

Epidemiology and Survival of the Patients with Tuberculosis Covered by the Zabol Tuberculosis Center from 2006 to 2014

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Abstract

Background: Tuberculosis (TB) primarily targets the lungs and stands as the leading cause of death globally among diseases caused by a single agent. It is estimated that one-third of the world's population is infected with TB. This study was undertaken due to the significant presence and incidence of TB in Zabol, an endemic city in Iran.

Methods: We examined patient records (n=4092) spanning from 2006 to 2014, analyzing the data using SPSS. The Kaplan-Meier model was employed to assess patient survival rates, the Cox regression model helped identify factors affecting survival and mortality, and the classic Mantel-Haenszel method was utilized to calculate the mortality rate.

Results: The patients' mean age was 53.97 years, with a standard deviation of 20.55. Females comprised 59.78% of the study population, and 84.93% of the TB cases were pulmonary. Furthermore, 89.85% of the patients underwent successful treatment. Throughout the study period, there were 240 recorded deaths among TB patients. The average survival duration for patients was 2638 days, with a five-year survival rate of 75%. An increase in age every 10 years significantly raised the risk of death among TB patients ($P < 0.05$). However, no significant impact on patient survival was observed in relation to other variables, such as gender, history of recurrence, treatment delay, place of conflict, residency, and nationality.

Conclusion: The findings of this study can provide useful information so that planners and health officials can take effective measures with appropriate interventions in order to diagnose the disease faster and follow up with appropriate treatment.

Keywords: Epidemiology, Tuberculosis, Survival analysis

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Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (1), ranks among the oldest and most well-known diseases affecting humans worldwide. Following HIV infection, it is the leading cause of death from single-agent diseases globally (1). TB is generally divided into two categories: pulmonary TB, which primarily affects the lungs and is more common, and extrapulmonary TB, which can affect either a single organ or multiple organs other than the lungs; indeed, over a third of TB cases involve organs other than the lungs (2). Prior to the HIV epidemic, approximately 80% of new TB cases were limited to the lungs. Nonetheless, in the context of concurrent HIV and TB infection, two-thirds of patients suffer from both pulmonary and extrapulmonary TB, including those with only the extrapulmonary form (1). If TB, caused by drug-sensitive strains, receives proper treatment, it is nearly always curable; without treatment, however, the disease can prove fatal within five years for 50%-65% of patients (1).

TB ranks as the second leading cause of death from infectious agents, following HIV. The latest World Health Organization (WHO) statistics from 2021 report 10.6 million new TB cases (both pulmonary and extrapulmonary) and 1.6 million deaths, with 187000 of these deaths occurring in individuals also infected with HIV (3). The highest incidence of TB and AIDS co-infection has been observed on the African continent (4). The death toll from TB has risen from 1.97 million individuals in 2010 to 1.3 million in 2022 (5). TB remains a leading cause of death among women of reproductive age.

Recognizing the significance and urgency of addressing TB and its control, the WHO designated this disease as the sixth goal of the United Nations Millennium Development Goals in 2015. The aim is to achieve a 90% reduction in both the prevalence and mortality rates of TB by 2030, relative to 2015 levels, worldwide (5).

TB is ranked seventh in terms of its global burden and is projected to maintain this position through 2020 (6).



It is estimated that one-third of the global population is infected with *M. tuberculosis*, with a significant number residing in developing countries, such as Iran; Africa and Southeast Asia report the highest numbers of TB cases (2).

TB is predominantly a chronic disease that disproportionately affects individuals in lower socio-economic classes, largely because these individuals struggle to adhere to their treatment regimens due to the financial burden. Moreover, over 90% of TB-related illnesses and deaths occur in developing countries, where 75% of TB cases involve individuals aged 15-45 years, the most economically active segment of the population (2,5,6). If current control measures are not enhanced, it is estimated that approximately 100 million people will contract new TB infections, 150 million will be infected, and 39 million will succumb to the disease (4).

The WHO's latest reports from 2022 indicate an expected TB rate of 11 cases per 100 000 people in Iran, identifying nearly 10 000 new cases, predominantly among those aged over 65 years (5,7,8). According to the 2021 report from Iran's General Directorate of TB and Leprosy at the Ministry of Health and Medical Education, the incidence rate of pulmonary TB with a positive sputum smear stood at 4.6 cases per 100 000 people. Of the total 7298 TB cases reported in Iran in 2022, 44% were female, and 23% were non-Iranian (mostly Afghans), with the highest incidence observed in the age group of 65 years and older (9). Given that disease can only be fully eradicated through a combination of clinical and epidemiological approaches and that a clinical approach alone is insufficient for tackling TB, understanding its epidemiology is essential.

To control TB effectively, it's essential to incorporate activities that enhance the timely detection and effective treatment of patients within each country. Epidemiological studies play a crucial role in developing a comprehensive disease control program within the TB control strategies of various countries. Consequently, this study was carried out to address the significance and prevalence of TB in the Zabul region.

Methods

The study adopted a retrospective cohort design, focusing on a cohort of pulmonary and extrapulmonary TB patients registered at the TB center in Zabul city from 2006 to 2014. The inclusion criterion was a TB infection between 2006 and 2014. Exclusion criteria included no migration and failure to initiate or continue treatment. Patients were followed until their death, withdrawal from the study, or until the current time, with relevant data being extracted for analysis.

This study utilized a census method to examine all patients diagnosed with TB in Zabul from 2006 to 2014 who were registered at the TB offices of the TB center. The principal investigator first visited the TB coordinating

center in Zabul city to gather necessary information via the patient registration offices or through general profile registration software. Additional details were obtained from records available at the TB center. For patients who had completed their treatment, the researcher located their addresses and phone numbers through the healthcare center responsible for their care and gathered information either by phone or in person. Patients were monitored until their death or withdrawal from the study, and their data were documented.

All necessary information was gathered using a checklist derived from the patient's files. This checklist captured details such as age, sex, date of symptom onset, treatment initiation and cessation dates, place of residence, treatment group, TB recurrence, patients' nationality, survival status, and date of death, where applicable.

The data were coded and entered into SPSS by an individual in a single-blind manner for statistical analysis. The Kaplan-Meier model was employed to assess patient survival rates, while the Cox regression model was utilized to identify factors affecting survival and mortality. The Cochran-Mantel-Haenszel method was applied to ascertain the mortality rate across different subgroups. The mortality rate was calculated by dividing the number of deaths by the total population over the study period.

Results

In this study, the files of 4290 TB patients from the years 2006 to 2014 were reviewed. Patients were included from the onset of their symptoms. A total of 198 patients with incomplete information were excluded, leaving 4092 patients for examination. The mean age of these patients was 53.97 ± 20.55 years. Additionally, 59.78% of the patients were women, and 84.93% had pulmonary TB. Furthermore, 85.89% of the patients belonged to treatment group 1, which included those treated with a 4-drug regimen, while 10.15% were in treatment group 2, encompassing cases of treatment absence and failure. Also, 26.79% of patients resided in urban areas, 72.77% in rural areas, and 0.44% lived outside of Iran. A history of TB recurrence was noted in 4.03% of the patients, with 87.78% being Iranian and 12.22% Afghan (Table 1).

During the research period, 240 deaths among TB patients were recorded. Figure 1 illustrates the survival time of the patients, with an average survival time of 2638 days. This indicates that 50% of the patients survived up to 2,638 days after symptom onset. The 5-year survival rate of patients was 75%, meaning 75% of patients were alive after 5 years. The number of surviving patients at the end of each year is detailed in Table 2. According to Table 3, the mortality rate during the study period was 0.18 deaths per thousand people per year, with rates of 0.22 for men and 0.16 for women per thousand people per year. Thus, monitoring a thousand TB patients for one year would result in 0.22 deaths for men and 0.16

Table 1. Frequency of investigated variables in patients with tuberculosis

| Variable | | Frequency | Percent |
|--------------------------|----------------|-----------|---------|
| Gender | Male | 1646 | 40.22 |
| | Female | 2446 | 59.78 |
| History of TB recurrence | No | 3927 | 95.97 |
| | Yes | 165 | 4.03 |
| Involvement area | Pulmonary | 3403 | 84.93 |
| | Extrapulmonary | 604 | 15.07 |
| Treatment group | 1 | 3656 | 89.85 |
| | 2 | 413 | 15.10 |
| Place of residence | Urban | 1094 | 26.79 |
| | Rural | 2971 | 72.77 |
| | Living abroad | 18 | 0.44 |
| Nationality | Iranian | 3591 | 87.78 |
| | Afghan | 500 | 12.22 |

for women. The mortality rate was 19 for Iranians and 18 for Afghans per thousand people per year. In urban and rural areas, the rates were 20 and 18 deaths per thousand people per year, respectively. The mortality rate for groups 1 and 2 was 18 and 24 deaths per thousand person-years, respectively. Concerning the type of TB, the mortality rate for pulmonary TB was 19 deaths, and for extrapulmonary TB was 17 deaths per thousand people per year. For individuals with a history of TB recurrence, the mortality rate was 31, compared to 18 per thousand people per year for those without such a history (Table 3).

Table 4 shows the effect of different factors on the death of TB patients. Regarding gender, the risk of death was higher in men than in women, indicating lower survival rates in men, although this was not statistically significant ($P > 0.05$). However, the incidence of TB was higher among women. A delay in treatment of up to two years did not significantly affect the risk of death for TB patients. Additionally, concerning the type of TB (pulmonary or extrapulmonary) and its impact on patient survival, extrapulmonary TB was associated with reduced survival rates in patients, yet this finding was not statistically significant ($P < 0.05$). With respect to the effect of treatment groups on survival, patients in treatment group 2, which included cases of treatment absence and failure, exhibited decreased survival compared to those in group 1, but this difference was not statistically significant ($P > 0.05$). In terms of residency, living in rural areas was associated with reduced survival rates, although this was not statistically significant ($P > 0.05$). Regarding nationality, Afghan patients had lower survival rates than Iranian patients, but this difference was not statistically significant ($P > 0.05$).

Discussion

This study analyzed the records of 4092 TB patients from 2006 to 2014. The average survival duration of the

Table 2. A survival rate of TB patients diagnosed between 2006 and 2014 in Zabul

| Year | Survival rate |
|--------------|---------------|
| First year | 0.9327 |
| Second year | 0.8779 |
| Third year | 0.8391 |
| Fourth year | 0.8391 |
| Fifth year | 0.7552 |
| Sixth year | 0.7552 |
| Seventh year | 0.7552 |
| Eighth year | 0.3776 |
| Ninth year | 0.3776 |

Curve 1: Survival rate of TB patients diagnosed from 2006 to 2014.

patients was 2638 days, and their 5-year survival rate was 75%. An increase in age every 10 years significantly raised the risk of death for TB patients ($P < 0.05$). Other variables, including gender, history of recurrence, delay in treatment, area of involvement, place of residence, and nationality, did not significantly impact patient survival.

The average age of the patients was 53.97 years, aligning with studies conducted in Birmingham, UK, where the highest incidence was in the age group of 45-64 years (10), and in America, where 68% of patients were aged 18-60 years (11). In Sofian and colleagues' research, the average age reported was 52.91 years, similar to this study (12). Rastegari and colleagues' study in Mashhad reported an average age of 64.65 years (13). The occurrence of TB in older age groups may be attributed to a decline in immune system efficiency, an increase in comorbidities, malnutrition, low literacy rates, more atypical disease manifestations, and delays in seeking healthcare services (14,15).

In our study, the prevalence of TB was higher among women, with 59.78% of the patients being female and 40.22% male. This finding aligns with Fader and colleagues' study in Kabul, Afghanistan, which reported a higher incidence of TB in women compared to men (16). Similarly, studies conducted by Rajabi and Abazari in Bam (17), as well as research in Arak city (12), Golestan province (18), Ardabil city (19), Shahriar city (20), and Metanat and colleagues' study in Zahedan (6), found TB to be more prevalent in women than in men. However, this contrasts with findings from Maryland, the United States (11), the United Kingdom (21), Turkey (22), and studies by Yazdani Charati et al in Mazandaran (23), Khazaei et al in Hamadan (24), and Gholami et al in Ardabil (25), where the rate of TB in men was higher than in women. According to WHO reports, TB tends to be more common in women than in men in Afghanistan and some border regions of Iran, possibly due to factors

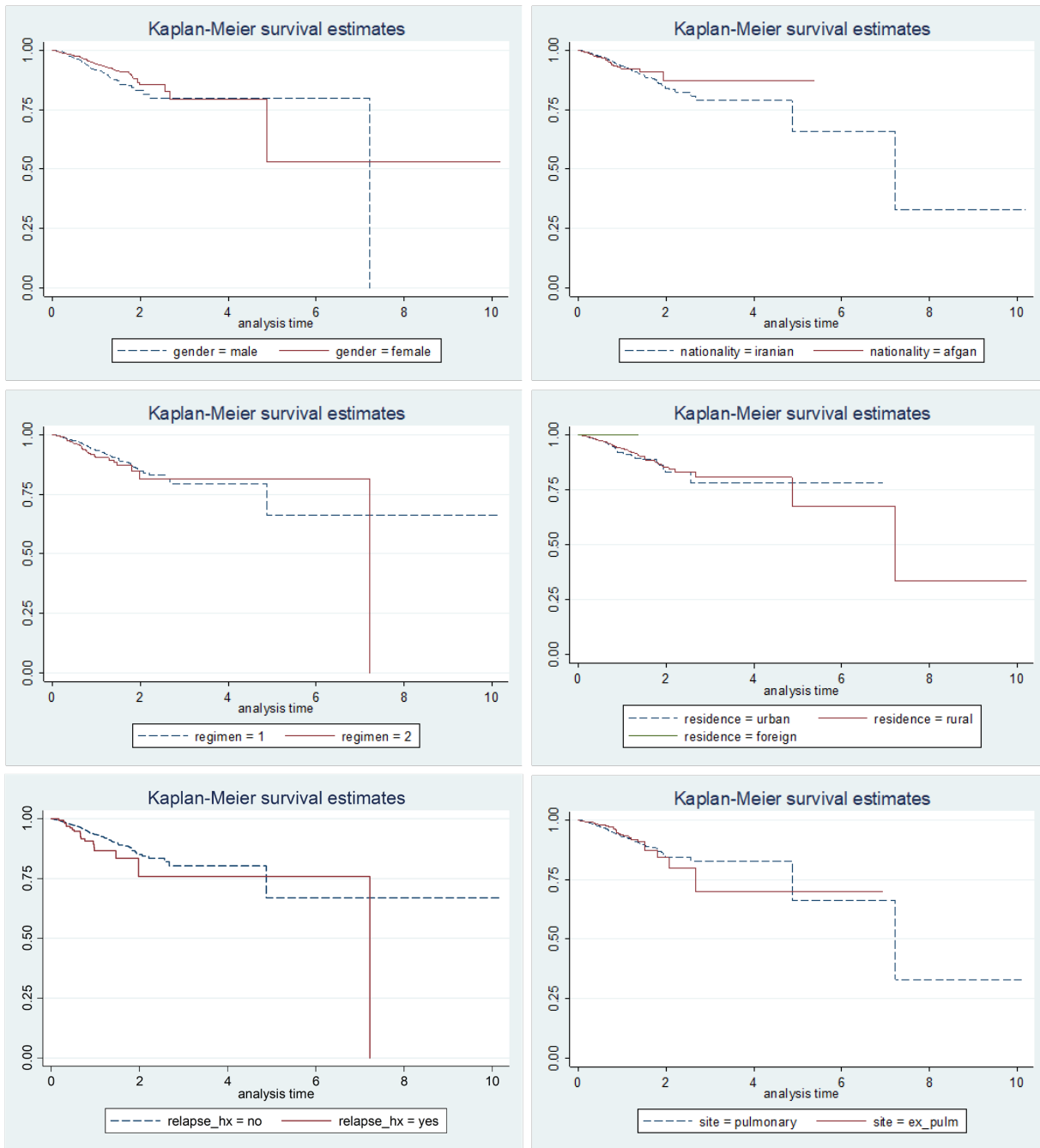


Figure 1. Survival time curve of TB patients by demographic and disease-related factors

such as malnutrition, insufficient food supply, and higher prevalence of diabetes in women (26). Dokht Forozani and colleagues' study highlighted malnutrition as a significant nutritional issue among women in Zabol city (27). In our research, 26.79% of TB patients lived in urban areas, 72.77% in rural areas, and 0.44% outside of Iran, with survival rates being lower among rural residents. This finding contrasts with studies in Mazandaran province by Yazdani Charati et al (23), in Hamadan (24), and in Ardabil (25). The disparity could be attributed to the proximity of many villages in Zabol to Afghanistan, inadequate hygiene practices, the presence of extremely

marginalized villages, and poverty (28).

In terms of treatment groups, 85.89% of the patients were in treatment group 1, and 10.15% were in treatment group 2. This distribution aligns with the findings from the United Kingdom, where 82.5% of patients underwent successful treatment, reflecting the efficacy of treatment systems in patient care (29). Similarly, in Hamburg, Germany, 80.3% of patients experienced successful TB treatment outcomes (30), and in France, 70% of patients had successful treatment results (31). Comparable statistics were reported by Sofian et al in Arak, with 86.5% of patients successfully treated (12). In Rasht city, 68.2%

Table 3. The death rate of patients per thousand people per year during the study period

| | | Number of deaths | The number of people at risk | Death rate (thousands per year) | 95% confidence interval |
|-----------------------|----------------|------------------|------------------------------|---------------------------------|-------------------------|
| Gender | Male | 117 | 521.83 | 0.22 | 0.19-0.27 |
| | Female | 121 | 762.33 | 0.16 | 0.13-0.19 |
| Nationality | Iranian | 211 | 1.1e+0.3 | 0.18 | 0.16-0.21 |
| | Afghan | 27 | 152.87 | 0.17 | 0.12-0.25 |
| Place of residence | Urban | 70 | 342.60 | 0.20 | 0.16-0.25 |
| | Rural | 168 | 933.64 | 0.17 | 0.15-0.20 |
| | Living abroad | 0 | 4.83 | 0.00 | 0 |
| Treatment group | 1 | 201 | 1.1e+0.3 | 0.17 | 0.15-0.20 |
| | 2 | 36 | 149.44 | 0.24 | 0.17-0.33 |
| TB type | Pulmonary | 199 | 1.1e+0.3 | 0.18 | 0.16-0.21 |
| | Extrapulmonary | 32 | 183.95 | 0.17 | 0.12-0.24 |
| History of recurrence | No | 219 | 1.2e+0.3 | 0.17 | 0.15-0.20 |
| | Yes | 19 | 60.15 | 0.31 | 0.20-0.49 |

Table 4. Factors affecting the death of TB patients

| Variable | Crude hazard ratio | P value | 95% confidence interval | | Variable | Adjusted hazard ratio* | P value | 95% Confidence interval | |
|------------------------------------|--------------------|---------|-------------------------|------|------------------------------------|------------------------|---------|-------------------------|------|
| Female gender | 0.70 | 0.008 | 0.54 | 0.91 | Female gender | 0.83 | 0.17 | 0.64 | 1.08 |
| History of recurrence | 1.76 | 0.017 | 1.10 | 2.82 | History of recurrence | 1.58 | 0.05 | 0.99 | 2.53 |
| Every two years delay in treatment | 0.53 | 0.105 | 0.25 | 1.14 | Every two years delay in treatment | 0.49 | 0.066 | 0.23 | 1.04 |
| Extrapulmonary TB | 0.93 | 0.719 | 0.64 | 1.35 | Extrapulmonary TB | 1.3 | 0.175 | 0.88 | 1.90 |
| Treatment group 2 | 1.34 | 0.1 | 0.94 | 1.92 | Treatment group 2 | 1.18 | 0.342 | 83/0 | 1.69 |
| Rural residence | 0.86 | 0.296 | 0.65 | 1.13 | Rural residence | 0.78 | 0.08 | 0.59 | 1.02 |
| Afghan nationality | 0.94 | 0.787 | 0.63 | 1.41 | Afghan nationality | 1.21 | 0.337 | 0.81 | 1.82 |
| Every 10 years of increase in age | 1.36 | 0 | 0.26 | 1.47 | Every 10 years of increase in age | 1.35 | 0 | 1.25 | 1.47 |

of patients received successful treatment, with 39.8% belonging to group 2 (32). In Ethiopia, 64.6% of patients were successfully treated (33). However, a study in India showed that only 48% of patients were in treatment group 1 (34), a variation that may stem from differences in treatment systems, challenges in implementing the DOTS system, or suboptimal hygiene standards.

Regarding the type of TB involvement, 84.93% of patients had pulmonary TB, and the remaining 15.07% had extrapulmonary TB, confirming the global prevalence of pulmonary TB as the more common form (1). Additionally, according to the most recent statistics from the Department of TB and Leprosy of the Ministry of Health in 2014, extrapulmonary TB represented 2795 of the total 10044 TB cases (35).

As for the survival rate, the median survival time for the patients was 2638 days, and the 5-year survival rate was 75%. In our study, survival decreased with every 10-year increase in age. This finding is consistent with studies from Mexico and India (14,15), Spain and Vietnam (36,37), and a study by Moosazadeh et al on 946 patients registered in the TB registry software in Iran (38). The

observed trend may be attributed to an increase in drug resistance and a higher prevalence of comorbidities.

Regarding the impact of gender on the survival of TB patients, survival rates were higher in women than in men (26), although this difference was not statistically significant. This outcome aligns with studies from India and Ireland, where no significant correlation between gender and the survival rate of the disease was found (39,40). In terms of nationality, survival rates in Afghan patients were lower compared to Iranians, yet this difference was not statistically significant. Regarding residence, living in rural areas was associated with reduced patient survival, but this observation was not statistically significant. Concerning the impact of the treatment group on survival, being in treatment group 2, which includes cases of absence from treatment and treatment failure, was associated with decreased survival, though this was not statistically significant. However, studies in India (15), Ireland (40), and Iran (38) have shown that absence from treatment and treatment failure are linked to reduced survival. The effect of the TB involvement area

on patient survival indicated that extrapulmonary TB led to decreased survival rates, but this was not statistically significant.

Limitations of the study

Our study faced limitations, including missing data in patient files within the TB center archives, particularly information from previous years, difficulties in locating patients or their families treated many years ago, and incomplete data for 2015.

Conclusion

This study identified increasing age as a factor contributing to the mortality of TB patients in Zabul. Based on the findings of this and other studies, we recommend greater emphasis on disease detection planning and conducting screenings in older age groups, especially in rural and underserved areas, to aid in TB prevention and the identification of TB patients. Additionally, enhancing public awareness through mass media, education, and continuous evaluation can play a crucial role in reducing TB incidence. The insights from this study offer valuable information that can assist planners and health officials in implementing effective strategies for quicker diagnosis and proper treatment follow-up.

Authors' Contribution

Conceptualization: Nasim Safa.

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Formal analysis: Fateme Safa, Kimia Hajizadeh.

Investigation: Adele Khodabakhshi.

Methodology: Nasim Safa.

Project administration: Adele Khodabakhshi.

Software: Adele Khodabakhshi.

Supervision: Adele Khodabakhshi.

Validation: Fateme Safa.

Visualization: Adele Khodabakhshi.

Writing—original draft: Nasim Safa.

Writing—review & editing: Adele Khodabakhshi, Kimia Hajizadeh.

Competing Interests

The authors declare that they have no competing interests.

Ethical Approval

This research received approval from the Ethics Committee of the Kerman University of Medical Sciences (KNRC/97-88/EC). Ethical considerations were strictly adhered to; all provided information was kept confidential, and the results were reported in a generalized and anonymous manner.

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