INTRODUCTION: Tuberculosis infection caused by Mycobacterium tuberculosis is one of the most common infectious diseases, especially in countries such as Iran. The course of treatment and the number of drugs used vary depending on the severity of the disease and the parts of the body involved. The resistant tuberculosis to treatment has increased in recent years. Thus, this study was conducted to investigate the frequency distribution of response to treatment of patients with tuberculosis in Sirjan, Iran.

METHODS: This descriptive cross-sectional study investigated all patients with tuberculosis in Sirjan city who had referred to health centers during the years 2011-2019. The data collection tool was a pre-prepared checklist that included information on age, sex, sputum smear results, sputum culture results, diabetes, patients' nationality, drug side effects, and response to treatment. Finally, data was entered into SPSS version 22, and analyzed.

RESULTS: In this study, the overall response rate was 83% and the mortality rate was 10%. Between the frequency distribution of response to treatment in terms of gender, age, sputum smear results, sputum culture results, diabetes, patients' nationality, drug side effects, and response to treatment. Also, no statistically significant difference was found between the frequency distribution of pulmonary TB treatment response in terms of drug allergy, drug hepatitis and other drug side effects.

CONCLUSION: According to results, can be concluded that none of the variables: age, sex, smear and culture result, and history of diabetes have no an effect on response to treatment and mortality of tuberculosis.
1. INTRODUCTION

The mortality rates of TB remain high around the world, despite attempts to eradicate tuberculosis (TB). This issue is still among the world's top ten causes of death [1-4]. A significant predictor of TB control systems is the treatment impact. Patients who have failed TB therapy are more likely to develop tuberculosis resistant to drugs [5, 6]. Elder age, type of tuberculosis disease, prior tuberculosis cure, very low income, incomplete contact to transport, distance from treatment center to the home, low information about the disease and its dealing, partial public funding, multidrug high resistance, and comorbidity specially with HIV have all been investigated to be associated with ineffective treatment consequences [7-12].

The ultimate goal of the strategy to end the global TB epidemic by 2035 is to reduce TB-related deaths by 95% and the prevalence rate of TB by 90% [13, 14]. Understanding the factors related to the outcomes of TB treatment is critical. Thus, this study was conducted to investigate the frequency distribution of response to treatment of patients with tuberculosis in Sirjan, Iran.

2. METHODS

This cross-sectional study was conducted in all patients with tuberculosis (95 cases) referred to health centers in Sirjan, Iran during 2011-2019. Sirjan population in 2019 was 299716. Tuberculosis affects about 16,000 Iranian people and killed about 2000 people each year (For Sirjan almost 8 cases/year). The treatment protocol included rifampicine and isoniazid as the first line of treatment. Pyrazinamide also reduced the duration of treatment to six months. Another effective first-line drug is ethambutol, which prevented the formation of resistant tuberculosis when added to the diet. Exclusion criteria included patients' dissatisfaction for participating in the study and patients with a history of drug allergy to first-line TB drugs.

Informed consent was obtained from all eligible patients. Patients' confidentiality was maintained in accordance with the Helsinki convention, and individuals were assured that their information would be confidential and would only be used for research purposes. Also, patients will not incur any additional costs in conducting this research. Our university ethics committee confirmed this study.

The frequency of non-response to treatment was assessed based on microbiological or clinical tests or other tests. Questionnaire information were including age, sex, nationality, smear at the beginning of treatment, smear at the end of the second month, smear at the end of the fourth and sixth months, patients 'deaths and patients' treatment status (success therapy, failure therapy, transfer to other centers, absence from treatment and treatment complications). Thus, resistant cases were identified and their frequency was compared based on age, sex, positive smear or negative smear. Indeed, analysis of the patients’ record (death and other records) was performed in this research.

Finally, the information was entered in SPSS software (version 22). Percentage, mean and standard deviation criteria were used for descriptive analysis.

3. RESULTS

This study was performed on 95 patients with tuberculosis, of which 49 (46.55%) were male and 46 (53.45) were female. Sputum smear was positive in 66% of patients and negative in 34%. There was a history of diabetes in 33% and a history of contact with the infected person in 43% of patients.

Table 1. Response to treatment based on gender and age

| Gender | Complete recovery | Lack of recovery | Death | Total |
|--------|------------------|-----------------|-------|-------|
| Female | 36 (77)          | 5 (11)          | 3 (6) | 44 (100) |
| Male   | 42 (89)          | 2 (4)           | 6 (13) | 50 (100) |
| Total  | 78 (83)          | 6 (7)           | 9 (10) | 59 |

| Age    | Complete recovery | Lack of recovery | Death | Total |
|--------|------------------|-----------------|-------|-------|
| 59-89 years | 39 (76)          | 4 (8)           | 8 (16) | 51 (100) |
| 11-49 years | 40 (93)          | 2 (5)           | 1 (2)  | 43 (100) |
| Total  | 79 (84)          | 6 (6)           | 9 (10) | 92 |
Among patients, 98% were treated with the four drugs isoniazid, rifampin, pyrazinamide, ethambutol and 2% were treated with multi-drug resistant (MDR). After starting drug treatment, drug allergy was observed in 9.5% and drug hepatitis in 12% of patients. Also, 12% of patients showed other reactions to the drug. No significant difference was found between response to treatment and parameters of gender and age (Table 1). Also, there was no significant difference between smear results and sputum culture with response to treatment (Table 2). Also, the difference in response to TB drug treatment in terms of diabetes (p=0.315) and drug allergy (p=0.166) was investigated and no significant relationship was found. Finally, no significant difference was found between the frequency distribution of TB treatment response in terms of drug hepatitis complication and other drugs side effects (Table 3).

## 4. DISCUSSION

At present study, the overall response rate to treatment was 83% and the mortality percentage was 10%. Between the frequency distribution of response to treatment based on gender, age, sputum smear results, sputum culture results, patients’ nationality and diabetes was not statistically notable difference. Also, no statistically significant difference was found between the frequency distribution of pulmonary TB treatment response based on drug allergy, drug hepatitis and other drug side effects. The main limitations in present study were drug consumption without a doctor’s prescription and also incomplete patient information.

A research in Busan, South Korea, found that the overall success rate for treatment was 83.9% and 8% of patients died. Also, female gender was correlated with lower mortality. Age (~ 75 years) and smear-positive TB were related to upper mortality [1]. The cure success rates were 95.02% for smear-positive patients and 95% for smear-negative patients in another study in Anqing, China. In addition, curing as ineffective among patients with negative smear was strongly correlated with age over 45 years, full-period treatment care model, uncontrolled chest X-ray, existence of chest X-ray miliary effect and period above 51 days [6]. The good treatment result percentage in Hamadan province, Iran was 83.1% and 9.4% of the patients died through the study period [13]. Ethiopia Mainstream 333 (94.6%) of TB treatment results were also effective in Addis Ababa, i.e. either healed or effectively fulfilled treatment, while only 19 (5.4%) of therapies were ineffective [15].

In Bahawalpur, Pakistan the success percentage of treatment was 67.8% for new patients with TB and retreating individuals and almost 69% for TB patients with smear positive. The older cases, retreatment patients and

| Drug hepatitis | No n (%) | Yes n (%) | Total n (%) | p-value |
|----------------|----------|-----------|-------------|---------|
| Complete recovery | 72 (86) | 7 (64) | 79 (83) | 0.165 |
| Lack of recovery | 5 (6) | 2 (18) | 7 (7) | |
| Death | 7 (8) | 2 (18) | 9 (10) | |
| Total | 84 (100) | 11 (100) | 95 (100) | |

| Other side effects | No n (%) | Yes n (%) | Total n (%) | p-value |
|--------------------|----------|-----------|-------------|---------|
| Complete recovery | 69 (82) | 10 (90.9) | 79 (83) | 0.584 |
| Lack of recovery | 8 (9) | 1 (9.1) | 9 (7) | |
| Death | 9 (11) | 0 (0) | 9 (10) | |
smokers were at bigger risk of having ineffective treatment results [2].
Inclusion criteria for the current study caused that did not make a statistical difference between the variables and outcomes of treatment.

5. CONCLUSIONS
Age, sex, smear and culture result, and history of diabetes have no an effect on response to treatment and mortality from tuberculosis. Therefore, other underlying diseases may also be effective in responding to treatment, and treatment should continue as before and also it is essential to investigate the more parameters.

6. REFERENCES
1. Mok J, An D, Kim S, Lee M, Kim C, Son H. Treatment outcomes and factors affecting treatment outcomes of new patients with tuberculosis in Busan, South Korea: a retrospective study of a citywide registry, 2014-2015. BMC Infect Dis. 2018;18(1):655. doi: 10.1186/s12879-018-3574-y.
2. Atif M, Anwar Z, Fatima RK, Malik I, Aqhar S, Seahill S. Analysis of tuberculosis treatment outcomes among pulmonary tuberculosis patients in Bahawalpur, Pakistan. BMC Res Notes. 2018;11(1):370. doi: 10.1186/s13104-018-3473-8.
3. Tola A, Mishore KM, Ayele Y, Mekuria AN, Legese N. Treatment Outcome of Tuberculosis and Associated Factors among TB-HIV Co-Infected Patients at Public Hospitals of Harar Town, Eastern Ethiopia: A five-year retrospective study. BMC Public Health. 2019;19(1):1638. doi: 10.1186/s12889-019-7980-x.
4. Mohammed T, Daniel K, Helamo D, Letu T. Treatment outcomes of tuberculosis patients in rift Eleni Mohammed general hospital, hoassa, southern nations, nationalities and peoples region, Ethiopia: a five year (June 2009 to August 2014) retrospective study. Arch Public Health. 2017;75:16. doi: 10.1186/s13690-017-0184-x.
5. Gao J, Ma Y, Du J, Zhu G, Tan S, Fu Y, et al. Later emergence of acquired drug resistance and its effect on treatment outcome in patients treated with Standard Short-Course Chemotherapy for tuberculosis. BMC Pulm Med. 2016;16:26. doi: 10.1186/s12890-016-0187-3.
6. Wen Y, Zhang Z, Li X, Xia D, Mo J, Dong Y, et al. Treatment outcomes and factors affecting unsuccessful outcome among new pulmonary smear positive and negative tuberculosis patients in Anqing, China: a retrospective study. BMC Infect Dis. 2018;18(1):104. doi: 10.1186/s12879-018-3019-7.
7. Gebrezgiabher G, Romha G, Ejeta E, Asebe G, Zemene E, Ameni G. Treatment Outcome of Tuberculosis Patients under Directly Observed Treatment Short Course and Factors Affecting Outcome in Southern Ethiopia: A Five-Year Retrospective Study. PLoS One. 2016;11(2):e0150560. doi: 10.1371/journal.pone.0150560.
8. Ahmad T, Haroon, Khan M, Khan MM, Ejeta E, Karami M, Ohia C. Treatment outcome of tuberculosis patients under directly observed treatment short course and its determinants in Shangla, Khyber-Pakhtunkhwa, Pakistan: A retrospective study. Int J Mycobacteriol. 2017;6(4):360-4. doi: 10.4103/ijmy.ijmy_69_17.
9. Ejeta E, Beyene G, Balay G, Bonsa Z, Abebe G. Factors associated with unsuccessful treatment outcome in tuberculosis patients among refugees and their surrounding communities in Gambella Regional State, Ethiopia. PLoS One. 2018;13(10):e0205468. doi: 10.1371/journal.pone.0205468.
10. Dale D, Nega D, Yimam B, Ali E. Predictors of poor tuberculosis treatment outcome at Arba Minch General Hospital, Southern Ethiopia: a case-control study. J Tuber Dis. 2017;2(1):110.
11. Feltzer K, Leow JS. Prevalence and factors associated with tuberculosis treatment outcome among hazardous or harmful alcohol users in public primary health care in South Africa. Afr Health Sci. 2014;14(1);157-66. doi: 10.4314/ahs.v14i1.24.
12. Getie A, Alemnew B. Tuberculosis Treatment Outcomes and Associated Factors Among Patients Treated at Wolde General Hospital in Northeast Ethiopia: An Institution-Based Cross-Sectional Study. Infect Drug Resist. 2020;13:3423-9. doi: 10.2147/IDR.S275568.
13. Khazaei S, Hassanzadeh J, Rezaeian S, Ghaderi E, Khazaei S, Hafshejani AM, et al. Treatment outcome of new smear positive pulmonary tuberculosis patients in Hamadan, Iran: A registry-based cross-sectional study, Egypt J Chest Dis Tuberc. 2016;65(4):825-30. doi: 10.1016/j.ejctd.2016.05.007.
14. Korhonen V, Lytyikkäinen O, Ollgren J, Soini H, Vasankari T, Rautu P. Risk factors affecting treatment outcomes for pulmonary tuberculosis in Finland 2007-2014: a national cohort study. BMC Public Health. 2020;20(1):1250. doi: 10.1186/s12889-020-0960-7.
15. Fentie AM, Jorgi T, Assefa T. Tuberculosis treatment outcome among patients treated in public primary healthcare facility, Addis Ababa, Ethiopia: a retrospective study. Arch Public Health. 2020;78(12). doi: 10.1186/s13690-020-0393-6.