Prevalence and Treatment outcome of Tuberculosis patient across different Age groups and gender at District swat from 2014-2019; A retrospective approach

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ABSTRACT

Background: The incidence of Tuberculosis (TB) is decreasing too slowly to meet the End TB Strategy's target, and Pakistan is one of the countries most affected by TB. TB can manifest as pulmonary or extra-pulmonary, with symptoms such as cough, chest pain, fever, night sweats, and weight loss. The study was conducted with the aim to identify the prevalence and outcome of the treatment among patient diagnose with pulmonary tuberculosis in district swat.

Method and Materials: The data was collected from October to December 2022, using a retrospective, observational design in district swat, Pakistan of patients who diagnosed and received treatment from 2015 to 2019. The total patients were 15,567 patients with drug-sensitive tuberculosis (DS-TB) among the total population of 2.3 million of district swat. The data was gathered from various sources, including laboratory request forms, TB registers, treatment cards, and GeneXpert test registries. Data analysis was performed using Microsoft Excel and SPSS, and the findings were presented in the form of tables and graphics.

Results: The total number of participants was 15,567, where 98.64% were new cases, while 1.36% was previously treated. The incidence of TB was higher in males than females. A higher number of TB cases were recorded in 2018, while the lowest number was observed in 2015. The proportion of TB cases decreased as age increased. The diagnosis revealed that 20.98% of patients had pulmonary smear-positive TB, while 39.41% had pulmonary smear-negative TB.

Moreover, 39.60% of patients had extra-pulmonary TB. The annual number of patients diagnosed with PBC, PCD, and EP TB increased significantly during the study period. The overall treatment success rates were 93.9% for PBC cases, 98.76% for PCD cases, and 97.85% for EP cases, varying by year and type of TB.

Conclusion: Early identification of the disease is essential in preventing the emergence of drug-resistant strains, highlighting the importance of timely culture and drug susceptibility testing. Improved diagnostic practices hold the potential to enhance treatment efficacy and play a pivotal role in the worldwide battle against tuberculosis.

KEYWORDS: tuberculosis, prevalence, outcome, treatment, MDR-TB, clinical environment, diagnosis

INTRODUCTION

Background

Tuberculosis (TB) is among the top ten causes of mortality globally caused by a single infectious pathogen, according to the World Health Organization [1]. An individual with TB can transmit the disease to as many as ten people if they are in close contact for a year, and two of them can develop active TB [2].

The global TB incidence rate decreased by an average of 1.7% per year from 2000 to 2019, with a recent increase of

2.3% annually from 2018 to 2019. However, this rate of decline is insufficient to meet the End TB Strategy's objective of a 20% reduction between 2015 and 2020. World Health Organization (WHO) 2019 report showed that the cumulative decrease between 2015 and 2019 was 9%, below the target reduction. The WHO ranks Pakistan as the fifth most TB-affected country out of 30. Pakistan has 369,548 confirmed cases of TB, according to a 2019 report published by the World Health Organization. When compared to 2017' total of 368,897 cases, this year's total indicates an increase of 651 [3]. According to data, The projected rates of tuberculosis incidence and mortality were 265.0 and 562.0 per 100,000 people, respectively, with a mortality rate of 340 [4].

There are two main types of tuberculosis (TB): pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB). PTB primarily affects the lungs, while EPTB can affect any part of the body [5]. In the case of extra-pulmonary TB, the main parts of the body that might be affected include the central nervous system, pleura, bones and joints, and lymphatic system [6]. However, if the infection left untreated, tuberculosis can be lethal [7].

When a person with tuberculosis coughs, sneezes, shouts, or screams, the organism in their respiratory tract are released into the air; droplet nuclei containing TB organisms pass through the mouth or nose, enter the upper respiratory system, enter the bronchia, and finally reach the alveoli of the lungs, and can infect a healthy person who breathes them in [8].

Multiple factors increase the likelihood of TB infection, with overcrowding and malnutrition being strongly correlated. Other significant risk factors include alcoholism, living conditions, smoking, and a history of TB [9]. As opposed to men, women were shown to be more susceptible to tuberculosis, most likely due to the influence of female hormones. Age is another factor that has been demonstrated to raise TB prevalence. [10].

The infected person may experience symptoms such as chest pain and a productive cough; however, roughly 25% of patients are symptom-free [11]. Patients with EPTB, however, may experience symptoms similar to PTB, including night sweats, fever, and weight loss [12].

To diagnose TB in a patient's test sample contains bacilli, TB can be diagnosed through a detailed medical examination together with additional testing, like microbiological tests, medical imaging, immune response tests, histopathology, and surgical biopsy, which may strongly suggest TB as the diagnosis [13]. A diagnostic assessment should follow the chest x-ray (CXR) to establish a diagnosis, and any abnormality in CXR anomaly compatible with TB should be evaluated by a bacteriological examination [14]. Radiography of PTB is complex and challenging to diagnose. To begin, understanding and distinguishing between active and latent tuberculosis is vital. Cavity lesions and lung consolidation are signs of active tuberculosis, which carries a higher risk of spreading the infection [15].

Sputum smear microscopy (SSM), the standard gold method for identifying pulmonary TB, counts the number of mycobacteria present in a patient's sputum samples. Despite its low sensitivity, smear microscopy has high specificity [13]. Furthermore, the GeneXpert MTB/RIF assay is a molecular diagnostic tool that exhibits enhanced sensitivity and specificity for the simultaneous detection of Mycobacterium tuberculosis (MTB) and drug-resistant tuberculosis (DR-TB) in sputum and other appropriate specimens [14]. The GeneXpert assay utilizes a polymerase chain reaction (PCR) methodology, enabling results to be obtained in less than two hours [15]. A clinical diagnosis of tuberculosis (TB) can be made based on signs and symptoms, even without a positive culture for Mycobacterium tuberculosis. For the detection of multidrug-resistant TB (MDR-TB), World Health Organization (WHO) endorsed gold standard methods such as molecular line-probe assays, and commercial liquid culture systems provide rapid and accurate results [16].

The IGRA or the Mantoux test can be used to identify latent TB, with the Mantoux test being less expensive and more appropriate for Low Countries. The IGRA test, on the other hand, is more accurate than the Mantoux test [16].

Research Objective

1. To assess the prevalence of patients with pulmonary bacterial confirmation (PBC), pulmonary clinical diagnosis (PCD), and extra-pulmonary diagnosis (EP) of tuberculosis, as well as treatment outcomes for all TB patients who participated in the TB control program in Swat district, Khyber Pakhtunkhwa, between 2015 and 2019.

MATERIALS AND METHODS

Study design and setting

This study used a retrospective, hospital-based, observational approach with secondary data collected from TB registers of all confirmed DS-TB patients who had been previously notified between 2015 and 2019 in district swat, Khyber pukhtankhwa from October to December 2022.

In this study, we included all cases of Drug-sensitive tuberculosis (DS-TB) cases that were confirmed between January 2015 and December 2019 and previously diagnosed by clinical signs and symptoms together with Genexpert MTB/RIF assay, Acid-Fast Bacilli (AFB) smear, X-ray /CT examination, pathological examination, X-ray/CT examination, and culture.

Most local government and commercial TB diagnostic centers offer the Ziehl-Neelsen (ZN) test. All samples of Presumptive TB patients negative on ZN-smear for TB bacilli are sent to the Genexpert laboratories in Swat.

Out of the patients who met the selection criteria, the study comprised 15,567 individuals with DS-TB.

The inclusion and Exclusion criteria

All patients diagnosed with tuberculosis, whether through clinical or microbiological means, were included in this study regardless of the type of TB (pulmonary or extra-pulmonary).

Patients without confirmed TB results were excluded from the study.

Data collection Procedure

The laboratory's "request for examination" forms were used to obtain patient data such as sample types, age, sex, address, HIV status, and previous history of anti-TB drugs.

Data of all enrolled TB patients were collected from the TB register, treatment cards, and Genexpert test registers.

Data analysis procedure

Two static software's were applied to analyze the information: Microsoft Excel (Microsoft Office Professional Plus 2016) and statistical package for social sciences (SPSS). Tables and graphics were then created to represent the data.

Ethical Consideration

The confidentiality of each participant was maintained while permission was taken from the management of TB control program to utilize the data only for data analysis.

RESULTS

Demographic data of the participants

Between January 2014 and December 2019, a total of 15,567 patients from 13 sites of TB in District swat with known ages and sexes were included; of the total, 15,356 (98.64%) were new patients, and 211 (1.36%) were re-treatment patients (See table 1).

Table 1: Distribution of all TB cases according to the type

Type of TB	*Total*	*Percent*
PBC	3266	20.98%
PCD	6136	39.42%
EP	6165	39.60%
Total Cases	*15567*	*100*

PBC= Pulmonary Bacteriologically confirmed, PCD= Pulmonary Clinically diagnosed, EP= Extra Pulmonary

According to the current analysis, most cases were reported in 2018, and the lowest number was reported in 2015. Fig: 1 show that since 2015, the total number of cases has increased significantly.

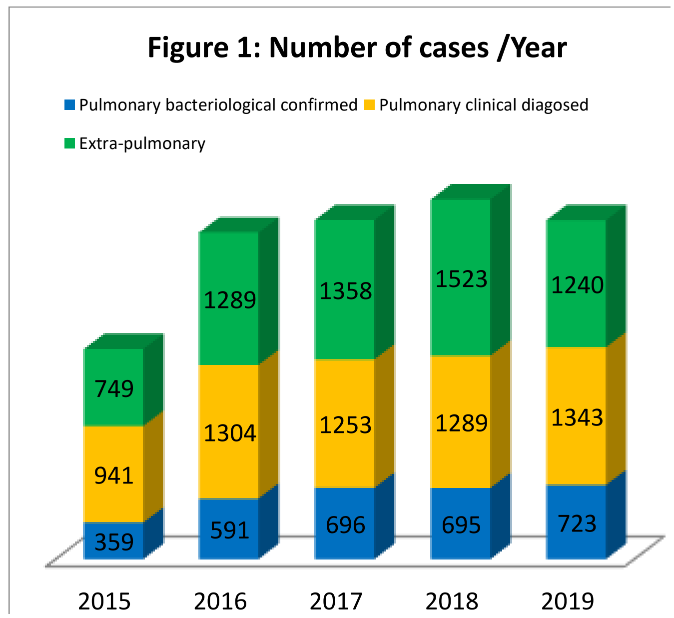

Table 2: Demographic data of tuberculosis cases

Age group (Y)	*Gender*		*Total (%)*
	Male (%)	*Female (%)*	
0 – 4	1382	1119	2501 (16.0%)
5 – 14	2735	2331	5,066 (32.5%)
15 – 24	1182	1522	2,704 (17.3%)
25 – 34	820	973	1793 (11.5%)
35 – 44	514	537	1,051 (6.7%)

45- 54	427	438	865 (5.5%)
55 – 64	448	334	782 (5.0%)
>65	575	230	805 (5.1%)
Total	8083(51.92)	7484(48.08)	15567

According to the results, male TB patients were higher than female TB patients. The study also found that there were 3.8% more cases of TB in males (N=599) than in females (Table 2).

TREATMENT OUTCOMES OF ALL TB PATIENTS

Of the 3266 PBC patients enrolled, 2,100 (64.2%) had been declared cured successfully, while 967 (29.6%) had completed their anti-TB treatment, 21 (0.6%) cases had failed treatment, 99 (3.0%) had been lost to follow-up, and 79 (2.4%) had died.

Table 3: TB Patients by the diagnostic site from 2014- 2019

Diagnostic site	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)	2019 n (%)	Total
PBC	371 (11.36%)	635 (19.44%)	737 (22.57%)	755 (23.12%)	768 (23.52%)	3266
PCD	941 (15.34%)	1304 (21.25%)	1253 (20.42%)	1290 (21.02%)	1348 (21.97%)	6136
EP	750 (12.17%)	1289 (20.91%)	1360 (22.06%)	1525 (24.74%)	1241 (30.13%)	6165

PBC= Pulmonary Bacteriologically confirmed, PCD= Pulmonary Clinically diagnosed, EP= Extra Pulmonary

All TB patients were divided into eight age groups, using ten-year intervals. Of the total, 32.5% of cases were found in children aged 5-14, and the percentage decreased as age increased.

(52.5%) to 563 (74.5%) but fell to 496 (64.5 %) in 2019; also the percentage of patients who completed their

Table 4: Gender-wise yearly Trend of Tuberculosis in District Swat

Gender	2015	2016	2017	2018	2019	Average
Male	1077(52.23%)	1702(52.73%)	1733(51.73%)	1806(50.59%)	1765(52.57%)	1616
Female	985 (47.77%)	1526(47.27%)	1617(48.27%)	1764(49.41%)	1592(47.42%)	1496
Total	2062	3228	3350	3570	3357	15567

The annual trends in the registration of TB patients by diagnostic site indicated that each year the number of PBC TB patients registered for treatment increased from 371 (11.36%) to 768 (23.52%). A statistically marked increase was also observed in PCD patients enrolled for anti-TB treatment, from 941 (15.34%) to 1348 (21.97%). Comparatively, the number of extra-pulmonary tuberculosis cases has also shown a statistically significant increase from 750 (12.07%) to 1241 (20.13%). (Table 3).

Table 4 shows that the maximum number of male and female cases was diagnosed in 2018, while the minimum number of patients was diagnosed in 2015. During the five-year study, an average of 1,616 males and 1,496 females were infected with tuberculosis each year.

in 2019, the number of patients who died while receiving treatment increased from 4 (1.0%) to 19. (2.4%). (Table 5). Out of the 6,136 PCD cases studied, the vast majority of patients, 6059 (98.76%), successfully completed their treatment regimen. The overall treatment success rate for PCD cases was 98.76%. However, a small percentage (0.78%) was lost to follow-up, and a slightly larger group (0.42%) died before completing the course; no incidence of unsuccessful treatment was reported.

6033 (97.85 %) of the 6165 patients with EPTB have completed the course of treatment (i.e., favorable treatment outcome). One hundred six patients (1.71%) were lost to follow-up during treatment, whereas 26 (0.42%) died, and no patient was recorded with treatment failure. The overall TSR for EP cases was 97.85%. The treatment success rate of the TB patients throughout the five-year study was 97.85%. Table (5).

DISUSSION

The study revealed that PTB was present in 60% of the patients, while EPTB was identified in 39%. Our findings closely resemble the outcomes reported in a study [19],

Table 5: Treatment outcome of registered TB patients from 2015 to 2019

Diagnostic Year	Total No. of cases	Cured n (%)	Treatment completed n (%)	Treatment failed n (%)	lost to follow-up n (%)	Died	Treatment success n (%)
Treatment outcome of Pulmonary Bacteriologically confirmed patients							
2015	371	195 (52.5)	149(40.1)	3(0.8)	20 (5.3)	4(1.0)	344 (92.7)
2016	635	334 (52.6)	259(40.7)	9(1.4)	16 (2.5)	17(2.6)	603 (94.9)
2017	737	512 (69.4)	190(25.7)	3(0.4)	16 (2.1)	16(2.1)	702 (95.2)
2018	755	563 (74.5)	143(18.9)	2 (0.2)	24 (3.1)	23(3.0)	706 (93.5)
2019	768	496 (64.5)	226(29.4)	4 (0.5)	23 (2.9)	19(2.4)	722 (94.0)
Total	**3266**	**2100 (64.2)**	**967(29.6)**	**21(0.6)**	**99 (3.0)**	**79 (2.5)**	**3097 (93.9)**
Treatment outcome of Pulmonary clinically diagnosed patients							
Diagnostic Year	Total No. of cases	Cured n (%)	Treatment completed n (%)	Treatment failed n (%)	Lost to follow-up n (%)	Died n (%)	Treatment success n (%)
2015	941	------	924 (15.2)	0	17(1.8)	0	924 (98.1)
2016	1304	------	1283 (21.2)	0	11(0.8)	10(0.7)	1283 (98.3)
2017	1253	------	1239 (20.4)	0	4(0.3)	10(0.8)	1239 (98.8)
2018	1290	------	1278 (21.0)	0	7(0.5)	5(0.3)	1278 (99.0)
2019	1348	------	1335 (22.0)	0	9(0.7)	4(0.6)	1355 (99.1)
Total	**6136**	------	**6059(98.7)**	**0**	**48(0.7)**	**29(0.4)**	**6059 (98.7**
Treatment outcome of Extra Pulmonary Bacteriologically Confirmed or clinically diagnosed							
Diagnostic Year	Total No. of cases	Cured n (%)	Treatment completed n (%)	Treatment failed n (%)	Lost to follow-up n (%)	Died n %	Treatment success n (%)
2015	750	------	724 (96.5)	0	26(3.46)	0	724 (96.5)
2016	1289	------	1258 (97.5)	0	23(1.7)	8(0.6)	1258 (97.5)
2017	1360	------	1337 (98.3)	0	18(1.3)	5(0.3)	1337 (98.3)
2018	1525	------	1499 (98.2)	0	18(1.1)	8(0.5)	1499 (98.2)
2019	1241	------	1215 (97.9)	0	21(1.6)	5(0.4)	1215 (97.9)

which found PTB and EPTB present in 63.3% and 36.7% of patients, respectively. Our results are also comparable to earlier studies conducted in Ethiopia, where the prevalence of PTB and EPTB was reported to be 67.4% and 32.3% in(Shargie & Lindtjørn, 2005) study [20], and 71.7% and 28.3%, in (Tessema et al., 2009) study [21]. Therefore, our findings are consistent with previous research conducted in Ethiopia regarding the prevalence of PTB and EPTB.

During our research, 20% were diagnosed with PTB+, 39% with PTB-, and 39% with EPTB. Similar findings in Ethiopia's northern part also indicated significant EPTB cases and lower notification rates for PTB+ patients (Hirpa et al., 2013; Tessema et al., 2009) [21]. Compared to the national average of nearly 40% reported by WHO between 2015 and 2016, the proportion of PTB+ patients was much lower [22]. There is also a notable difference in the proportion of bacteriologically confirmed TB cases in this area compared to the national average of 48 percent (WHO, 2019) [3]. Some research indicated that as altitude increases, the prevalence of PTB decreases, even though it has no influence on EPTB incidence (Pérez-Guzmán et al., 2014) [23]. The percentage of EPTB in Pakistan's North-west is substantial, according to (Tahseen et al., 2020) [24].

Even though the underlying causes have not yet been determined, there are several probable reasons at this juncture: Anti-TB medicine over-prescription and the zoonotic spread of the disease [25]. Private healthcare institutions allegedly lack the equipment and knowledge required to accurately diagnose smear-negative PTB and EPTB; Estimates show that 15% of all EPTB cases and 97.3% of PTB smear-negative individuals had the misdiagnosis [26]. Based on an analysis carried out by (Fatima et al., 2019), A high number of children's TB cases were registered by private practitioners, and the majority of children (89 %)) were clinically diagnosed; Following the recorded linkage, the number of confirmed cases of tuberculosis in children's was meager, and a considerable underreporting rate of 78 % was observed. Because of the ZN's low sensitivity and low pathology testing, Clinicians sometimes declares tuberculosis suspected patients as confirmed pulmonary smear-negative patient [27].

Like the findings from Ethiopia, this research found that 51.92 % of the TB patients were men [19]. Women may have had lower rates of TB than men for several reasons, including a lack of health-seeking behavior, poor financial management, and the stigma associated with having TB. In addition, a multitude of variables, including sex-related genetic background, sexual hormones, and metabolism, among others, might contribute to gender disparities in vulnerability [12]. Moreover, It was found that 48.61% of all reported TB cases among the age group 0-14 years were in children. The notification rates of childhood TB for children aged 0-4 and 5-14 were 33.07 %and 66.92 %, respectively, which is more than the national estimate of 13 %. When feasible, rapid and reliable bacteriologically diagnostic tests should be used to confirm TB in children instead of clinical diagnosis [28]. Diagnostic criteria for pediatric tuberculosis in Pakistan are not being followed to the full extent recommended by the World Health Organization in private healthcare facilities. Screening for pediatric tuberculosis (TB) using children's symptoms is effective and affordable [29]. There is also the possibility of over diagnosis of TB in children. TB patients' treatment results and related reasons must be evaluated in order to determine the DOTS program's success. Failure to treat tuberculosis can lead to a wide range of issues, including drug resistance, extended infectiousness, and even death.

In the current study there was a steady rise in the treatment success rate over the course of the study. More EPTB patients (97.85%) than PTB patients (96.33%) were successfully treated when compared to all TB patients. As many as 98.76 % of the smear-negative PTB patients were successfully treated, compared to smear-positive PTB patients (93.90 %). Patients with sputum smear-negative and smear-positive PTB in our study achieved an impressive success rate of 96%, surpassing the results reported in Ethiopia by (Endris et al., 2014) at 94.8% (Tola et al., 2019) at 92.5% and in China by (Wen et al., 2018), also yielded success rates lower than ours [30, 31, 32]. Furthermore, our treatment success rate was much higher than the rates recorded in Southern Ethiopia by

(Gebrezgabiher et al., 2016); at 85.2%, Uzbekistan at 83% (Gadoev et al., 2015);, in the EU and European Economic Area at 78% (Karo et al., 2015) [33, 34, 35].

Our study found that EPTB patients had a higher treatment success rate of 97.85%. Countries with a high incidence of tuberculosis, such as Nigeria (52.3%), India (78.1%), and China (76.7%), have shown that EPTB patients had considerably lower rates of treatment success (Adamu et al., 2017; Ai et al., 2010; Sharma et al., 2014) [36, 37]. Only Pulmonary smear-positive individuals in the study had a treatment failure rate of 0.64 %, which was lower than the average TB treatment failure rate in high-TB-burden countries. (WHO, 2019) [3]. Our study indicates that a higher smear conversion rate of PTB that was smear-positive at the end of the intensive treatment phase, a key indicator of TB treatment failure, may be associated with a lowered treatment failure rate in patients (Namukwaya et al., 2011) [38], This might be linked to a lower rate of medication resistance in the district. (Hamusse et al., 2016) [39].

CONCLUSION

There was an overall low TB mortality rate in the research, which may be due to better treatment of TB patients, access of patients to advance mycrobacteriology labs, and better care of patients in the hospital. Loss to follow-up (LTFU) is a significant issue for TB control programs as it can lead to TB epidemics and bacterial resistance. Our research found that the prevalence of LTFU was 1.62%, but there was no association between LTFU and early risk indicators, such as smear-negative PTB or EPTB. The reason for the lower frequency of LTFU in our study could be attributed to the effective implementation of DOT measures in the region, such as defaulter supervision, tracing systems, and health education campaigns. Factors such as increased utilization of TB control services, improved DOTS performance, and better patient knowledge and access to healthcare may be contributing to the higher treatment success rate in the Swat district.

REFERENCES

1. WHO. (2021). *Global tuberculosis report 2021*.
2. Narasimhan, P., Wood, J., MacIntyre, C. R., & Mathai, D. (2013). Review Article Risk Factors for Tuberculosis. *Risk Factors for Tuberculosis*, *2013*, 8. https://doi.org/10.1155/2013/828939
3. WHO. (2019). *GLOBAL TUBERCULOSIS REPORT 2019*. World Health Organization. https://doi.org/10.16309/j.cnki.issn.1007-1776.2003.03.004
4. NTP. (2019). *NATIONAL TB CONTROL PROGRAM PAKISTAN ANNUAL REPORT 2019*. 76. https://ntp.gov.pk/wp-content/uploads/2020/10/Annual Report TB Pakistan 2019.pdf
5. Sepkowitz, K. A. (1996). How contagious is tuberculosis? *Clinical Infectious Diseases*, *23*(5), 954–962.
6. Bennett, J. E., Dolin, R., & Blaser, M. J. (2014). *Mandell, douglas, and bennett's principles and practice of infectious diseases: 2-volume set* (Vol. 2). Elsevier Health Sciences.
7. Xie, X., Li, F., Chen, J.-W., & Wang, J. (2014). Risk of tuberculosis infection in anti-TNF-α biological therapy: From bench to bedside. *Journal of Microbiology, Immunology and Infection*, *47*(4), 268–274.
8. Farhat, M. R., Shapiro, B. J., Kieser, K. J., Sultana, R., Jacobson, K. R., Victor, T. C., Warren, R. M., Streicher, E. M., Calver, A., Sloutsky, A., Kaur, D., Posey, J. E., Plikaytis, B., Oggioni, M. R., Gardy, J. L., Johnston, J. C., Rodrigues, M., Tang, P. K. C., Kato-Maeda, M., … Murray, M. (2013). Genomic analysis identifies targets of convergent positive selection in drug-resistant Mycobacterium tuberculosis. In *Nature Genetics* (Vol. 45, Issue 10, pp. 1183–1189). https://doi.org/10.1038/ng.2747
9. Patel, S., Parsyan, A. E., Gunn, J., Barry, M. A., Reed, C., Sharnprapai, S., & Horsburgh Jr, C. R. (2007). Risk of progression to active tuberculosis among foreign-born persons with latent tuberculosis. *Chest*, *131*(6), 1811–1816.
10. Cailhol, J., Decludt, B., & Che, D. (2005). Sociodemographic factors that contribute to the development of extra-pulmonary tuberculosis were identified. *Journal of Clinical Epidemiology*, *58*(10), 1066–1071.
11. Lawn, S. D., & Zumla, A. I. (2011). Tuberculosis. *Lancet (London, England)*, *378*(9785), 57–72. https://doi.org/10.1016/S0140-6736(10)62173-3
12. Möller, M., & Hoal, E. G. (2010). Current findings, challenges and novel approaches in human genetic susceptibility to tuberculosis. *Tuberculosis*, *90*(2), 71–83.
13. Steingart, K. R., Henry, M., Ng, V., Hopewell, P. C., Ramsay, A., Cunningham, J., Urbanczik, R., Perkins, M., Aziz, M. A., & Pai, M. (2006). Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. *The Lancet Infectious Diseases*, *6*(9), 570–581.
14. WHO. (2013). *Systematic screening for active tuberculosis: principles and recommendations*. World Health Organization.
15. Nachiappan, A. C., Rahbar, K., Shi, X., Guy, E. S., Mortani Barbosa Jr, E. J., Shroff, G. S., Ocazionez, D., Schlesinger, A. E., Katz, S. I., & Hammer, M. M. (2017). Pulmonary tuberculosis: role of radiology in

diagnosis and management. *Radiographics*, *37*(1), 52–72.
16. Kuhn, J. E. (2013). Current Concepts. *Current Sports Medicine Reports*, *12*(5), 311–315. https://doi.org/10.1249/jsr.0000000000000000
17. Hanifa, Y. (2019). *Investigation pathways for tuberculosis among HIV-positive adults in South Africa* [London Sch o ol of Hygiene & Tropical Medicine]. https://doi.org/https://doi.org/10.17037/PUBS.04655980
18. Zijenah, L. S. (2018). The World Health Organization Recommended TB Diagnostic Tools. *Tuberculosis*, 71.
19. Alem, Y., & Gebre-Selassie, S. (2017). Treatment Outcome of Tuberculosis Patients in Selected Health Centres in Addis Ababa: a Five Year Retrospective Study. *Journal of Lung Health and Diseases*, *1*(1).
20. Shargie, E. B., & Lindtjørn, B. (2005). DOTS improves treatment outcomes and service coverage for tuberculosis in South Ethiopia: a retrospective trend analysis. *BMC Public Health*, *5*(1), 1–11.
21. Tessema, B., Muche, A., Bekele, A., Reissig, D., Emmrich, F., & Sack, U. (2009). Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, North-west Ethiopia. A five-year retrospective study. *BMC Public Health*, *9*(1), 1–8.
22. WHO. (2016). Global tuberculosis report. *Geneva: World Health Organization*, 1–214.
23. Pérez-Guzmán, C., Hernández-Cobos, S., Vargas, M. H., del Rosario Arellano-Macías, M., García-Ituarte, A. Z., & Serna-Vela, F. J. (2014). Clinical and epidemiological features of extra-pulmonary tuberculosis in a high incidence region. *Salud Pública de México*, *56*(2), 189–196.
24. Tahseen, S., Khanzada, F. M., Baloch, A. Q., Abbas, Q., Bhutto, M. M., Alizai, A. W., Zaman, S., Qasim, Z., Durrani, M. N., Khalid Farough, M., Ambreen, A., Safdar, N., & Mustafa, T. (2020). Extra-pulmonary tuberculosis in Pakistan- A nation-wide multicenter retrospective study. *PLoS ONE*, *15*(4), 1–16. https://doi.org/10.1371/journal.pone.0232134
25. Berg, S., Schelling, E., Hailu, E., Firdessa, R., Gumi, B., Erenso, G., Gadisa, E., Mengistu, A., Habtamu, M., & Hussein, J. (2015). Investigation of the high rates of extra-pulmonary tuberculosis in Ethiopia reveals no single driving factor and minimal evidence for zoonotic transmission of Mycobacterium bovis infection. *BMC Infectious Diseases*, *15*(1), 1–10.
26. Ehlers, V. J., & Aragaw, G. S. (2014). An audit of diagnosis and treatment of tuberculosis in Ethiopia. *African Journal of Primary Health Care & Family Medicine*, *6*(1), 1–6.
27. Fatima, R., Yaqoob, A., Qadeer, E., Hinderaker, S. G., Ikram, A., & Sismanidis, C. (2019). Measuring and addressing the childhood tuberculosis reporting gaps in Pakistan: The first ever national inventory study among children. *PloS One*, *14*(12), e0227186.
28. Marais, B. J., & Graham, S. M. (2016). Childhood tuberculosis: a roadmap towards zero deaths. *Journal of Paediatrics and Child Health*, *52*(3), 258–261.
29. Mandalakas, A. M., Hesseling, A. C., Gie, R. P., Schaaf, H. S., Marais, B. J., & Sinanovic, E. (2013). Modelling the cost-effectiveness of strategies to prevent tuberculosis in child contacts in a high-burden setting. *Thorax*, *68*(3), 247–255.
30. Endris, M., Moges, F., Belyhun, Y., Woldehana, E., Esmael, A., & Unakal, C. (2014). Treatment Outcome of Tuberculosis Patients at Enfraz Health Center, North-west Ethiopia: A Five-Year Retrospective Study. *Tuberculosis Research and Treatment*, *2014*, 726193. https://doi.org/10.1155/2014/726193
31. Tola, A., Minshore, K. M., Ayele, Y., & Mekuria, A. N. (2019). Tuberculosis Treatment Outcomes and Associated Factors among TB Patients Attending Public Hospitals in Harar Town, Eastern Ethiopia: A Five-Year Retrospective Study. *Tuberculosis Research and Treatment*, *2019*, 1503219. https://doi.org/10.1155/2019/1503219
32. Wen, Y., Zhang, Z., Li, X., Xia, D., Ma, J., Dong, Y., & Zhang, X. (2018). Treatment outcomes and factors affecting unsuccessful outcome among new pulmonary smear positive and negative tuberculosis patients in Anqing, China: a retrospective study. *BMC Infectious Diseases*, *18*(1), 104. https://doi.org/10.1186/s12879-018-3019-7
33. Gebrezgabiher, G., Romha, G., Ejeta, E., Asebe, G., Zemene, E., & Ameni, G. (2016). 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*, *11*(2), e0150560.
34. Gadoev, J., Asadov, D., Tillashaykhov, M., Tayler-Smith, K., Isaakidis, P., Dadu, A., Colombani, P. de, Gudmund Hinderaker, S., Parpieva, N., & Ulmasova, D. (2015). Factors associated with unfavorable treatment outcomes in new and previously treated TB patients in Uzbekistan: a five year countrywide study. *PloS One*, *10*(6), e0128907.
35. Karo, B., Hauer, B., Hollo, V., van der Werf, M. J., Fiebig, L., & Haas, W. (2015). Tuberculosis treatment outcome in the European Union and European Economic Area: an analysis of surveillance data from 2002–2011. *Eurosurveillance*, *20*(49), 30087.
36. Adamu, A. L., Gadanya, M. A., Abubakar, I. S., Jibo, A. M., Bello, M. M., Gajida, A. U., Babashani, M. M., & Abubakar, I. (2017). High mortality among tuberculosis patients on treatment in Nigeria: a retrospective cohort study. *BMC Infectious Diseases*, *17*(1), 1–11.
37. Sharma, S. K., Soneja, M., Prasad, K. T., & Ranjan, S. (2014). Clinical profile & predictors of poor outcome of adult HIV-tuberculosis patients in a tertiary care centre in north India. *The Indian Journal of Medical Research*, *139*(1), 154.
38. Namukwaya, E., Nakwagala, F. N., Mulekya, F., Mayanja-Kizza, H., & Mugerwa, R. (2011). Predictors of treatment failure among pulmonary tuberculosis patients in Mulago hospital, Uganda. *African Health Sciences*, *11*, 105–111.

39. Hamusse, S. D., Teshome, D., Hussen, M. S., Demissie, M., & Lindtjørn, B. (2016). Primary and secondary anti-tuberculosis drug resistance in Hitossa District of Arsi zone, Oromia regional state, Central Ethiopia. *BMC Public Health*, *16*(1), 1–10.

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