Research Article

Determinants of Multidrug Resistance Tuberculosis: A Systematic Review and Meta-analysis

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Abstract

Objective: The aim of this systemic review and meta-analysis was to determine demographic, behavioral and clinical risk factors for multiple drug-resistant.

19 studies were included in the systemic review and meta-analysis.

Materials and Methods: Search engines: PubMed/Medline, Web of Science, Scopus and Google scholar were used to search related literatures on MDR TB and selected determinates of MDRTB. All data were independently extracted. We used a random-effects model according to the DerSimonian and Laird method.

Results: The risk of having MDR-TB in patients who have informal education was 0.67 times lower than that of patients who have formal education (RR = 0.67; 95% CI, 0.46 to 0.96).

The risk of having MDR-TB in patients who have Diabetes Mellitus was 1.33 times higher than that of patients who have no Diabetes Mellitus (RR of 1.33 and 95% CI, 1.01 to 1.77).

Conclusion: This systemic review and meta-analysis indicated that the risk of having MDR-TB in patients who have informal education was 0.67 times lower than that of patients who have formal education and the risk of having MDR-TB in patients who have Diabetes Mellitus was 1.33 times higher than that of patients who have no Diabetes Mellitus.

Our review did not showed the presence of association between MDR TB and other selected variables gender, smoking and alcohol.

We recommend interested researchers on MDR TB to do further research on patient's educational level as a risk factor for MDR-TB in order to explain the variation in MDR TB among patients with formal education and patients with informal education.

Keywords: Multidrug Resistance Tuberculosis; Alcohol; Smoking; Diabetes Mellitus; Gender; Educational Status

Introduction

- Multidrug resistance tuberculosis is a tuberculosis caused by a tubercle bacilli that is resistant to isoniazid and rifampicin [1].

- Worldwide, an estimated 10.0 million people diseased with TB in 2018 [2].

- In 2018, WHO reported that there were 484,000 incident cases of MDRTB cases and 44.21 (214,000 deaths) [3].

- In the world, MDR-TB among TB patients who are new cases and previously treated cases was estimated to be 3.5% and 20.5% respectively [4]).

- MDR-TB has received increased attention in Africa and it is under-reported [5,6]

- In Sub-Saharan Africa the magnitude reaches 14% of the world new MDR-TB cases [5].

- In six countries of Africa including (new/retreatment % respectively) Angola (2.6/18%), DR Congo (2.2/17%), Kenya (1.3/9.4%), Nigeria (4.3/25%), Somalia (8.7/47%) and Zimbabwe (4.6/14%) [4].

- In the African Region, the frequency of resistance per country ranged Burundi in the third position with 66% after Rwanda (87%), Democratic Republic of the Congo (68%) [7].

- In Ethiopia prevalence of MDR TB is 2.7% and 14.0% in newly and treated previously TB patients respectively [4].

- In Ethiopia, many of the MDR-TB patients are undiagnosed due to the poor socioeconomic status of people, low level of knowledge and decreased access to health service.

- In Ethiopia the number of patients tested for MDR-TB was < 1% of new cases and < 4% of retreatment cases [8].

- Previous studies identified some risk factors associated with MDRTB like gender [9,10], smoking or other substance misuse [11-13] and diabetes [14].

- Previous studies in Ethiopia and China also reported that HIV/AIDS smoking cigarette, and drinking alcohol, overcrowding, and poor adherence to DOTS (Directly Observed Treatment Short-course) program are factors associated with MDR-TB [15-20].

- Few authors worldwide had the concern of investigating the patient's educational level as a risk factor for MDR-TB [21,22].

Aim of the Study

The aim of this systemic review and meta-analysis was to determine demographic, behavioral and clinical risk factors for multiple drug-resistant TB and for this we have selected two demographic variables gender and educational status, two behavioral factors alcohol and smoking and one clinical factor that is Diabetes Mellitus.

Methodology

Literature search strategy

This systematic reviews and meta analyses was done in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guideline [23] and we have done the search for different literatures that include data on magnitude of MDR-TB in relation to two socio demographic variables gender and educational status, two behavioral variables alcohol and smoking and one clinical variable, Diabetes Mellitus.

Search engines: PubMed/Medline, Web of Science, Scopus and Google scholar were used to search related literatures on MDR TB and selected determinates of MDRTB.

Combination of words used to search were: "MDRTB", "Gender and MDRTB", "Diabetes Mellitus and MDRTB", "alcohol and MDRTB", "educational status and MDRTB" and "smoking and MDRTB".

In addition the reference of selected articles were used to search additional studies not found in our initial search.

Selection/eligibility criteria

Studies that reported five selected determinants of MDR-TB and this are gender, educational status, alcohol, smoking and Diabetes Mellitus and published in English language regardless of the design and setting were included.

Studies were included in the review irrespective of their study year.

Outcome of interest

MDR-TB is TB that caused by strains of *M. tuberculosis* that are resistant to isoniazid and RMP [4,24].

Data extraction and quality assessment

The titles and abstracts were assessed for reporting the outcome and for fulfilling the eligible criteria.

From studies that fulfill the eligible criteria the following data was extracted using prepared form.: Name of author, prevalence of MDR-TB in the selected variables gender, smoking, alcohol, educational status and Diabetes Mellitus.

All data were independently extracted. Returned abstracts were reviewed to check whether they contained relevant information.

Each selected research was assessed using the Newcastle-Ottawa Scale (NOS) for assessing the quality of non randomized studies in meta-analyses [25].

Data analysis

- An outcome of interest was MDR-TB.

- We used a random-effects model according to the DerSimonian and Laird method [26].

- Heterogeneity was assessed by the I^2 and values greater than 50% considered representing significant heterogeneity.

- When there is heterogeneity between studies we used random-effect models [27]. Results were presented in forest plots. Publication bias was assessed using funnel plots and Beggs and eggers regression test

- Analysis was performed using Rev Man software version 5.3 [28].

Results

Studies included

- Our initial search using the search terms gave 1170 articles. Out of these, 559 researches which do not match with the aim of the study were excluded after reviewing their titles and abstracts.

- Then the remaining articles were checked for duplications and 77 articles were selected for full text review.

- Of the 77 articles reviewed in full text, 19 articles [29-47] were included in the final analysis based on the inclusion-exclusion criteria and quality assessment and 58 studies were removed prior to analysis for reasons of not reporting at least one variable from the five selected variables to be studied as determinants of MDRTB

- The selection process of study is presented in figure 1.

Description of findings

- 19 studies were included in the systemic review and meta-analysis [29-47].

- 10 studies measured magnitude of MDR-TB among Informal and/or formal educated patients [29,30,32,33,35,37,38,44,46,47].

- 16 studies measured magnitude of MDR-TB among male and/or female patients [29-40,43,45-47]

- 7 studies measured magnitude of MDR-TB among Diabetes mellitus and/or no diabetes mellitus patients [29,32,36,38,40,42,45]

- 8 studies measured magnitude of MDR-TB among alcohol drinking patients and/or no alcohol drinking patients [29-33,35,45,47]

- 13 studies measured magnitude of MDR-TB among Smoking patients and/or no Smoking patients [29-33,35,37,38,41,42,45-47].

Figure 1: Flow chart for the process of searching, selection and screening of the systemic review and meta-analysis.

Gender and MDR TB

- The meta-analysis of gender and MDR-TB did not demonstrate a statistically significant association of MDR-TB with Gender (An overall RR of 0.96 and 95% CI, 0.86 to 1.07).

- As presented in figure 2, except for three studies [30,38,39], all other studies showed no association of MDR-TB to male or female Patients.

- Heterogeneity testing showed significant variation among the studies (I^2 = 53%).

Educational status and MDR TB

- The risk of having MDR-TB in patients who have informal education was 0.67 times lower than that of patients who have formal education (overall RR = 0.67; 95% CI, 0.46 to 0/96).

Figure 2: Risk ratio of multidrug resistant TB (MDR-TB) in relation to Gender status (Male vs Female), a meta-analysis on Determinates of MDR TB.

- The combined effect size indicated that there is a statistically significant association of MDR-TB with educational status of patients, five studies [30,32,37,46,47] were exceptions.

- There is heterogeneity between the studies (I2 = 84%) (Figure 3).

Source of heterogeneity for educational status and MDRTB

There is a statistical significant association between effect size and magnitude of informal education as shown in the moderator analysis as prevalence of informal education increase, the effect size for MDRTB decrease (B=-3.67, p value < 0.0001).

Figure 3: Risk ratio of multidrug resistant TB (MDR-TB) in relation to educational status (informal education vs formal education), a meta-analysis on Determinates of MDR TB.

Figure 4: Moderator analysis for educational status and MDRTB.

Figure 5: Funnel plot for educational status and MDRTB.

Assessment of publication bias for educational status and MDRTB

We used Beggs test for asymmetry of funnel plot (p value = 0.531) and Eggers regression test (p value 0.903) to test publication bias and both indicated that there is no publication bias for the meta-analysis of educational status and MDRTB.

Alcohol and MDR TB

- The meta-analysis of Alcohol and MDR-TB did not also demonstrate a statistically significant association of MDR-TB with Drinking Alcohol (overall RR of 0.97 and 95% CI, 0.75 to 1.25).

- As presented in figure 6, except for two studies [32,33], all other studies showed no association of MDR-TB to Alcohol drinking patients or No alcohol drinking patients.

- There is Heterogeneity between the studies (I^2 = 74%).

Smoking and MDR TB:
- The meta-analysis of smoking and MDR-TB did not also demonstrate association of MDR-TB with smoking status (an overall RR of 1.18 and 95% CI, 0.87 to 1.60).

- As presented in figure 7, except for five studies [29,32,38,42,47], all other studies showed no association of MDR-TB to smoking patients or no smoking patients.

- There is Heterogeneity between the studies (I^2 = 87%).

Figure 6: Risk ratio of multidrug resistant TB (MDR-TB) in relation to Drinking Alcohol (Drinking Alcohol vs No Drinking Alcohol), a meta-analysis on Determinates of MDR TB.

Figure 7: Risk ratio of multidrug resistant TB (MDR-TB) in relation to smoking status (smoking vs No smoking), a meta-analysis on Determinates of MDR TB.

Diabetes mellitus and MDR TB
- The meta-analysis of Diabetes Mellitus and MDR-TB showed that there is a statistically significant association of MDR-TB with Diabetes Mellitus.

- The risk of having MDR-TB in patients who have Diabetes Mellitus was 1.33 times higher than that of patients who have no Diabetes Mellitus (an overall RR of 1.33 and 95% CI, 1.01 to 1.77).

- As presented in figure 8, except for three studies [29,38,40], all other studies showed no association of MDR-TB to Diabetes Mellitus patients or no Diabetes Mellitus patients.

- Heterogeneity testing showed significant variation among the studies (I^2 = 66%).

Discussion

MDRTB and gender
- The finding of this systemic review and meta-analysis showed that there is no statistical significant difference between male and female with respect to Multi Drug Resistance Tuberculosis and our study is similar with previous studies [29,30,32,33,37,38,48,49].

- Our finding is not similar with previous studies [39,43].

- The explanations for the association between gender and MDRTB in previous studies are socio economic factors, health seeking behavior, prolonged delays in female patients (due to lack of control at household levels on financial resources), increased immune suppression with pregnancy, lactation and increased magnitude of HIV.

Figure 8: Risk ratio of multidrug resistant TB (MDR-TB) in relation to Diabetes Mellitus (Diabetes Mellitus vs No Diabetes Mellitus), a meta-analysis on Determinates of MDR TB.

MDRTB and smoking

- This systemic review and meta-analysis did not indicate the presence of association between smoking and Multi Drug Resistance Tuberculosis.

- Further studies need to be done on smoking and resistance to anti-tuberculosis drugs [32].

- This systemic review and meta-analysis is not similar with previous studies [13,38].

- The reason for the difference in findings might be variation in sample size, study design and study participants characteristics.

Alcohol and MDRTB

- Our finding showed that there is no statistical significant association between MDR TB and drinking alcohol and we could not found similar findings in our search for literature but our findings is not similar with previous studies [49].

- The explanation for the observed association between alcohol and MDR TB in previous studies is that alcohol drinking is associated with elevated probability of MDR-TB due to decreased adherence immunosuppression and adverse drug effects.

- Drinking Alcohol was associated with increased risk of MDR-TB [37].

Diabetes mellitus and MDRTB

In our systemic review and meta-analysis there is an association between Diabetes Mellitus and MDR TB and our finding is similar with previous studies [29].

Educational status and MDRTB

- Our systemic review and meta-analysis indicated that the risk of having MDR-TB in patients who have informal education was 0.67 times lower than that of patients who have formal education (overall RR = 0.67; 95% CI, 0.46 to 0/96) and our finding is consistent with previous studies [38,39,42].

- This study is not similar with previous studies [49].

- The possible explanation for difference in findings between our review and other studies might be difference in study participants characteristics, sample size and study areas.

Conclusion

- This systemic review and meta-analysis indicated that the risk of having MDR-TB in patients who have informal education was 0.67 times lower than that of patients who have formal education and the risk of having MDR-TB in patients who have Diabetes Mellitus was 1.33 times higher than that of patients who have no Diabetes Mellitus.

- Our review did not showed the presence of association between MDR TB and other selected variables gender, smoking and alcohol.

- We recommend interested researchers on MDR TB to do further research on patient's educational level as a risk factor for MDR-TB in order to explain the variation in MDR TB among patients with formal education and patients with informal education.

Data Availability

All data are included in the paper.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

- Kaleab Tesfaye Tegegne was responsible for conceptualization, project administration, software, supervision, and development of the original drafting of the manuscript.

- Kaleab Tesfaye Tegegne, Eleni Tesfaye Tegegne, Abiyu Ayalew Assefa, Mekibib Kassa Tessema, Berhanu Bifato, Alelign Tadele Abebe, Muse Rike and Andualem Zenebe were participated in quality assessment of articles, methodology, validation, and screening of research papers

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