



Evaluation of Drug Resistance and Treatment Outcomes among TB Patients with Diabetes Mellitus at Tertiary Care Hospital of Sindh, Pakistan

**Kahaf Khan^{1*}, Ayaz Ali Unar², Khalida Unar³, Faraz Qurban Rajper⁴
and Mirza Tasawar Baig⁵**

¹Department of Pharmacology, Peoples University of Medical and Health Sciences, Shaheed Benazir Abad, Sindh, Pakistan.

²Institute of Pharmacy, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Sindh, Pakistan.

³Department of Microbiology, Shah Abdul Latif University, KhairpurMirs, Sindh, Pakistan.

⁴Institute of Pharmaceutical Sciences, Peoples University of Medical and Health Sciences, Shaheed Benazir Abad, Sindh, Pakistan.

⁵Department of Pharmacy practice, Faculty of Pharmacy, Ziauddin University Karachi, Sindh, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. Author KK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AAU, KU and FQR managed the analyses of the study. Author MTB managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI:10.9734/JPRI/2021/v33i27B31501

Editor(s):

(1) Dr. R. Deveswaran, M.S. Ramaiah University of Applied Sciences, India.

Reviewers:

(1) Elena V. Budanova, Sechenov University, Russia.

(2) Maseabata Ramathebane, National University of Lesotho, Lesotho.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/67647>

Original Research Article

Received 15 February 2021

Accepted 20 April 2021

Published 01 May 2021

ABSTRACT

The objective of the study is to evaluate of drug resistance and treatment outcomes among tuberculosis patients with diabetes mellitus at tertiary care hospital of Sindh, Pakistan. Tuberculosis (TB) is considered as very dangerous infectious disease caused by *Mycobacterium tuberculosis* or other tubercle bacilli pathogen affects the lungs and it can be spread from person to person through very minute droplet released by infected person via coughing or sneezing. Descriptive cross-sectional study was carried out at different Tuberculosis setting located at tertiary

*Corresponding author: E-mail: tahseen.channa89@gmail.com;

care hospital of Sindh, Pakistan for the period of 10 months. Tuberculosis OPD is considered as major health care facility for the TB, MDR-TB and XDR-TB patients for the local population and peripheries. Total 389 samples were collected through purposive sampling techniques. From the given data, there were 209 Males and 180 females, all participants belong to different areas, so 216 patients belong to rural areas, 121 study participants were house wives, 134 were employed and 41 were have their own business. From the clinical data, 229 participants shown positive response with TB smear test, whereas; 156 participants had positive results with TB culture test. 247 patients had previous history of Tuberculosis, 120 had developed drug resistance and 24 had developed multi-drug resistance (MDR). 312 patients were recently diagnosed with Diabetes mellitus and they had one year of duration of diabetes. Complication of tuberculosis developed among 113 patients and complication of diabetes developed among 194 participants. 39 people were using oral therapy for the management of diabetes and 341 participants had successfully completed their therapy and cured whereas 2 patients were died due to complication. It was concluded from the current research that there were many chances for developing drug resistance and multi-drug resistance among the patients suffering from co-morbid including tuberculosis along with Diabetes mellitus. Proper counseling should be conducted, in order to reduce the complication of either type of disease.

Keywords: Diabetes mellitus; tuberculosis; Multi-Drug Resistance (MDR); oral therapy.

1. INTRODUCTION

Internationally, approximately 9 million new cases of Tuberculosis (TB) reported every year and according to WHO reports there were almost 350 million people, who had diagnosed with diabetes mellitus [1,2]. Diabetes Mellitus is considered as major hazardous aspect for the development of tuberculosis cases [3,4] and almost 18% of active tuberculosis patients had diabetes mellitus [5]. There was strong correlation between Tuberculosis and Diabetes Mellitus as both disease possess high dominance globally and since last few decades, mortality and morbidity rates of diabetes increased enormously [2,6,7]. The cases of multi drug resistant tuberculosis (MDR-TB) are also increased very fast [8], so the significance of understanding about the correlation of diabetes and tuberculosis is also developing [9]. Literatures from India, Spain, Turkey and Pakistan elaborate that diabetes with active cases of tuberculosis was very much common among these countries. 25% of MDR-TB patients were having diabetes mellitus [10-13]. According to various studies there was strong correlation between diabetes and MDR-TB [14,15]. Due to lack of medical facilities and diagnostic criteria, there was very low data available for the MDR-TB patients with diabetes. Moreover, patients of MDR-TB had lack of knowledge and attitude towards the relation of Diabetes with other diseases and their control along with clinical impact [16,17]. Among the low socio-economic nations, the burden of MDR-TB is almost very high and frequency of diabetes patients is expected to grow in coming 20 years [16,7]. In 2020, the incidence of MDR-

TB in Pakistan was 230 per 1 lac individual that is quite greater among south Asian countries [18]. On national level the patients of MDR-TB were never treated when previously diagnosed with tuberculosis that was considered as major risk factor for developing Multi Drug Resistance [8]. In the same case, the burden of Diabetes was also raised in Pakistan. The frequency of diabetic patients among the urban areas was quite greater than the local residents of rural areas [13]. As per national epidemic report of diabetes, the rate of cases of new diagnosed diabetes was high among the adults [19] and it is expected to enhance by 9% up to 2030 [20-23]. Diabetes and Tuberculosis routinely increase the burden on the population of Pakistan so it becomes very difficult to manage such types of co-morbidities simultaneously. [24-27] Although, it is necessary to understand the relationship between diabetes and tuberculosis. If tuberculosis is properly managed without creating any hindrance to management of diabetes so the chances of developing MDR-TB were also increased. [28-30] So, the aim of the study was to evaluate the characteristics of Tuberculosis patients' assessment for MDR-TB along with and without Diabetes Mellitus and clinical aspect of Diabetes with medical care correlate with drug resistance among the patients with Diabetes and Tuberculosis and also determine the management of diabetes associated with the best TB regimen. [31-32]

2. METHODOLOGY

Descriptive cross-sectional study was carried out at different Tuberculosis setting located at tertiary

care hospital of Sindh, Pakistan for the period of 10 months. Tuberculosis OPD is considered as major health care facility for the TB, MDR-TB and XDR-TB patients for the local population and peripheries. Total 389 samples were collected through purposive sampling techniques. All participants were facilitated with questionnaire and guided regarding its filling and data was collected and Statistical analysis was done by using SPSS version 20.00

3. RESULTS AND DISCUSSION

Descriptive cross-sectional study was carried out at different Tuberculosis setting located at tertiary care hospital of Sindh, Pakistan for the period of 10 months. Total 389 samples were collected through purposive sampling techniques; from

them 209 were males and 180 females as mentioned in Table 1.

From all study subjects, 209 were belongs to rural areas where as 173 participants belongs to urban areas of Sindh as mentioned in Table.

All the study subjects were divided in accordance with different age groups as described in Table 3.

All the participants were also divided in the different groups according to their marital status as mentioned in Table 4.

Job status of study subjects were also described in Table 5.

Qualification of study subjects were also mentioned in Table 6.

Table 1. Gender wise distribution of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	209	53.7	53.7	53.7
	Female	180	46.3	46.3	100.0
	Total	389	100.0	100.0	

Table 2. Area wise distribution of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Rural	216	55.5	55.5	55.5
	Urban	173	44.5	44.5	100.0
	Total	389	100.0	100.0	

Table 3. Age wise distribution of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	15-24 Years	79	20.3	20.3	20.3
	24-34 Years	134	34.4	34.4	54.8
	35-44 Years	86	22.1	22.1	76.9
	45-54 Years	40	10.3	10.3	87.1
	55 and above	50	12.9	12.9	100.0
	Total	389	100.0	100.0	

Table 4. Marital Status wise distribution of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Married	202	51.9	51.9	51.9
	Single	146	37.5	37.5	89.5
	Divorced/Separated	41	10.5	10.5	100.0
	Total	389	100.0	100.0	

Table 5. Job Status of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	House wives	121	31.1	31.1	31.1
	Employed	134	34.4	34.4	65.6
	Un-employed	93	23.9	23.9	89.5
	Landlord/Self Business	41	10.5	10.5	100.0
	Total	389	100.0	100.0	

Tuberculosis was measured through TB Smear test and the results of TB smear test was mentioned in Table 7.

Some time smear test didn't get positive results of TB so for the confirmation of TB, culture test was also conducted and the resultant of Culture test was mentioned in Table 8

History of TB among the patients was mentioned in Table 9.

Patients who had already taken the treatment of TB and their results were mentioned in Table 10.

With irregular drug therapy, number of participants had developed various drug resistant including Pan susceptible, drug resistant, Multi

Drug Resistant and XDR and their data is mentioned in Table 11.

TB patients had developed many symptoms such as weight loss, dyspnea, blood in sputum, dry coughing, yellowish eyes, dry mouth, abdominal cramps and results for each symptoms were mentioned in Table 12.

Various risk factors were also observed among the TB patients and the results of each risk factor is mentioned in Table 13.

Each participants had different diabetes types such as Type I and Type II and the results for Types of diabetes is mentioned in Table 14

Table 6. Qualification wise distribution of study subjects

		Frequency	Percent	Valid percent	Cumulative percent
Valid	Primary	203	52.2	52.2	52.2
	Secondary	90	23.1	23.1	75.3
	Graduation	88	22.6	22.6	97.9
	Post graduation	8	2.1	2.1	100.0
	Total	389	100.0	100.0	

Table 7. Tuberculosis Smear Test results of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positive	229	58.9	58.9	58.9
	Negative	160	41.1	41.1	100.0
	Total	389	100.0	100.0	

Table 8. Tuberculosis Culture Test results of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positive	156	40.1	40.1	40.1
	Negative	233	59.9	59.9	100.0
	Total	389	100.0	100.0	

Table 9. Previous history of Tuberculosis of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	247	63.5	63.5	63.5
	NO	142	36.5	36.5	100.0
	Total	389	100.0	100.0	

Table 10. Previously taken Tuberculosis treatment by study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	201	51.7	51.7	51.7
	No	188	48.3	48.3	100.0
	Total	389	100.0	100.0	

Table 11. Drug Susceptibility of study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Pan Susceptible	243	62.5	62.5	62.5
	Drug Resistance	120	30.8	30.8	93.3
	Multi Drug Resistance	24	6.2	6.2	99.5
	Extended Drug Resistance	2	.5	.5	100.0
	Total	389	100.0	100.0	

Table 12. Symptoms of Tuberculosis found among study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	weight loss	22	5.7	5.7	5.7
	Dyspnea	88	22.6	22.6	28.3
	Blood in Sputum	83	21.3	21.3	49.6
	Dry Coughing	118	30.3	30.3	79.9
	Yellowish Eyes	19	4.9	4.9	84.8
	Dry Mouth	40	10.3	10.3	95.1
	Abdominal Cramps	19	4.9	4.9	100.0
	Total	389	100.0	100.0	

Table 13. Risk factors of Tuberculosis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	HIV Positive	100	25.7	25.7	25.7
	TB Contact at Home	138	35.5	35.5	61.2
	MDR-TB contacts at Home	28	7.2	7.2	68.4
	Tobacco consumption	80	20.6	20.6	88.9
	Alcohol Consumption	43	11.1	11.1	100.0
	Total	389	100.0	100.0	

Table 14. Types of Diabetes among study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	TYPE-I	77	19.8	19.8	19.8
	TYPE-II	312	80.2	80.2	100.0
	Total	389	100.0	100.0	

Table 15. Duration of Diabetes mellitus among study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Below one year	192	49.4	49.4	49.4
	Below 05 years	182	46.8	46.8	96.1
	Above 05 years	15	3.9	3.9	100.0
	Total	389	100.0	100.0	

Table 16. Management of Diabetes by study subjects

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Oral Medicine	39	10.0	10.0	10.0
	Insulin therapy	350	90.0	90.0	100.0
	Total	389	100.0	100.0	

Table 17. Characteristics of study subjects after using proper management of Tuberculosis and Diabetes Mellitus

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Cure and complete therapy	341	87.7	87.7	87.7
	Failed	46	11.8	11.8	99.5
	Adequate and Died	2	.5	.5	100.0
	Total	389	100.0	100.0	

Table 18. Cross tabulation of Gender along with Tuberculosis Smear Test

		TB Smear test		Total
		Positive	Negative	
Gender	Male	153	56	209
	Female	76	104	180
Total		229	160	389

Each participant had different diabetes history as mentioned in Table 15.

Management of Diabetes among the study subjects were controlled through oral therapy and Insulin and the results for the management of Diabetes were mentioned in Table 16.

Characteristics of study subjects after using proper management of Tuberculosis and Diabetes Mellitus were mentioned in Table 17.

4. CONCLUSION

It was concluded from the current study that there were many chances for developing drug resistance and multi-drug resistance among the patients suffering from co-morbid including tuberculosis along with Diabetes mellitus (DM). Proper counseling and seminar should be conducted, for the patients, in order to reduce the complication of either type of disease. People from remote areas were unaware of complexities of symptoms and their proper management, so they were properly guided for dosing. Oral therapy for DM had developed number of drug-drug interaction, so the patients were facilitated regarding proper insulin therapy.

CONSENT

As per international standard or university standard, respondents’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Muñoz-Torrico M, Luna JC, Migliori GB, D’Ambrosio L, Carrillo-Alduenda JL, Villareal-Velarde H, Torres-Cruz A, Flores-Ergara H, Martínez-Mendoza D, García-Sancho C, Centis R. Comparison of bacteriological conversion and treatment outcomes among MDR-TB patients with and without diabetes in Mexico: Preliminary data. *Revista Portuguesa de Pneumologia (English Edition)*. 2017 Jan 1;23(1):27-30.
- Baghaei P, Tabarsi P, Abrishami Z, Mirsaedi M, Faghani YA, Mansouri SD, Masjedi MR. Comparison of pulmonary TB patients with and without diabetes mellitus type II; 2010.
- Chung-Delgado K, Guillen-Bravo S, Revilla-Montag A, Bernabe-Ortiz A. Mortality among MDR-TB cases: Comparison with drug-susceptible tuberculosis and associated factors. *PloSOne*. 2015;10(3):e0119332.
- Bashar M, Alcabes P, Rom WN, Condos R. Increased incidence of multidrug-resistant tuberculosis in diabetic patients on the Bellevue Chest Service, 1987 to 1997. *Chest*. 2001;120(5):1514-1519.
- Singla R, Khan N, Al-Sharif N, Al-Sayegh MO, Shaikh MA, Osman MM. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. *The International Journal of Tuberculosis and Lung Disease*. 2006;10(1):74-79.
- Kang YA, Kim SY, Jo KW, Kim HJ, Park SK, Kim TH, Shim TS. Impact of diabetes on treatment outcomes and long-term survival in multidrug-resistant tuberculosis. *Respiration*. 2013;86(6):472-478.
- Chang JT, Dou HY, Yen CL, Wu YH, Huang RM, Lin HJ, Shieh CC. Effect of type

- 2 diabetes mellitus on the clinical severity and treatment outcome in patients with pulmonary tuberculosis: a potential role in the emergence of multidrug-resistance. *Journal of the Formosan Medical Association*. 2011;110(6):372-381.
8. Viswanathan V, Vigneswari A, Selvan K, Satyavani K, Rajeswari R, Kapur A. Effect of diabetes on treatment outcome of smear-positive pulmonary tuberculosis—a report from South India. *Journal of Diabetes and its Complications*. 2014; 28(2):162-165.
 9. Carreira S, Costeira J, Gomes C, André JM, Diogo N. Impact of diabetes on the presenting features of tuberculosis in hospitalized patients. *Revista Portuguesa de Pneumologia (English Edition)*. 2012; 18(5):239-243.
 10. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: evidence from a systematic review and meta-analysis. *Systematic Reviews*. 2018;7(1):1-13.
 11. Hsu AH, Lee JJ, Chiang CY, Li YH, Chen LK, Lin CB. Diabetes is associated with drug-resistant tuberculosis in Eastern Taiwan. *The International Journal of Tuberculosis and Lung Disease*. 2013; 17(3):354-356.
 12. Salindri AD, Kipiani M, Kempker RR, Gandhi NR, Darchia L, Tukvadze N, Magee MJ. Diabetes reduces the rate of sputum culture conversion in patients with newly diagnosed multidrug-resistant tuberculosis. In *Open forum infectious diseases*. Oxford University Press. 2016 May;3(3).
 13. Gómez-Gómez A, Magaña-Aquino M, López-Meza S, Aranda-Álvarez M, Díaz-Ornelas DE, Hernández-Segura MG, Noyola DE. Diabetes and other risk factors for multi-drug resistant tuberculosis in a Mexican population with pulmonary tuberculosis: case control study. *Archives of Medical Research*. 2015;46(2):142-148.
 14. Muñoz-Torrice M, Caminero-Luna J, Migliori GB, D'Ambrosio L, Carrillo-Alduenda JL, Villareal-Velarde H, Pérez-Padilla R. Diabetes is associated with severe adverse events in multidrug-resistant tuberculosis. *Archivos de Bronconeumología (English Edition)*. 2017;53(5):245-250.
 15. Magee MJ, Kempker RR, Kipiani M, Gandhi NR, Darchia L, Tukvadze N, Blumberg HM. Diabetes mellitus is associated with cavities, smear grade, and multidrug-resistant tuberculosis in Georgia. *The International Journal of Tuberculosis and Lung Disease*. 2015; 19(6):685-692.
 16. Liu Q, Li W, Xue M, Chen Y, Du X, Wang C, He JQ. Diabetes mellitus and the risk of multidrug resistant tuberculosis: a meta-analysis. *Scientific Reports*. 2017;7(1):1-7.
 17. Huangfu P, Ugarte-Gil C, Golub J, Pearson F, Critchley J. The effects of diabetes on tuberculosis treatment outcomes: an updated systematic review and meta-analysis. *The International Journal of Tuberculosis and Lung Disease*. 2019; 23(7):783-796.
 18. Magee MJ, Kempker RR, Kipiani M, Tukvadze N, Howards PP, Narayan KV, Blumberg HM. Diabetes mellitus, smoking status, and rate of sputum culture conversion in patients with multidrug-resistant tuberculosis: A cohort study from the country of Georgia. *PloSOne*. 2014; 9(4):e94890.
 19. Saktiawati AM, Subronto YW. Influence of diabetes mellitus on the development of multi drug resistant-tuberculosis in Yogyakarta. *Acta Med Indones*. 2018; 50(1):11-17.
 20. Shewade HD, Jeyashree K, Mahajan P, Shah AN, Kirubakaran R, Rao R, Kumar AM. Effect of glycemic control and type of diabetes treatment on unsuccessful TB treatment outcomes among people with TB-Diabetes: A systematic review. *PloSOne*. 2017;12(10):e0186697.
 21. Young F, Critchley JA, Johnstone LK, Unwin NC. A review of co-morbidity between infectious and chronic disease in Sub Saharan Africa: TB and diabetes mellitus, HIV and metabolic syndrome, and the impact of globalization. *Globalization and Health*. 2009;5(1):1-9.
 22. Perez-Navarro LM, Restrepo BI, Fuentes-Dominguez FJ, Duggirala R, Morales-Romero J, López-Alvarenga JC, Zenteno-Cuevas R. The effect size of type 2 diabetes mellitus on tuberculosis drug resistance and adverse treatment outcomes. *Tuberculosis*. 2017;103:83-91.
 23. Joseph P, Desai VBR, Mohan NS, Fredrick JS, Ramachandran R, Raman B, Thomas A. Outcome of standardized treatment for patients with MDR-TB from Tamil Nadu, India. *The Indian Journal of Medical Research*. 2011;133(5):529.

24. Zhang Q, Xiao H, Sugawara I. Tuberculosis complicated by diabetes mellitus at Shanghai Pulmonary Hospital, China. *Jpn J Infect Dis.* 2009;62(5):390-391.
25. Fisher-Hoch SP, Whitney E, McCormick J. B, Crespo G, Smith B, Rahbar MH, And The Nuevo Santander Tuberculosis Trackers. Type 2 diabetes and multidrug-resistant tuberculosis. *Scandinavian Journal of Infectious Diseases.* 2008; 40(11-12):888-893.
26. Harries AD, Kumar AM, Satyanarayana S, Lin Y, Zachariah R, Lönnroth K, Kapur A. Addressing diabetes mellitus as part of the strategy for ending TB. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* 2016;110(3):173-179.
27. Jali MV, Mahishale VK, Hiremath MB. Bidirectional screening of tuberculosis patients for diabetes mellitus and diabetes patients for tuberculosis. *Diabetes & Metabolism Journal.* 2013;37(4):291.
28. Pinto CM, Carvalho AR. Diabetes mellitus and TB co-existence: Clinical implications from a fractional order modelling. *Applied Mathematical Modelling.* 2019;68:219-243.
29. Tegegne BS, Habtewold TD, Mengesha MM, Burgerhof JG. Association between diabetes mellitus and multi-drug-resistant tuberculosis: a protocol for a systematic review and meta-analysis. *Systematic Reviews.* 2017;6(1):1-5.
30. Mi F, Jiang G, Du J, Li L, Yue W, Harries AD, Lin Y. Is resistance to anti-tuberculosis drugs associated with type 2 diabetes mellitus? A register review in Beijing, China. *Global Health Action.* 2014;7(1):24022.
31. Baghaei P, Tabarsi P, Javanmard P, Farnia P, Marjani M, Moniri, A, Velayati A. A. Impact of diabetes mellitus on tuberculosis drug resistance in new cases of tuberculosis. *Journal of Global Antimicrobial Resistance.* 2016;4:1-4.
32. Restrepo BI. Diabetes and tuberculosis. Understanding the Host Immune Response against *Mycobacterium Tuberculosis Infection.* 2018;1-21.

© 2021 Khan et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/67647>*