766–795.
- Shah, N. H., Khan, M. M., Ahmad, A., Hanif, M., & Ali, M. (2014). THE PHARMA INNOVATION - JOURNAL Comparative Incidence of serious side effects from first-line anti-tuberculosis drug in patients treated for active tuberculosis and treatment outcomes, 74–84.
- Wahome, E., Makori, L., Gikera, M., Wafula, J., Chakaya, J., Edginton, E. M., and Kumar, V. M. A. (2013) ‘Tuberculosis treatment outcomes among hospital workers’, *Public Health Action*, 3(4), pp. 323–327

WHO. (2017). *Global Tuberculosis Report 2017*. Who.
<https://doi.org/WHO/HTM/TB/2017.23>

WHO. (2014). *Definitions and reporting framework for tuberculosis – 2013 revision*. World Health Organisation. <https://doi.org/WHO/HTM/TB/2013.2>

WHO.(2010) ‘Treatment of tuberculosis: guidelines’, *4Th Edition*, p. 160. doi: 10.1164/rccm.201012-1949OC.