

FACTORS INFLUENCING POOR ADHERENCE LEADING TO POOR OUTCOMES IN TUBERCULOSIS TREATMENT: A CROSS-SECTIONAL STUDY

Original Research

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ABSTRACT

Background: Tuberculosis (TB) remains one of the leading causes of infectious disease-related mortality worldwide. Despite the availability of effective first-line antituberculous therapy, non-adherence continues to undermine treatment success, leading to prolonged infectiousness, drug resistance, and disease relapse. Multiple behavioral, clinical, and logistical factors influence adherence levels, particularly in low-resource settings. Understanding these factors is vital for improving treatment compliance and strengthening TB control strategies at the regional level.

Objective: To determine the prevalence and major contributing factors associated with non-adherence to anti-tuberculous treatment among patients attending a tertiary care hospital in Peshawar, Pakistan.

Methods: A cross-sectional study was conducted from 21st December 2024 to 20th April 2025 at the Department of Pulmonology, Hayatabad Medical Complex, Peshawar. A total of 181 male and female patients aged 20–60 years with poor adherence to antituberculous treatment were enrolled using a convenient sampling technique. Factors evaluated included pill burden, medication adverse effects, concurrent medical illness, forgetfulness, and transportation difficulties. Data were collected through structured interviews, transcribed into English, and analyzed using SPSS version 26. Continuous variables were expressed as mean \pm SD, while categorical variables were reported as frequencies and percentages.

Results: The mean age of participants was 37.83 ± 11.99 years, and the mean BMI was 22.58 ± 1.59 kg/m². Males constituted 55.8% (n = 101) of the sample, while 43.6% (n = 79) were older than 40 years. A BMI above 23 kg/m² was observed in 35.9% (n = 65). Forgetfulness emerged as the leading cause of non-adherence (23.8%, n = 43), followed by medication adverse effects, concurrent medical illness, and transportation barriers, each affecting 19.9% (n = 36). Pill burden was the least frequent factor (11.6%, n = 21).

Conclusion: A considerable proportion of TB patients failed to adhere to their prescribed therapy, primarily due to forgetfulness, adverse drug reactions, concurrent illness, and limited access to healthcare facilities. Targeted patient education, early side effect management, and decentralization of DOTS services are essential to enhance adherence and improve treatment outcomes.

Keywords: Adverse Drug Reaction, Anti-Tuberculous Agents, Medication Adherence, Pill Burden, Tuberculosis, Treatment Compliance, Transportation Barriers.

INTRODUCTION

Tuberculosis (TB) remains one of the world's most devastating infectious diseases, ranking among the top ten global causes of mortality. Despite the availability of effective treatment, TB continues to impose a substantial burden on public health systems, particularly in low- and middle-income countries. In 2018 alone, an estimated 10 million people were infected worldwide, and approximately one-quarter of the global population was either affected or at risk of developing active disease (1). The World Health Organization (WHO) emphasizes that early diagnosis and strict adherence to treatment are critical components for TB control and prevention. TB is a curable disease when treated with a standardized six-month course of first-line antibiotics. However, non-adherence to this regimen remains a major obstacle to eradication efforts. To achieve complete recovery, a patient must take at least 90% of the prescribed medications, while a compliance rate of 95% or higher is categorized as "high adherence" (2). According to WHO guidelines, patients who interrupt therapy for more than two months are classified as treatment failures (3). Such discontinuation not only compromises individual recovery but also facilitates the emergence of drug-resistant strains, thereby escalating morbidity, mortality, and transmission risk at both personal and community levels (4). Several studies have sought to identify the determinants of non-adherence to TB therapy, revealing a multifactorial interplay of behavioral, socioeconomic, and health system factors. A systematic review reported a non-adherence rate of 21.3%, attributing it to forgetfulness, fear of adverse drug effects, prolonged waiting times at healthcare facilities, and distance from treatment centers (5). Similarly, another study found that 5% of patients were lost to follow-up, while 20% exhibited poor adherence, with significant associations observed with TB-HIV co-infection, transportation costs, poor awareness, adverse drug reactions, low educational level, and psychological distress (6). Additional findings highlighted that 8.2% of non-adherent patients were HIV-positive, 14.6% had diabetes, 59.6% reported transportation difficulties, and 24.2% experienced side effects from medication (7,8). Despite these findings, a considerable knowledge gap persists regarding the contextual and regional determinants of treatment non-adherence, particularly in resource-limited settings where cultural, logistical, and systemic barriers may differ. Addressing these factors is crucial for optimizing therapeutic outcomes, reducing transmission rates, and curbing the emergence of multidrug-resistant TB. Therefore, the present study aims to determine the prevalence and associated factors contributing to non-adherence to TB treatment. The findings are expected to provide valuable insights for policymakers and healthcare providers to design targeted interventions that enhance adherence and ultimately reduce the disease burden.

METHODS

This cross-sectional study was conducted at the Department of Pulmonology, Hayatabad Medical Complex, Peshawar, from 21st December 2024 to 20th April 2025, with the objective of identifying factors contributing to non-adherence among patients receiving antituberculous treatment (ATT). Both male and female patients who were diagnosed with non-adherence to ATT were included, while those with a history of hypersensitivity to ATT medications, dementia, chronic kidney disease, liver disease, or immunocompromised states were excluded. Tuberculosis (TB) was defined by the presence of fever and productive cough with sputum positive for acid-fast bacilli (AFB). Non-adherence was defined as an interruption of treatment for at least one week or failure to complete the prescribed therapy duration as outlined in the WHO Directly Observed Treatment, Short-course (DOTS) protocol. The study assessed multiple factors potentially associated with non-adherence. These included both treatment-related and patient-related determinants. Adverse drug effects were identified when patients reported yellowish discoloration of the sclera, reddish discoloration of urine, or gastrointestinal symptoms such as nausea or vomiting (visual analog scale >3) occurring after two weeks of ATT initiation. Transportation issues were defined as travel distances exceeding 20 km to collect medications. Pill burden was considered significant when patients had to take more than two tablets daily for more than four consecutive weeks. This threshold was selected based on clinical observations and patient feedback indicating that an increased number of tablets and prolonged polypharmacy can lead to psychological fatigue, reduced motivation, and difficulties in maintaining adherence—particularly in low-resource settings where patients may have limited health literacy or inadequate treatment support. Although the specific cutoff is not universally standardized, it reflects a pragmatic operational definition relevant to the local population's adherence behavior patterns.

Concurrent illness was defined as the presence of any chronic comorbidity, including diabetes mellitus (fasting blood sugar >130 mg/dL), hepatitis C virus infection (positive HCV RNA by PCR), hepatitis B virus infection (positive HBV DNA by PCR), or human

immunodeficiency virus infection (HIV antigen or antibody positive on ELISA). Forgetfulness was assessed based on self-reported inability to consistently remember medication intake. The sample size was calculated as 181 using the WHO sample size calculator, assuming an anticipated proportion of concurrent medical illness of 8.2%, a 4% margin of error, and a 95% confidence interval (7). Participants were enrolled through a convenient sampling technique from the outpatient department. Ethical approval was obtained from the Institutional Review Board of Hayatabad Medical Complex. Written informed consent was obtained from all participants prior to data collection. Data were gathered using a semi-structured questionnaire that covered domains such as medication adverse effects, transportation challenges, pill burden, concurrent illnesses, and forgetfulness. The questionnaire was translated into the language best understood by each participant, and responses were subsequently transcribed into English to maintain data accuracy. Data analysis was carried out using SPSS version 26. Continuous variables were summarized as means \pm standard deviations (SD) or medians with interquartile ranges (IQR), while categorical variables were expressed as frequencies and percentages. Stratification was performed to control for potential effect modifiers, and post-stratification chi-square tests were applied to determine associations between variables, with a p -value ≤ 0.05 considered statistically significant.

RESULTS

The study included 181 participants with a mean age of 37.83 ± 11.99 years and a mean body mass index (BMI) of 22.58 ± 1.59 kg/m². Of these, 79 participants (43.6%) were older than 40 years, while 102 (56.4%) were 40 years or below. Males constituted 55.8% ($n = 101$) of the sample, and females 44.2% ($n = 80$). More than one-third of participants (35.9%, $n = 65$) had a BMI greater than 23 kg/m². The majority resided in rural areas (55.8%), whereas 44.2% were from urban settings. Among the determinants of treatment non-adherence, forgetfulness emerged as the most frequent factor, affecting 43 participants (23.8%). Medication adverse effects, concurrent illnesses, and transportation difficulties were each reported by 36 participants (19.9%), while pill burden was the least common cause of non-adherence, observed in 21 participants (11.6%). Age was found to have a statistically significant association with several factors influencing non-adherence. Adverse drug effects were more frequently reported among patients older than 40 years (61.1%) compared to those aged 40 years or below (38.9%) ($p = 0.018$). Similarly, pill burden was higher in the older age group (66.7% vs 33.3%, $p = 0.024$). Concurrent medical illness showed a highly significant association with age, being exclusively present in patients over 40 years ($p < 0.001$). Transportation difficulties were also more common among older participants (58.3% vs 41.7%, $p = 0.047$). Forgetfulness, however, did not demonstrate a statistically significant difference across age groups ($p = 0.225$). No statistically significant association was observed between gender and any of the factors related to treatment non-adherence ($p > 0.05$). Males and females showed comparable frequencies across all variables, including adverse effects, pill burden, concurrent illness, transportation issues, and forgetfulness.

When analyzed by BMI, medication adverse effects were significantly more common among participants with a BMI ≤ 23 kg/m² ($p < 0.001$). In this subgroup, all 36 reported cases of adverse effects occurred exclusively among patients with lower BMI, suggesting a possible association between body composition and drug tolerance. No significant associations were observed between BMI and other factors such as pill burden ($p = 0.793$), concurrent illness ($p = 0.677$), transportation difficulties ($p = 0.056$), or forgetfulness ($p = 0.600$). Overall, the analysis highlighted forgetfulness as the predominant cause of non-adherence, followed by adverse drug effects, concurrent illness, and transportation barriers, while pill burden contributed to a smaller extent. Age and BMI were the only variables significantly associated with specific non-adherence factors. When analyzed by place of residence, notable variations were observed in the factors contributing to treatment non-adherence. Patients from rural areas demonstrated higher frequencies of transportation-related issues (66.7%) compared to their urban counterparts (30.0%), reflecting the challenges of long travel distances to healthcare facilities. Similarly, medication adverse effects were slightly more common among rural residents (22.8%) than urban residents (16.3%), possibly due to delayed follow-up and limited clinical monitoring. Forgetfulness was also marginally more frequent among rural patients (25.7%) compared to urban (21.3%), whereas concurrent medical illnesses were relatively balanced between the two groups (rural 19.8%, urban 20.0%). In contrast, pill burden appeared more prominent among urban participants (13.8%) than rural (9.9%). Statistical analysis revealed that the association between residence and transportation issues was significant ($p = 0.002$), indicating that rural residence is an important determinant of access-related non-adherence. Other associations were not statistically significant ($p > 0.05$).

Table 1: Descriptive statistics of study participants (n = 181)

| Parameters | Mean | Std. Deviation |
|-------------|--------|----------------|
| Age (years) | 37.83 | 11.986 |
| BMI (kg/m2) | 22.583 | 1.5898 |

Table 2: Baseline characteristics of study participants (n = 181)

| Parameters | Subgroups | Frequency | Percent |
|-------------|----------------|-----------|---------|
| Age (years) | 40 or below | 102 | 56.4 |
| | More than 40 | 79 | 43.6 |
| Gender | Male | 101 | 55.8 |
| | Female | 80 | 44.2 |
| BMI (kg/m2) | 23.0 or below | 116 | 64.1 |
| | More than 23.0 | 65 | 35.9 |
| Residence | Rural | 101 | 55.8 |
| | Urban | 80 | 44.2 |

Table 3: Factors leading to non-adherence among study participants (n = 181)

| Factors leading to non-adherence | Subgroups | Frequency | Percent |
|----------------------------------|-----------|-----------|---------|
| Medication adverse effects | Yes | 36 | 19.9 |
| | No | 145 | 80.1 |
| Pill burden | Yes | 21 | 11.6 |
| | No | 160 | 88.4 |
| Concurrent illness | Yes | 36 | 19.9 |
| | No | 145 | 80.1 |
| Transportation issue | Yes | 36 | 19.9 |
| | No | 145 | 80.1 |
| Forgetfulness | Yes | 43 | 23.8 |
| | No | 138 | 76.2 |

Table 4: Stratification of factors leading to nonadherence with age (n = 181)

| | | Age (years) | | Total | P value |
|-----------------------------|-----|-----------------------|-----------------------|--------|---------|
| | | 40 or below (n = 102) | More than 40 (n = 79) | | |
| Medications adverse effects | Yes | 14 | 22 | 36 | 0.018 |
| | | 38.9% | 61.1% | 100.0% | |
| | No | 88 | 57 | 145 | |
| | | 60.7% | 39.3% | 100.0% | |

| | | Age (years) | | Total | P value |
|----------------------|-----|-----------------------|-----------------------|--------|---------|
| | | 40 or below (n = 102) | More than 40 (n = 79) | | |
| Pill Burden | Yes | 7 | 14 | 21 | 0.024 |
| | | 33.3% | 66.7% | 100.0% | |
| | No | 95 | 65 | 160 | |
| | | 59.4% | 40.6% | 100.0% | |
| Concurrent illness | Yes | 0 | 36 | 36 | 0.000 |
| | | 0.0% | 100.0% | 100.0% | |
| | No | 102 | 43 | 145 | |
| | | 70.3% | 29.7% | 100.0% | |
| Transportation issue | Yes | 15 | 21 | 36 | 0.047 |
| | | 41.7% | 58.3% | 100.0% | |
| | No | 87 | 58 | 145 | |
| | | 60.0% | 40.0% | 100.0% | |
| Forgetfulness | Yes | 21 | 22 | 43 | 0.225 |
| | | 48.8% | 51.2% | 100.0% | |
| | No | 81 | 57 | 138 | |
| | | 58.7% | 41.3% | 100.0% | |

Table 5: Stratification of factors leading to nonadherence with gender (n = 181)

| | | Gender | | Total | P value |
|-----------------------------|-----|----------------|-----------------|--------|---------|
| | | Male (n = 101) | Female (n = 80) | | |
| Medications adverse effects | Yes | 21 | 15 | 36 | 0.732 |
| | | 58.3% | 41.7% | 100.0% | |
| | No | 80 | 65 | 145 | |
| | | 55.2% | 44.8% | 100.0% | |
| Pill Burden | Yes | 14 | 7 | 21 | 0.286 |
| | | 66.7% | 33.3% | 100.0% | |
| | No | 87 | 73 | 160 | |
| | | 54.4% | 45.6% | 100.0% | |
| Concurrent illness | Yes | 22 | 14 | 36 | 0.474 |
| | | 61.1% | 38.9% | 100.0% | |
| | No | 79 | 66 | 145 | |
| | | 54.5% | 45.5% | 100.0% | |
| Transportation issue | Yes | 22 | 14 | 36 | 0.474 |
| | | 61.1% | 38.9% | 100.0% | |

| | | Gender | | Total | P value |
|---------------|-----|-----------------------|------------------------|--------------|----------------|
| | | Male (n = 101) | Female (n = 80) | | |
| Forgetfulness | No | 79 | 66 | 145 | 0.078 |
| | | 54.5% | 45.5% | 100.0% | |
| | Yes | 29 | 14 | 43 | |
| | | 67.4% | 32.6% | 100.0% | |
| | No | 72 | 66 | 138 | |
| | | 52.2% | 47.8% | 100.0% | |

Table 6: Stratification of factors leading to nonadherence with BMI (n = 181)

| | | BMI (kg/m2) | | Total | P value |
|-----------------------------|-----|--------------------------------|--------------------------------|--------------|----------------|
| | | 23.0 or below (n = 116) | More than 23.0 (n = 65) | | |
| Medications adverse effects | Yes | 36 | 0 | 36 | 0.000 |
| | | 100.0% | 0.0% | 100.0% | |
| | No | 80 | 65 | 145 | |
| | | 55.2% | 44.8% | 100.0% | |
| Pill Burden | Yes | 14 | 7 | 21 | 0.793 |
| | | 66.7% | 33.3% | 100.0% | |
| | No | 102 | 58 | 160 | |
| | | 63.7% | 36.3% | 100.0% | |
| Concurrent illness | Yes | 22 | 14 | 36 | 0.677 |
| | | 61.1% | 38.9% | 100.0% | |
| | No | 94 | 51 | 145 | |
| | | 64.8% | 35.2% | 100.0% | |
| Transportation issue | Yes | 28 | 8 | 36 | 0.056 |
| | | 77.8% | 22.2% | 100.0% | |
| | No | 88 | 57 | 145 | |
| | | 60.7% | 39.3% | 100.0% | |
| Forgetfulness | Yes | 29 | 14 | 43 | 0.600 |
| | | 67.4% | 32.6% | 100.0% | |
| | No | 87 | 51 | 138 | |
| | | 63.0% | 37.0% | 100.0% | |

Table 7: Stratification of Factors Leading to Non-Adherence with Residence (n = 181)

| Factors Leading to Non-Adherence | Subgroups | Rural (n = 101) | Urban (n = 80) | Total | p-value |
|----------------------------------|-----------|-----------------|----------------|-------|---------|
| Medication adverse effects | Yes | 23 (22.8%) | 13 (16.3%) | 36 | 0.291 |
| Pill burden | Yes | 10 (9.9%) | 11 (13.8%) | 21 | 0.428 |
| Concurrent illness | Yes | 20 (19.8%) | 16 (20.0%) | 36 | 0.982 |
| Transportation issue | Yes | 24 (23.8%) | 12 (15.0%) | 36 | 0.002 |
| Forgetfulness | Yes | 26 (25.7%) | 17 (21.3%) | 43 | 0.494 |

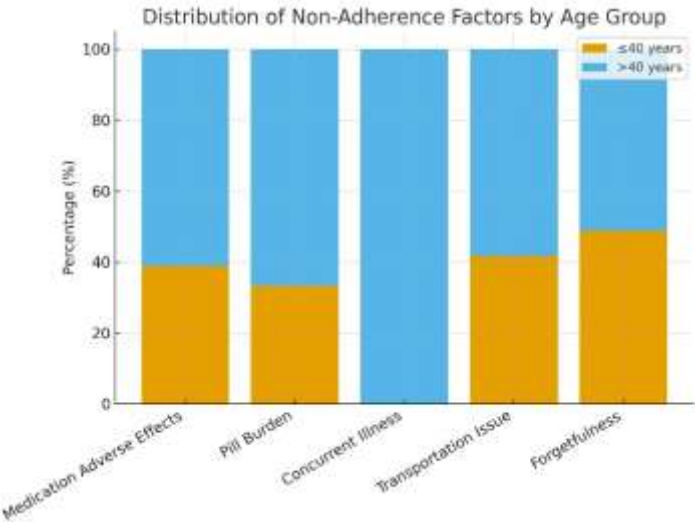


Figure 2 Distribution of Non-Adherence Factors by Age Group

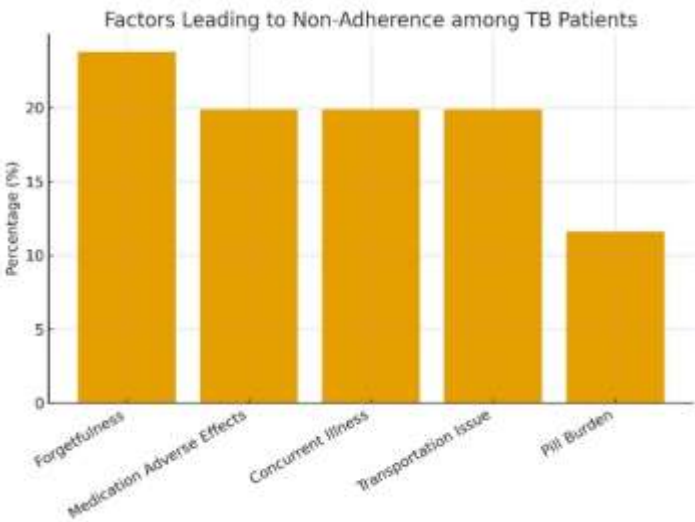


Figure 2 Factors Leading to Non-Adherence Among TB Patients

DISCUSSION

A significant proportion of patients receiving antituberculous therapy (ATT) remain non-adherent to treatment despite the availability of effective and affordable medications. The present study demonstrated that forgetfulness, medication adverse effects, concurrent medical illness, and transportation difficulties were the most frequent contributors to non-adherence among tuberculosis (TB) patients. These findings are consistent with earlier studies conducted in Southeast Nigeria and Ethiopia, where non-adherence rates were reported at 24.2% and 55.8%, respectively, though lower rates were documented in China (9–11). Variability in adherence across regions may be attributed to differences in study populations, healthcare accessibility, patient education, and treatment monitoring practices. Non-adherence was particularly higher among patients in the continuation phase of therapy compared with those in the intensive phase, aligning with studies from Ethiopia that identified the perception of clinical improvement as a common reason for treatment discontinuation (12,13). Patients often equate symptomatic relief with complete recovery and therefore discontinue medications prematurely. This pattern highlights the crucial role of continuous patient education and counseling throughout the entire treatment course. Socioeconomic and educational factors have a strong influence on adherence behavior. The current findings support earlier reports indicating that patients with limited education, low income, or unstable employment exhibit higher rates of non-adherence due to inadequate understanding of disease relapse, treatment duration, and the consequences of incomplete therapy (14–17). In this study, forgetfulness was the most common cause of non-adherence, particularly among older patients, suggesting that cognitive decline, dementia, or age-related memory impairment may contribute to missed doses. Similar findings were documented in several Ethiopian studies where general forgetfulness significantly impacted adherence to TB therapy (18).

Physical and logistical barriers also emerged as key determinants of non-adherence. Rural residence, long commuting distances, and extended waiting times at healthcare facilities were strongly associated with missed doses and treatment interruption. These observations align with findings from Peru and Russia, where distance to healthcare centers and lack of family or community support were leading

causes of treatment discontinuation (19,20). The current study further corroborates that in DOTS-based TB programs, daily clinic visits required for supervised dosing may pose a considerable burden for patients living far from treatment centers. Decentralized drug delivery, mobile health interventions, or community-based DOTS models may improve accessibility and adherence rates in such populations. Adverse drug effects also contributed substantially to non-adherence, with patients experiencing hepatotoxicity, gastrointestinal discomfort, or discoloration of urine demonstrating nearly double the risk of treatment discontinuation. This finding is comparable to previous reports from Northern Ethiopia, where medication-related side effects were identified as a major predictor of poor adherence (21,22). Regular monitoring, patient reassurance, and early management of drug-related toxicities may mitigate this issue.

The strength of the present study lies in its comprehensive evaluation of demographic, clinical, and behavioral determinants of non-adherence in a tertiary care setting, supported by standardized operational definitions and structured data collection. However, several limitations must be acknowledged. The use of a convenience sampling method may have introduced selection bias, limiting generalizability. Self-reported adherence and recall-based responses might have led to under- or overestimation of certain behavioral factors such as forgetfulness or perceived side effects. Additionally, the cross-sectional design restricts the ability to establish temporal causality between determinants and non-adherence. Future research should adopt longitudinal or mixed-method approaches to explore the psychosocial and contextual dimensions of adherence in greater depth. Incorporating qualitative interviews could enhance understanding of patient perceptions, stigma, and healthcare system barriers. Moreover, interventional studies evaluating the impact of mobile health reminders, community-based support systems, and medication packaging innovations could provide evidence-based strategies to reduce non-adherence in high-burden settings. Overall, this study underscores that TB treatment adherence is influenced by a combination of behavioral, clinical, and structural factors. Addressing these challenges through integrated patient education, accessible healthcare delivery, and supportive follow-up systems is essential to improving treatment outcomes and reducing disease transmission in the community.

CONCLUSION

The study concluded that a substantial number of tuberculosis patients failed to adhere fully to their prescribed treatment regimen, with non-adherence primarily influenced by behavioral, clinical, and accessibility-related factors such as forgetfulness, drug side effects, concurrent illness, and long travel distances to health facilities. These findings emphasize the urgent need for patient-centered strategies to strengthen treatment compliance through continuous education, early identification of adverse effects, and improved accessibility of care. Decentralizing DOTS services to peripheral healthcare levels and establishing structured follow-up mechanisms could significantly enhance adherence and treatment success, thereby reducing disease transmission and improving overall TB control efforts.

AUTHOR CONTRIBUTION

| Author | Contribution |
|--------------------|--|
| Romesa Khattak* | Substantial Contribution to study design, analysis, acquisition of Data |
| | Manuscript Writing |
| | Has given Final Approval of the version to be published |
| Muhammad Asif Khan | Substantial Contribution to study design, acquisition and interpretation of Data |
| | Critical Review and Manuscript Writing |
| | Has given Final Approval of the version to be published |
| Hasnan Ibrahim | Substantial Contribution to acquisition and interpretation of Data |
| | Has given Final Approval of the version to be published |
| Fatima Fareed | Contributed to Data Collection and Analysis |

| Author | Contribution |
|-----------|--|
| | Has given Final Approval of the version to be published |
| Aimen Zeb | Contributed to Data Collection and Analysis Has given Final Approval of the version to be published |

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