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Original article

A RETROSPECTIVE CROSS-SECTIONAL STUDY INVESTIGATING THE PREVALENCE OF COVID-19 AND TB COINFECTION IN PATIENTS IN KWAZULU-NATAL, SOUTH AFRICA.

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Abstract.

Background:

The co-occurrence of tuberculosis (TB) and Covid-19 poses significant challenges to public health systems worldwide. This study aimed to investigate the prevalence of TB and Covid-19 co-infection, explore the correlation between TB status and Covid-19 results, and examine the distribution of co-infection across different age groups in KwaZulu-Natal, South Africa.

Methods:

A retrospective analysis was conducted using data retrieved from a laboratory database, including 1241 TB patient results between April 2020 and April 2021. Diagnostic methods for TB included microscopy, culture, GeneXpert, and line probe. Covid-19 test results were categorized as positive, negative, or inconclusive. Statistical analysis, including statistical significance tests, was performed to assess the correlation between TB status, Covid-19 co-infection, and age groups.

Results:

Among the TB patients, 3.95% were diagnosed using microscopy, 7.01% using culture, 88.80% using GeneXpert, and 0.24% using line probe. Out of the 1241 TB patients, 50% were males and 49% were females. Among the tested patients, 84% tested negative for Covid-19, 14.5% tested positive, and 1% had inconclusive findings. The statistical significance analysis indicated no significant correlation between TB status and Covid-19 co-infection ($p > 0.05$). However, a significant association was observed between age groups and Covid-19 co-infection ($p < 0.05$).

Conclusion:

This study provides insights into the prevalence and correlation of TB and Covid-19 co-infection among a diverse patient population. Although no significant correlation was found between TB status and Covid-19 co-infection, there was a significant association between age groups and co-infection rates. These findings highlight the need for tailored screening, prevention, and treatment strategies considering different age groups. The study contributes to the existing literature and can inform healthcare policies and interventions related to TB and Covid-19 co-infection.

Recommendation:

To address the co-infection, we recommend strengthening surveillance, enhancing awareness, conducting further research, improving infection control, and developing integrated healthcare approaches.

Keywords: Tuberculosis, Covid19, coinfection, prevalence, correlation, age group, Submission: 2023-05-07 Accepted: 2023-05-11

1. Background:

The year 2019 marks the advent of a global pandemic, the coronavirus disease of 2019 (Covid-19), which dominated both the scientific community and mainstream media. The Covid-19 pandemic became a major public health threat due to its rapid spread across the world causing significant morbidity and mortality as well as economic disruption (1-4). According to World Health Organisation (WHO), in 2020, Sub-Saharan African countries reported 33 92117 Covid-19 cases with 83 787 deaths in Africa (5). Approximately 40% of these confirmed cases (12 14176) were from South Africa (5). While Covid-19 took center stage, it is important to remember the existence of other serious and gruesome diseases of the respiratory tract such as Tuberculosis (TB) which did not disappear because of the Covid-19 pandemic. Similar to Covid-19, TB is a communicable disease of the respiratory tract caused by the bacillus Mycobacterium tuberculosis which to date has killed more than 1.6 million globally (5). According to WHO in 2021, Sub-Saharan African countries accounted for two-thirds of the total number of TB cases globally (6).

Both TB and Covid-19 are transmitted via respiratory droplets and aerosols (7). Both diseases cause severe acute respiratory syndrome that commonly presents with symptoms that include a dry cough, fever, headache, and shortness of breath (7-9). In high-burden and resource-limited settings, this makes it difficult for healthcare workers to distinguish between the two diseases (8). This is concerning when considering the potential effect that co-infection would have on the mortality of infected individuals. The immune system abnormalities brought on by each pathogen frequently result in an out-of-control inflammatory response, which can speed up the progression and severity of both diseases (10, 11). The Covid-19 infection causes a transient immune deficiency which leads to chronic stimulation of T-cells causing cytokine storm and T-cell exhaustion (12-14). These cytokine storms and hyper-inflammation can lead to multiple-organ failure and reactivation of diseases like Latent TB (11, 15, 16). Although this has been investigated, the prevalence of TB and Covid-19 coinfection in different settings has not been well investigated. In light of the above-reported fatality rate due to Covid-19 and TB co-infection, the effect of quality healthcare service providers to address this challenge is crucial. Therefore, when considering the limited access to services, including healthcare, which was experienced during the periodic Covid-19 pandemic lockdowns, knowledge about the prevalence of Covid-19 and TB co-infection during this period is important.

In addition to this being an important issue for South Africa nationally, it is even more important for the province of KwaZulu-Natal (KZN) which is heavily burdened with TB infections including cases of extensively drug-resistant TB (XDR-TB) (17-20). A potential concern to public health was the lack of prompt attention given to TB diagnosis and treatment during the Covid-19 pandemic, which could have resulted in a surge of drug-resistant MTB strains (21, 22). This population was likely under-represented in the published cohorts on Covid-19. As such the current study was conducted using retrospective results of patients who had been tested for TB and Covid-19 in Durban KZN in South Africa. It was anticipated that the study findings would inform medical practitioners on how to manage TB patients in the advent of Covid-19.

This study aimed to investigate the prevalence of TB and Covid-19 co-infection, explore the correlation between TB status and Covid-19 results, and examine the distribution of co-infection across different age groups.

2. Methodology:

A cross-sectional study was conducted on retrospective results of TB patients who had tested for Covid-19. The results were conveniently selected from a hospital-based laboratory database in a hospital in Durban, KZN. Durban is a metropoli-

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tan city in KZN which is located on the eastern seaboard of South Africa. To eliminate bias, the researcher established clear eligibility criteria for TB patient results to help minimize selection bias. By specifying the eligibility criteria upfront, the researcher ensured that the sample was representative of the intended population.

2.1. The following eligibility criteria were employed:

2.1.1. Inclusion Criteria:

- Patients diagnosed with tuberculosis (TB) within a specified timeframe (April 2020 - April 2021).
- Patients whose TB diagnosis was confirmed using microscopy, culture, GeneXpert, or line probe techniques.
- Patients for whom results of TB and Covid-19 testing were available in the laboratory database.
- Patients of various age groups, including children and adults.

2.1.2. Exclusion Criteria:

- Patients with incomplete or missing TB diagnostic results.
- Patients with incomplete or missing Covid-19 test results.
- Patients whose age group information was not recorded.
- Patients who were not tested for Covid-19.

Before data access, the researcher submitted a formal request for data through an online application system used by the laboratory. The results utilized for this study were those of specimens that had been tested using polymerase chain reaction diagnostics assays and sputum culture techniques. The retrospective results retrieved from the laboratory's results repository were sorted and checked for discrepancies, such as missing information, inaccurate addresses, and duplicate entries. All duplicate information was deleted. Microsoft Excel 2013 was used for descriptive statistical analysis and to determine the correlation between variables. Categorical variables were also discovered using the chi-square.

3. Results:

A total of 1241 TB patient results were retrieved from the laboratory database between April 2020 – April 2021 and included in this study. Out of 1241 TB patients, 49 (3.95%) were diagnosed with TB using microscopy, and 87 (7.01%) were diagnosed using culture. A total of 1102 (88.80%) patients were diagnosed using GeneXpert, and only 3 (0.24%) were diagnosed using a line probe. From the retrieved results 623 (50%) were from males and 618 (49%) from female TB patients who had been tested. Out of 1241 TB patient results tested for Covid-19, 13 (1%) were younger than 10 years of age of which 1 was from a female patient and 1 from a male patient. A total of 12 (1%) results were from patients aged 10-19 years where 5 were females and 7 were males. In the age group of 20-29 years 360 (29%) results were retrieved among which 268 were from females and 92 from males. A total of 501 (40%) results were from patients in the age group of 30-39 years of which 297 were females and 20 were males. In the age group 40-49 years 246 (20%) results were retrieved of which 22 were female and 224 were male. In the age group 50-59 years there were 89 (7%) results of which 13 were from females and 76 from males, 10 (0.8%) results were those of patients aged 60-69 years among which 6 were from females and 4 from males, a total of 8 (0.64%) results were from 70 – 80 years in which 6 were from females and 2 from males, only 2 (0.16%) results were those of male patients aged 80 years and above.

3.1. Gender distribution of Covid-19 test results

Table 2 presents Gender and Covid-19 result counts.A total of 1048 (84%) TB patients tested negative for Covid-19 and 180 (14.5%) tested positive for Covid-19. Out of the 180 (14.5%) Covid-19 positive results, 94 were among female patients while 86 were from among male patients. Additionally, there were 13 results which gave inconclusive findings of which 5 (0.40%) were from female patients and 8 (0.64%) from male patients.

Table 1: **Socio-demographic profile of patients whose results were retrieved**

Age group in years	**Total number of test results**	**Female**	Percentage of females	**Male**	Percentage of males
<10	13	1	0.08%	12	1%
10-19	12	5	0.4%	7	0.6%
20-29	360	268	22%	92	7%
30-39	501	297	24%	204	16%
40-49	246	22	2%	224	18%
50-59	89	13	1%	76	6%
60-69	10	6	0.5%	4	0.3%
70-80	8	6	0.5%	2	0.2%
>80	2	0	0%	2	0.2%

Table 2: **Covid-19 results distribution by age**

Age group	**Female (n = 94)**		**Males (n = 86)**	
Age group	**Positive results**	**Inconclusive results**	**Positive results**	**Inconclusive results**
<10	0	0	0	0
10-19	0	0	0	0
20-29	37	2	13	1
30-39	48	2	21	2
40-49	2	0	33	0
50-59	3	0	16	5
60-69	3	0	1	0
70-80	1	1	2	0
80>	0	0	0	0
TOTAL	**94**	5	**86**	8

3.2. Statistic correlation

Table 2 presents the calculated statistical significance p value investigating correlation between TB status and Covid-19 co-infection. The resulting p value after correlation of TB status and Covid-19 results was 0.21600652 ($p > 0.05$). Correlation between age group of TB patients tested and Covid-19 was also investigated. The resulting p value of this investigation was 0.000289446 ($p<0.05$).

4. Discussion:

The results of this study provide valuable insights into the diagnostic methods and gender distribution of TB patients and their co-infection with Covid-19. Among the 1241 TB patients included in the study, microscopy and culture were less commonly used for diagnosis, with only 3.95% and 7.01% of patients diagnosed using these methods, respectively. This contrasts with the widespread use of GeneXpert, which accounted for the diagnosis of 88.80% of the patients. These findings suggest that GeneXpert has become the preferred diagnostic method for TB due to its speed and accuracy in detecting Mycobacterium tuberculosis. This is in keeping with the World Health Organisation's recommendations to use GeneXpert as the first diagnostic test for TB (23).

Regarding the gender distribution, approxi-

Table 3: **Statistical significance through p value**

Correlation between Variables	Statistical significance	P value
Clinical findings and Covid-19 results	No	0.21600652
Age group and Covid-19 results	yes	0.000289446

mately equal numbers of male and female TB patients were tested, with 50% of the retrieved results coming from males and 49% from females. This indicates that TB affects both genders relatively equally, emphasizing the importance of targeted interventions and awareness campaigns for both male and female populations. This contrasts the findings of a study on gender distribution on a study conducted in Kenya, which revealed that TB prevalence was higher in males than females (24). In another study conducted in Pakistan TB prevalence was higher in women than men (25). A study conducted in South Africa revealed more men than women are suspected of having TB as a possible reason for a higher prevalence of TB in men than women (26).

The study also examined the co-infection of TB patients with Covid-19. Among the 1241 TB patients tested for Covid-19, 84% tested negative and 14.5% tested positive for Covid-19. The higher percentage of negative results suggests that TB patients may have a lower susceptibility to Covid-19, although further investigation is required to understand the underlying factors contributing to this trend. Research on Covid-19 prevalence in TB patients is conflicting, however, a systematic review on the subject revealed that TB and Covid-19 infection is common across the globe (27). Furthermore, the correlation analysis revealed that there was no statistically significant correlation between TB status and Covid-19 co-infection ($p>0.05$). This finding suggests that TB infection does not necessarily increase the risk of co-infection with Covid-19 or vice versa. However, several studies on TB and Covid-19 coinfection reported that coinfection promotes the progression of both diseases and increases morbidity and mortality (10, 11). It is important to note that both diseases pose significant public health challenges independently, and appropriate measures should be taken to prevent and manage each condition effectively.

In terms of age distribution, the study identified variations in the number of TB patients across different age groups. The highest number of results (29%) was retrieved from the age group of 20-29 years, followed by the age group of 30-39 years (40%). These findings are not unexpected considering that TB prevalence is highest in young adults. However, the findings highlight the need for targeted interventions and screening programs focusing on younger populations who are more susceptible to TB infection. Additionally, it is worth noting that there were relatively fewer results from patients aged 80 years and above, indicating a potential underrepresentation of this age group in the study population.

The strengths of the study were as follows: The study included a large number of TB patients (1241) with varied demographic characteristics, including different age groups and genders. This diversity enhances the representativeness of the findings and allows for better generalizability to similar populations. The study retrieved data from a laboratory database, which may have provided comprehensive and accurate information on TB and Covid-19 test results. This minimizes the risk of recall bias or reliance on self-reported data. The study employed statistical analysis to investigate the correlation between TB status, Covid-19 co-infection, and age groups. The use of statistical methods adds rigor to the study and helps draw valid conclusions from the data. The study examined the relationship between TB and Covid-19, which is a timely and relevant topic given the ongoing global pandemic. Understanding the co-infection rates and their implications can contribute to better management strategies and public health interventions. This study adds to the body of knowledge on TB and Covid-19

co-infection, particularly regarding the age distribution of affected patients. The findings may help fill gaps in the current literature and guide future research in this field. The study's results could have important implications for healthcare policies and interventions related to TB and Covid-19. The identification of a correlation between age groups and co-infection rates may inform targeted screening, prevention, and treatment strategies for specific populations. The study builds upon previous research by exploring the relationship between TB, Covid-19, and age groups. By using a more recent dataset (April 2020 - April 2021) and conducting statistical analyses, the study provides an updated understanding of this relationship. The findings of this study may have direct implications for clinical practice. Understanding the co-infection rates and factors associated with TB and Covid-19 can help healthcare providers in diagnosing, managing, and treating patients effectively.

This study also had limitations firstly including the study design, which was retrospective, relying on data collected from the laboratory database. This may have introduced selection bias or incomplete data, as not all relevant variables or patient characteristics may have been recorded. The accuracy and reliability of the laboratory data used in the study could be a potential limitation. Errors in data entry or misclassification of TB or Covid-19 results could impact the validity of the findings. The study may have lacked comprehensive information about individual patients, such as their comorbidities, treatment history, or socioeconomic factors. These variables could have influenced the outcomes but were not included in the analysis. The study focused specifically on the correlation between TB status, Covid-19 co-infection, and age groups of patients. Other factors that could potentially impact the outcomes, such as HIV co-infection or treatment outcomes, were not considered. The study design was cross-sectional, capturing data from a specific time. Longitudinal studies or prospective designs would provide a more comprehensive understanding of the dynamics between TB and Covid-19 over time. The study may not have accounted for potential confounding factors that could influence the relationship between TB, Covid-19, and age groups. Factors such as socioeconomic status, access to healthcare, or behavioral characteristics were not included in the analysis.

5. Conclusion

This study provides important insights into the diagnostic methods, gender distribution, and co-infection status of TB patients with Covid-19. The gender distribution of TB patients is relatively equal, emphasizing the importance of gender-specific interventions. The results suggest that while there is no significant correlation between TB status and Covid-19 results, there is a significant correlation between age group and Covid-19 results. Targeted interventions and screening programs should be developed, particularly for younger age groups who are more vulnerable to TB. However, the underrepresentation of patients aged 80 years and above in the study warrants attention in future research. Overall, these findings contribute to our understanding of TB and its co-infection with Covid-19, supporting evidence-based strategies for the prevention, diagnosis, and management of both diseases.

6. Recommendations

Strengthen TB and Covid-19 surveillance: Given the co-infection rate of TB and Covid-19, it is important to strengthen surveillance systems to monitor and detect cases of co-infection. This will help in understanding the epidemiological link between the two diseases and guide appropriate interventions for prevention and control. Enhance awareness and education: Public health campaigns should focus on increasing awareness about TB and Covid-19, their modes of transmission, and the importance of early diagnosis and treatment. Targeted educational programs should be developed to reach different populations, considering gender-specific messaging and age-specific interventions. Conduct further research: While this study provided valuable insights, further research is needed to explore

the factors contributing to the lower susceptibility of TB patients to Covid-19 and vice versa. Strengthen infection control measures: Given the potential transmission risks of both TB and Covid-19, healthcare facilities should prioritize strict infection control measures. This includes proper ventilation, use of personal protective equipment, and adherence to standard precautions to prevent the spread of both diseases within healthcare settings. Develop integrated healthcare approaches: Considering the co-occurrence of TB and Covid-19, there is a need for integrated healthcare approaches that address both diseases comprehensively. This includes coordination between TB and Covid-19 programs, ensuring that patients receive appropriate care and management for both conditions.

By implementing these recommendations, healthcare systems can improve the diagnosis, prevention, and management of TB and its co-infection with Covid-19, leading to better health outcomes for affected individuals and reduced transmission rates in the community.

7. Ethical considerations

Ethical clearance obtained from the university prior to data collection.

8. Abbreviations

Covid-19: Corona virus disease of 2019
KZN: KwaZulu-Natal
TB: Tuberculosis
WHO: World Health Organisation
XDRTB: Extensively drug-resistant TB

9. Funding

No funding obtained.

10. Data availability

De-identified laboratory data will be made available if requested.

11. Conflict of interest.

There is no conflict of interest.

12. Consent.

Not applicable because the study analysed retrospective results from the laboratory database.

13. Author contribution.

VH and ZNJ developed the research concept together; VH wrote the draft manuscript; ZNJ reviewed and edited the draft manuscript; ZNJ supervised the research project; VH and ZNJ both agreed on the final version of the manuscript.

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