

Trends and Public Health Implications of Tuberculosis Coinfections with HIV, Diabetes, and COVID-19: A Five-Year Study in Srikakulam District

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ABSTRACT

The primary objective of this study was to analyse the trends and public health implications of tuberculosis (TB) coinfections with HIV, diabetes (DM), and COVID-19 in the Srikakulam district over a five-year period (2018-2022). This cross-sectional study utilized data from the Government General Hospital in Srikakulam, focusing on trends in TB notifications, particularly the increasing incidence of extra-pulmonary TB, the declining trend of HIV-reactive TB, and the consistent prevalence of TB-DM coinfections. Additionally, the study explored the low incidence of TB-COVID coinfections. Data analysis was performed using logistic regression and chi-square tests to assess the relationship between variables. The results revealed a significant rise in extra-pulmonary TB cases, a decrease in TB-HIV coinfections, and a stable rate of TB-DM coinfections. Interestingly, TB-COVID coinfections were found to be minimal, suggesting limited interaction between these diseases. The study concludes that integrated healthcare strategies, including enhanced screening, diagnostics, and public awareness campaigns, are essential for effectively managing TB and its associated coinfections. The findings underscore the need for continued research and monitoring to adapt public health interventions to the evolving dynamics of TB coinfections, thereby improving patient outcomes and reducing the overall burden of tuberculosis.

Keywords:

GGH (Govt General Hospital), HIV (Human Immune Virus), MTBC (Mycobacterium tuberculosis complex), RIMS (Rajiv Gandhi Institute of Medical Sciences), Coinfections, Diabetes.

INTRODUCTION

Coinfections of tuberculosis are defined as the presence of two or more microbial infections in a patient with tuberculosis. These coinfections can be classified into viral, bacterial, parasitic, or fungal infections. The presence of coinfections can complicate the diagnosis, treatment, and overall outcome of tuberculosis [1]. Tuberculosis incidence and mortality computed from the Global Burden of Disease study: This article presents an analysis of global tuberculosis (TB) incidence and mortality from 2018 to 2022, using data from the epidemiological analysis. The study found that TB is still a serious public health issue, with high TB occurrence and ephemerality in low-income countries. The study also identified a decline in TB incidence and mortality rates in high-income countries, but highlights the need for continued efforts to reduce the global TB burden [2].

TB-HIV co-infection:

Co-infection between tuberculosis and HIV is a serious global health issue, especially in areas where both illnesses are common. HIV impairs immunity and raises the risk of tuberculosis

(TB) infection, which can hasten the development of HIV into AIDS. The World Health Organisation (WHO) estimated that among HIV-positive people, there were 1.4 million new cases of tuberculosis (TB) in 2019 and 208,000 deaths due to TB-HIV coinfection [3]. This article discusses the prevalence and impact of HIV and TB co-infection in, which has the highest burden of both diseases. The article highlights the importance of addressing the co-epidemic of HIV and TB in through coordinated efforts in healthcare [4].

TB-Diabetes Co-infections:

A chronic metabolic condition known as diabetes affects millions of people globally. Diabetes increases a person's likelihood of getting an active TB infection and are more likely to have poor TB treatment outcomes. The interaction between TB and diabetes is complex, and can lead to a range of health complications. The WHO estimates that in 2019, there were approximately 1.2 million new cases of TB among people with diabetes [5]. According to an Indian study, TB patients had a greater prevalence of DM than the general population, and that patients with DM were more likely to develop TB disease. Other research showing a relationship between diabetes and tuberculosis risk in both HIV-positive and HIV-negative groups does not modify these findings [6]. Several studies have investigated the prevalence and impact of coinfections of tuberculosis. A study conducted and found that nearly half of the patients with tuberculosis had at least one coinfection, with HIV being the most common. This study reported that coinfections were associated with longer hospital stays and higher mortality rates among tuberculosis patients [7]. The coexistence of HIV, DM, and TB presents a complex clinical challenge. Effective management often requires an integrated approach to care that takes into account the multiple chronic conditions and their interrelated health consequences. Notwithstanding these challenges, there are tactics that may be implemented to mitigate the prevalence of illness within this demographic, including better screening for DM and TB, improved access to antiretroviral therapy, and efforts to promote lifestyle changes that can reduce the risk of DM and other chronic conditions [8]. Extra-pulmonary tuberculosis (EPTB) refers to tuberculosis (TB) infection that occurs outside the lungs. It may impact the body's lymph nodes, bones and joints, gastrointestinal tract, genitourinary tract, central nervous system, and other organs and tissues. Here are some key points about extra-pulmonary tuberculosis, along with references for further reading: Prevalence and Distribution: EPTB accounts for about 15-20% of all tuberculosis cases worldwide, with significant regional variations. The distribution and prevalence of EPTB can vary depending on the population studied and geographical region. [9].

Common Types of Extra-pulmonary Tuberculosis:

- i. Lymphatic tuberculosis: Involves lymph nodes and is the typical form of EPTB.
- ii. Skeletal tuberculosis: Affects the bones and joints, commonly the spine (Pott's disease).
- iii. Genitourinary tuberculosis: Affects the kidneys, bladder, and genital organs.
- iv. Gastrointestinal tuberculosis: Affects the gastrointestinal tract, including the intestines, stomach, and peritoneum.

- v. Central nervous system tuberculosis: Affects the brain and spinal cord.
- vi. Other types include pericardial tuberculosis, miliary tuberculosis, and cutaneous tuberculosis.[10].

Diagnosis: Diagnosis of EPTB can be challenging due to its varied presentation and the difficulty in obtaining samples for testing. Various diagnostic methods include imaging (X-rays, CT scans), laboratory tests (microscopy, nucleic acid amplification tests), and invasive procedures (biopsy, fine-needle aspiration). [11]. **Treatment:** Treatment of EPTB generally follows the same principles as pulmonary tuberculosis, involving a combination of multiple anti-tuberculosis drugs for an extended duration. The kind of infection and based on the disease's location and intensity, the course of treatment may vary. Surgical intervention may be necessary in certain cases, such as spinal tuberculosis with neurological complications.[12].

Tuberculosis (TB) coinfection with COVID-19 is a salient clinical study due to the potential interaction between these two respiratory infections. Although research on the specific interactions between TB and COVID-19 is ongoing, I can provide you with some information based on the available studies and guidelines up until my knowledge cutoff in 2022. Please observe that the situation may have raised since then, so it's always advisable to review the latest scientific literature and medical guidelines. **Increased susceptibility:** Individuals suffering from tuberculosis may have compromised immune systems, rendering them more vulnerable to COVID-19. The immunosuppression associated with TB could potentially increase the risk of severe illness from COVID-19.[13]. **Diagnostic challenges:** Distinguishing between TB and COVID-19 can be challenging because they share similar clinical symptoms, such as fever, cough, and respiratory distress. Laboratories and healthcare systems may face difficulties in conducting timely and accurate diagnostic tests for both diseases simultaneously.[14]. **Disease severity:** Some studies suggest that individuals with concurrent TB and COVID-19 may experience more severe illness compared to those with either infection alone. The combined effects of both infections on the respiratory system could lead to worsened clinical outcomes.[15]. **Treatment challenges:** Managing TB and COVID-19 coinfection can present challenges due to potential drug interactions, prolonged treatment regimens, and monitoring complications. The management of both diseases requires careful consideration of individual patient characteristics and collaboration among different healthcare specialties.[16].

MATERIALS AND METHODS

1. Study design: The Cross-sectional research conducted at health facilities on people with PTB who attended and required TB treatment in RIMS, GGH was carried out from January 2018 to December 2022. The study of cases included all persons with tuberculosis suspicion who sought treatment at the medical facility during the research period. All TB-assumed patients who demonstrated clinical TB symptoms, such as a fever, a persistent cough lasting more than two weeks, and night sweats, and who were willing to take part in the study, were comprised.

2. Study site description: The study was presented in the Srikakulam district of India's North Coastal Andhra Pradesh. The distance between the district, Andhra Pradesh's capital city, is 464 kilometres. There are 23,19,061 people living in the district as a whole, and 62.17% of them depend on farming for their livelihood. Where the current study was conducted, RIMS, GGH, Srikakulam, has 800 beds, 60 of which were designated for treating TB in the Srikakulam district.

3. Sampling method: A practical and intentional sampling approach was used. Identification of the respondents who complied with the inclusion requirements and were approachable was aided by a licensed health professional at the location.

4. Data collection procedure: Patients received thorough explanations of the research purpose and the provided accord. A standardized inquiry form was utilized to collect information on participants' demographic and socioeconomic traits as well as their knowledge about tuberculosis, its treatment, and the factors that affect adherence. Due to the respondents' desire for anonymity and privacy, their names were not comprehended on the survey.

5. Data Analysis: Microsoft Excel version 16 was utilized for analysis after data entry. Thus, logistic regression analysis and the chi-square test were employed to ascertain the relationship between variables and adherence as well as plausible factors that could influence adherence to TB medication. Variables having Chi-square test analysis p values less than or near to 0.05 were taken into account in the logistic regression study. A p value less than 0.05 was regarded as statistically significant at a 95% level of confidence.

RESULT AND DISCUSSION

The study conducted on TB patients along with co infections having HIV-AIDS, DM, & COVID and adding the condition like extra pulmonary tuberculosis. In this overview the research of five years data was recorded i.e., 2018-2022 in Srikakulam, Government General Hospital TB case notifications. Here we enclosed the coinfections like as trends in proportion of HIV & HIV reactive TB notifications, TB-DM & TB-COVID.

Trends in proportion of extra-pulmonary TB case notifications

Year	TB notification - pulmonary TB	TB notification - extra-pulmonary	% of extra-pulmonary TB notification
2018	2716	296	10.90
2019	2920	538	18.42
2020	1460	498	34.11
2021	2025	826	40.79
2022	2169	1062	48.96

Table-1. Trend in proportion of extra pulmonary TB case

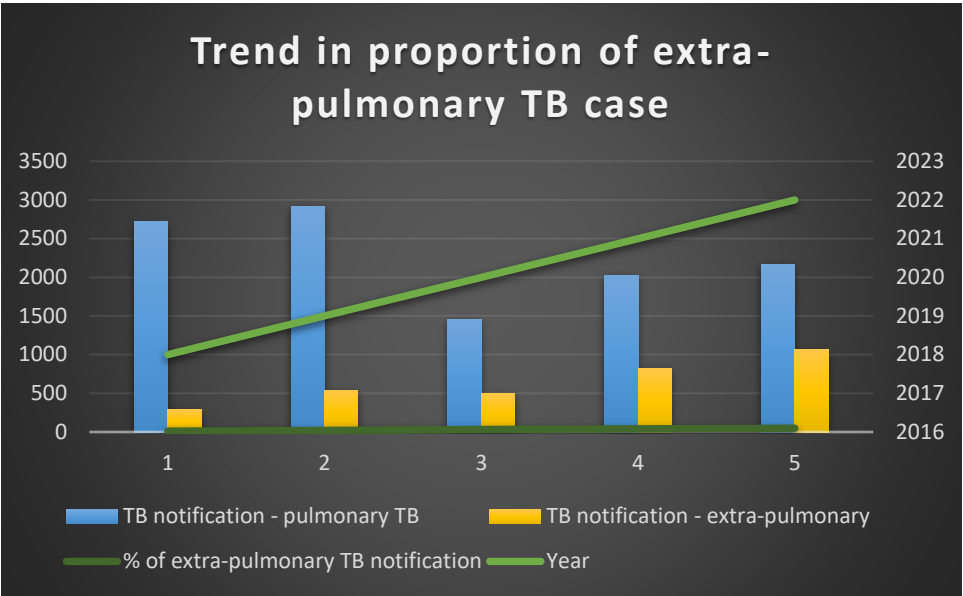


Figure-1. Graph of trend in proportion of extra pulmonary TB case

From the Table-1, the TB pulmonary case notifications in the subsequent years 2018 to 2022, 11,290 patients were observed. The pulmonary tuberculosis is former and most common and the extra pulmonary TB involves and effecting remaining organs other than lungs. Mostly there is 10-20% of chance in occurring pulmonary TB, according to the data 3,220 extra pulmonary cases are recorded in overall TB pulmonary cases (Figure-1).

Trend in proportion of HIV reactive TB notifications

Year	TB notification - Total	TB notification - with HIV reactive result	% of HIV reactive TB notification
2018	2742	167	6.09
2019	3851	200	5.19
2020	1990	99	4.97
2021	2695	94	3.49
2022	3231	83	2.57

Table-2. Trend in proportion of HIV reactive TB notifications

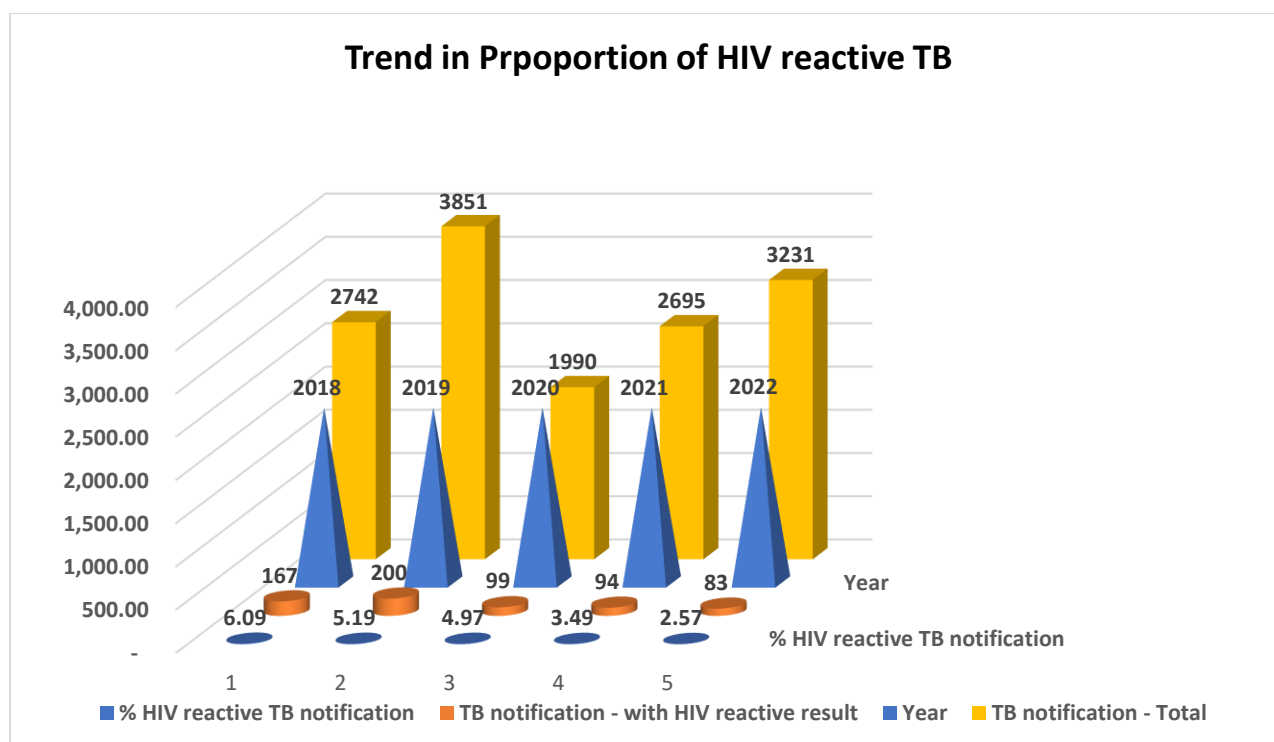


Figure-2. Graph of trend in proportion of HIV reactive TB

Total TB notification according to Table-2 are 2742, 3851, 1990, 2695, 3231 for the 5 years i.e., 2018, 2019, 2020, 2021 and 2022. Over all percentage of HIV reactive TB notification are 6.09%, 5.19%, 4.97%, 3.49% and 2.57% according to the HIV reactive result. Figure-2 shows the increase in HIV reactive TB cases along with the year i.e., 2020, 2021, 2022. Where 2018 and 2019 years shown hike in cases and sudden drop seen in the next year as per graph.

TB-HIV

Year	TB-HIV patients (Total number)	HIV patients registered in the district Total number (on active care)
2018	167	783
2019	200	662
2020	99	356
2021	94	466
2022	83	512

Table-3. TB-HIV Patients

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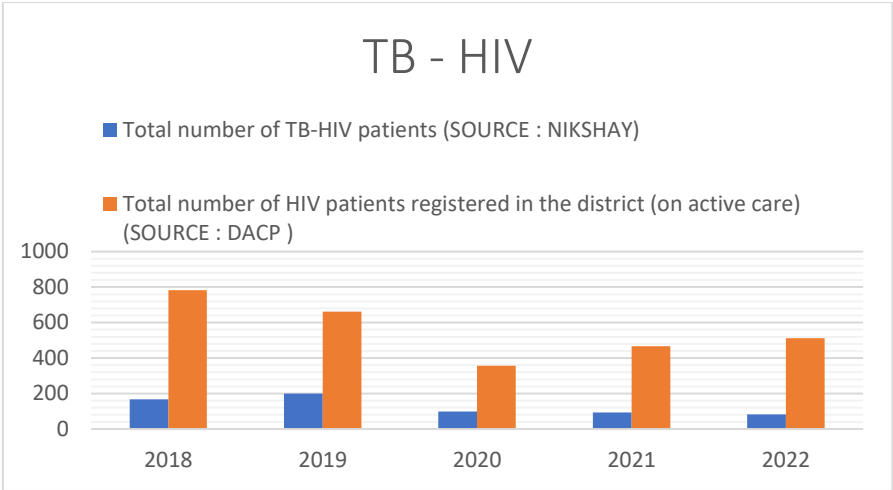


Figure-3. Graph of TB-HIV Patients vs TB Patients

Table-3 represents the total number of TB-HIV patients vs total number of HIV patients registered in Srikakulam district. As per the 3rd table and figure, the total number of only HIV patients for 5 years (2018 – 2022) are 2779 and the total number of TB-HIV patients are 643 which shows approximate percentage of TB-HIV patients is 23%.

TB-DIABETES

Year	Total number of TB-DM patients	Diabetic patients registered in the district Total number
2018	72	NOT AVILABLE
2019	133	58695
2020	119	56665
2021	308	104993
2022	308	34909

Table-4. TB-DIABETES

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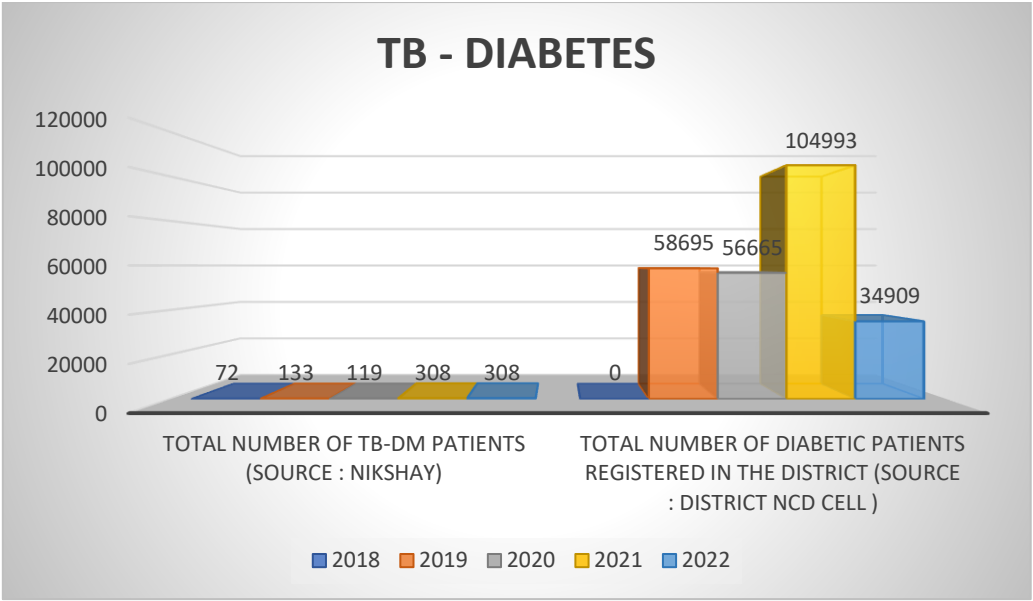


Figure-4. Graph of TB-Diabetic patients vs Diabetic patients

From the table-4 total number of TB-DM patients were 940 and last two years (2021 and 2022) shows no change in the patients’ number. Where the only diabetic patients number registered in the district are 2,55,262. According to the 4th table and figure only 0.36% of TB-DM patients were registered in the total number of diabetic patients in the district.

TB-COVID

Year	TB-COVID patients’ number	COVID patients diagnosed number in the district (on active care)
2020	5	46254
2021	2	77425
2022	0	10625

Table-5. TB-COVID Patients

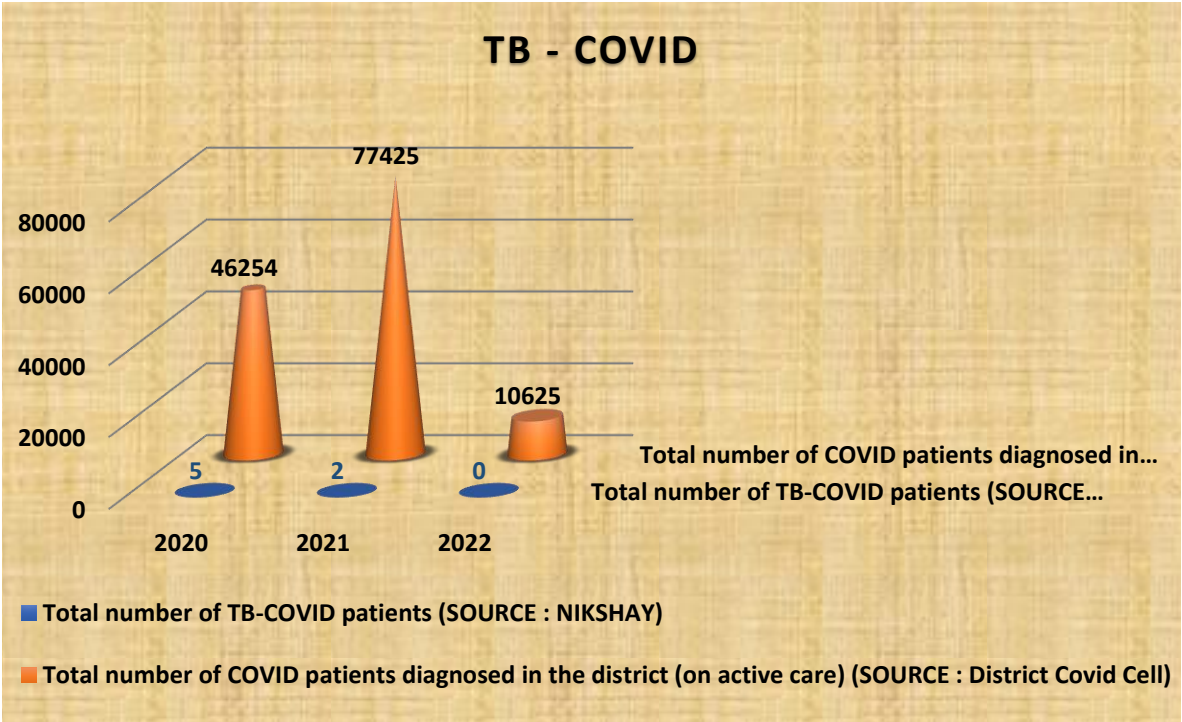


Figure-5. Graph of TB-Covid patients vs Covid patients

As per the results noted in the 5th table which represents in the Figure-5 graph, In 2022, there were nearly "zero" TB-COVID patients, and the district had 10625 total COVID patients with diagnoses. Comparing the overall number of patients with COVID-19 with the total number of patients with COVID-19 alone it was almost nil and which represents there is very less effect of TB on covid patients.

Discussion

This study offers an in-depth analysis of tuberculosis (TB) coinfections with HIV, diabetes (DM), and COVID-19 over a five-year period (2018-2022) in the Srikakulam district. The findings highlight the evolving nature of TB coinfections and their significant public health implications.

Trends in Extra-Pulmonary TB Cases: The observed increase in extra-pulmonary TB cases, rising from 10.90% in 2018 to 48.96% in 2022, suggests a shift in the diagnosis and recognition of TB that affects organs outside the lungs. This trend may be driven by improved diagnostic techniques, greater awareness among healthcare providers, or changing disease patterns. The data underscores the need for enhanced diagnostic and treatment strategies tailored to address extra-pulmonary TB with the same rigor traditionally reserved for pulmonary TB. This shift in focus is critical for improving patient outcomes and reducing the overall burden of TB.

TB-HIV Coinfection Trends: The study shows a decline in HIV-reactive TB notifications, from 6.09% in 2018 to 2.57% in 2022. This decrease can be attributed to effective HIV management strategies, including the widespread use of antiretroviral therapy (ART), which has been shown to reduce the risk of TB in HIV-positive individuals. However, the persistence of TB-HIV coinfections highlights the need for ongoing integrated healthcare services that address both TB and HIV, particularly in high-prevalence areas. Continuous efforts are required to further reduce TB-HIV coinfections and to maintain the gains achieved in HIV management.

TB-Diabetes Coinfection: The data reveals a concerning trend of TB-DM coinfections, with a steady proportion of TB patients being diagnosed with diabetes. This finding aligns with global research that identifies diabetes as a significant risk factor for TB. The interaction between these two conditions complicates treatment and requires a comprehensive approach that includes regular screening for diabetes among TB patients and vice versa. Integrated care strategies that address both TB and diabetes are essential to mitigate the risks and improve patient outcomes.

TB-COVID Coinfection: Interestingly, the study found a very low incidence of TB-COVID coinfection, with nearly zero cases reported in 2022. This suggests that TB may not exacerbate the severity of COVID-19 as initially feared, or it may reflect the effectiveness of public health interventions in controlling the spread of both infections. However, the potential interactions between TB and COVID-19 warrant further investigation, particularly as new variants of the virus continue to emerge. Continuous monitoring and research are essential to fully understand the dynamics between these two infections.

The study's findings have significant implications for public health policies and practices. The rising incidence of extra-pulmonary TB and TB-DM coinfections, coupled with the ongoing challenge of TB-HIV coinfections, calls for more robust and integrated healthcare strategies. Public health interventions should focus on:

Enhanced Screening and Diagnostics: Improve the detection and treatment of extra-pulmonary TB and TB-DM cases through advanced diagnostic tools and comprehensive screening programs. **Integrated Healthcare Services:** Maintain and enhance integrated care for TB-HIV coinfections, ensuring continuous access to ART and other critical services. **Public Awareness Campaigns:** Raise awareness about the risks of TB-DM coinfections and promote lifestyle changes that can reduce the incidence of diabetes, thereby lowering the risk of TB. **Continuous Monitoring:** Keep a close watch on the interactions between TB and emerging infections like COVID-19 to adapt public health strategies as needed.

Conclusion

This study provides a comprehensive analysis of TB coinfections with HIV, diabetes, and COVID-19 over a five-year period in the Srikakulam district. The findings underscore the complexity of TB coinfections and the need for tailored public health strategies to address the specific challenges they present.

The rising incidence of extra-pulmonary TB and the steady prevalence of TB-DM coinfections highlight the need for enhanced diagnostic and treatment approaches. The decline in TB-HIV coinfections reflects the success of integrated healthcare services, but continued efforts are necessary to maintain these gains. The low incidence of TB-COVID coinfections suggests limited interaction between these two infections, but ongoing research is essential to confirm this finding.

Overall, this study emphasizes the importance of integrated healthcare strategies that address the multifaceted nature of TB coinfections. By focusing on the specific needs of patients with TB-HIV, TB-DM, and TB-COVID coinfections, healthcare providers can improve treatment outcomes and contribute to the global effort to reduce the burden of tuberculosis. Continued research and monitoring are crucial to adapting public health strategies to the changing dynamics of TB coinfections and ensuring effective disease management across diverse populations.

REFERENCES

1. Dhasmana DJ, Ross C, Armstrong-James D. Coinfection of tuberculosis and other opportunistic infections in HIV-infected patients. *Clin Chest Med.* 2013;34(2):239-50.
2. Global tuberculosis incidence and mortality during 1990-2016 as computed from the Global Burden of Disease 2016 study: <https://www.ncbi.nlm.nih.gov/pubmed/29150277>
3. World Health Organization (WHO). Global tuberculosis report 2020. Available at: <https://www.who.int/publications/i/item/9789240013131>
4. HIV and tuberculosis co-infection in Southeast Asia: <https://www.ncbi.nlm.nih.gov/pubmed/22581435>
5. World Health Organization (WHO). Global report on diabetes. Available at: <https://www.who.int/publications/i/item/9789241565257>
6. Wang, Q., Ma, A., Han, X., Li, X., Chen, X., Feng, B., & Zhao, H. (2017). Diabetes mellitus and the risk of multidrug resistant tuberculosis: a meta-analysis. *Scientific Reports*, 7, 1090.
7. Cruz AT, Starke JR. Clinical manifestations of tuberculosis in children. *Paediatr Respir Rev.* 2007;8(2):107-17.
8. . Basit, A., & Fawwad, A. (2014). Diabetes mellitus and its complications in tuberculosis. *Journal of Diabetes and Metabolic Disorders*, 13(1), 37.

9. Zumla, A., Raviglione, M., Hafner, R., & von Reyn, C. F. (2013). Tuberculosis. *New England Journal of Medicine*, 368(8), 745-755. doi:10.1056/NEJMra1200894
10. World Health Organization. (2020). Global Tuberculosis Report 2020. Retrieved from https://www.who.int/tb/publications/global_report/en/
11. Theron, G., Jenkins, H. E., Cobelens, F., Abubakar, I., Khan, A. J., Cohen, T., & Dowdy, D. (2015). Data for action: collection and use of local data to end tuberculosis. *The Lancet*, 386(10010), 2324-2333. doi:10.1016/S0140-6736(15)00321-1
12. World Health Organization. (2019). Treatment Guidelines for Drug-Resistant Tuberculosis. Retrieved from <https://www.who.int/tb/publications/2019/consolidated-guidelines-drug-resistant-TB-treatment/en/>
13. Tadolini M, Codecasa LR, García-García J-M, et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur Respir J*. 2020;56(1):2001398. doi:10.1183/13993003.01398-2020
14. Tadolini M, Codecasa LR, García-García J-M, et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur Respir J*. 2020;56(1):2001398. doi:10.1183/13993003.01398-2020
15. Gupta RK, Harrison EM, Ho A, et al. Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. *Lancet Respir Med*. 2021;9(4):349-359. doi:10.1016/S2213-2600(20)30559-7
16. World Health Organization. Tuberculosis and COVID-19: Considerations for tuberculosis (TB) care in the context of COVID-19. Published 2020. Accessed September 25, 2021. https://www.who.int/tb/COVID_19considerations_tuberculosis_services.pdf.