The prevalence of patients with undiagnosed pulmonary tuberculosis, undergoing surgery at Pelonomi Tertiary Hospital.

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DECLARATION OF AUTHORSHIP

I, Dr. Anna Margaretha Botha with the student number 2007009950, declare that the coursework Master's Degree THE PREVALENCE OF PATIENTS WITH UNDIAGNOSED PULMONARY TUBERCULOSIS, UNDERGOING SURGERY AT PELONOMI TERTIARY HOSPITAL that I herewith submit in a publishable manuscript format for the M.Med qualification in Anesthesiology at the University of the Free State, is my independent work and that I have not previously submitted it for a qualification at another institution of higher education. All sections of the paper that use quotes or describe an argument or concept developed by another author have been duly referenced, including all secondary literature used.

Dr. AM Botha

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ABSTRACT

Introduction: Tuberculosis (TB) is a significant cause of death in South Africa (SA), resulting in a massive financial burden on the economy of the country. Delayed diagnosis is a problem in low and middle-income countries and can unintentionally cause other patients and personnel exposure, especially in enclosed areas such as theatres. The short and long-term consequences of occupational acquired TB affect the health care worker's physical, physiological, and financial health. This might put much strain on the health care workers themselves, their families and the health care system.

Method: This was a retrospective descriptive study done in May 2020, investigating all patients over the age of thirteen years that underwent surgery at Pelonomi Tertiary Hospital for one month (from 1 November 2019 till 30 November 2019) to evaluate how many of these patients might have had active tuberculosis (known or unknown) on the day that they underwent surgery. All available laboratory TB test results of the patients were included from three months before the documented surgery date and up to three months post the surgery date. Any patient with a documented positive TB laboratory test result during this period and not on TB treatment for at least two weeks, was considered potentially infectious.

Results: A total of 583 patients underwent surgery in November 2019. Of these 583 patients, 21 had a TB test done during the mentioned period, and results were captured on the National Health Laboratory Service database. Only one patient of the total 21 who was tested for tuberculosis had a positive TB test, which was done on the day of surgery. On admission, the patient presented with a lower respiratory tract infection before receiving his open L4 biopsy for possible infective spondylolysis surgery. The staff screened the patient for pulmonary TB (PTB), and an Xpert® MTB/RIF Ultra (Xpert® Ultra) test was done on 12/11/2019. The Xpert® Ultra results reported on 13/11/2019 were positive and sensitive to Rifampicin, and the patient was subsequently started on treatment. On the day of surgery, the patient was assumed to only have a bacterial lower respiratory tract infection and was not managed as a TB infected patient, and the necessary precautions were not taken, leading to exposure of the theatre staff and other patients to PTB.

Conclusion: The proportion of undiagnosed TB infection under patients who were perioperatively tested was 4,8%. However, since only patients who were expected to be admitted to ICU after surgery or who had respiratory symptoms before surgery were tested for TB, this study could not determine the prevalence of TB in patients receiving surgery.

KEYWORDS AND GLOSSARY OF TERMS

Drug resistance	Reduced effectiveness of drugs.
Emergent cases	The patient has a life-threatening condition and needs to be managed immediately.
Interferon-γ release assays	Whole blood tests that can aid in the diagnosis of latent tuberculosis.
Latent infection	When bacteria are present in the body, without causing disease.
Respiratory hygiene	Covering the mouth and nose when coughing, dispose of tissues in the nearest waste after usage, washing hands after contact with respiratory secretions or contaminated materials/objects.
Tuberculin skin test	A skin test to determine whether a person has developed an immune response to TB bacteria is used to diagnose latent TB.
Tuberculosis	Tuberculosis is a disease caused by members of the *Mycobacterium tuberculosis* complex and primarily affects the lung tissue. It spreads via aerosols from one person to the next and can potentially cause severe infection.
Upper room germicidal ultraviolet system	Ultraviolet lights create in the upper portion of the room a germicidal zone where it interrupts the transmission of airborne infective diseases.
Urgent cases	A patient who needs quick, within six hours, but not immediate management.
World Health Organization	An United Nations specialized agency responsible for international public health.

LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
COIDA	Compensation for Occupational Injuries and Disease Act
DOH	Department of Health
FS	Free State
GUV	Germicidal ultraviolet
HCW	Health care workers
HEPA	High-efficiency particulate air
HIV	Human immunodeficiency virus
HOD	Head of Department
HSREC	Health Sciences Research Ethics Committee
HVAC	Heating, ventilation, and air-conditioning systems
ICU	Intensive Care Unit
IGRAs	Interferon-γ release assays
IPC	Infection prevention and control
LTBI	Latent tuberculosis infection
MDR	Multidrug resistant
NHLS CDW	NHLS Corporate Data Warehouse
PTB	Pulmonary Tuberculosis
RR	Rifampicin resistant
SA	South Africa
TB	Tuberculosis
TST	Tuberculin Skin Test

UFS	University of the Free State
WHO	World Health Organization
XDR	Extensive drug resistant
Xpert® Ultra	Xpert MTB/RIF Ultra test
μm	Micrometer

CHAPTER 1

Critical and Synthesized Review of Literature

INTRODUCTION

The World Health Organization's (WHO) Global Tuberculosis Report in 2016 reported that almost 10 000 health care workers (HCW) in the world contracted tuberculosis (TB) at that time.[1] Tuberculosis in developing countries is one of the top 10 causes of death worldwide and a leading cause of death in human immunodeficiency virus (HIV) infected people in 2018.[2] According to the Global Tuberculosis Report of 2019, the estimated number of new TB cases in 2018 were 10 (9,0 – 11,1) million globally, of which 5,7 million were men, 3,2 million women, and 1,1 million cases were children.[2] The report also showed that the total number of cases co-infected with HIV was 9%. According to the report, the global death toll due to TB infections was 1,5 (1,4 -1,6) million, and of those cases, 251 000 (223 000 – 281 000) were HIV positive. The national epidemic severity varies widely among countries. In 2019 the Global Tuberculosis Report indicated that less than ten new cases per 100 000 population were diagnosed and reported in most high-income countries, whereas 150 to 400 new cases were reported in the highest-burden countries. Furthermore, 500 per 100 000 cases were reported in a few countries, including Mozambique, the Philippines, and South Africa (SA). The eight countries with the highest TB burden accounted for 66% of the new cases and included India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and SA.[2]

The Global Tuberculosis Report of 2019 continued to state that although the TB mortality rate fell by 42% from 2000 to 2018, antimicrobial resistance is still a significant cause of TB-related deaths. The global statistics in 2018 indicated that 484 000 (417 000 – 556 000) people developed Rifampicin-resistant TB (RR-TB), with 78% of those cases having multidrug-resistant TB (MDR-TB).[2] These MDR-TB cases have TB resistance to both Rifampicin and Isoniazid, the backbone of TB treatment regimens. A total of 187 000 cases with MDR/RR-TB were detected, treated, and notified, and 156 000 were enrolled and started on second-line treatment, including more extended regimens with more side effects. However, only 56% of the 156 000 treated cases had successful outcomes, suggesting that the treatment success rate in patients with MDR/RR-

TB remains very low globally. The global estimate of extensive drug-resistant TB (XDR-TB) according to the Global Tuberculosis Report of 2019 was 6,2%.[2] XDR-TB is resistant to even the newest and repurposed anti-TB agents like Bedaquiline and Linezolid.[2]

Health care workers are at an approximately two times higher risk of developing latent and three times higher risk of developing active TB through nosocomial transmission.[3] The annual incidence of latent TB infection (LTBI), diagnosed with a positive tuberculin skin test (TST), ranges between 0,5% to 14,3% in the general population and between 33% to 79% in HCW.[4] Risk factors identified for developing LTBI in HCW included male gender, advanced age, BCG scar/vaccination, education level, household contact with TB, a smoking history, chronic disease, immunosuppression, and diabetes mellitus.[5]

Xpert® MTB/RIF Ultra test (Xpert® Ultra) and Xpert® MTB/RIF is currently the WHO recommended initial test for the diagnosis of TB globally.[6] In 2016, a prospective multicenter diagnostic accuracy study was done in eight countries, including SA, to compare the specificity and sensitivity of Xpert® Ultra with Xpert® MTB/RIF.[7] Both Xpert® MTB/RIF and Xpert® Ultra are automated molecular tests used to detect TB and Rifampicin resistance. Xpert® MTB/RIF is less sensitive to paucibacillary disease and in HIV-positive individuals. The study showed superior sensitivity of Xpert® Ultra in HIV and paucibacillary disease and showed decreased specificity in patients with a TB history. Rifampicin resistance was similar in these tests.[7] In 2018, the Xpert® Ultra replaced Xpert® MTB/RIF as a first-line diagnostic test in SA, with results available within three hours.[7]

PREVENTATIVE MEASURES

Despite the awareness of the high TB burden and risk of transmission to HCW and patients, there is still an inadequate implementation of infection control measures in health care facilities.[8] In 2018, the United Nations (UN) General Assembly Political Declaration recognized HCW as an occupational group at risk for developing TB and recommended TB infection prevention and control (IPC) and TB screening and surveillance to be implemented.[9]

Nosocomial infections are spread primarily via droplet transmission. Droplets mainly consist of water with different inclusions that depend on where or how the droplet is generated. In humans,

droplets are produced by breathing, talking, coughing, sneezing and singing, and contain various cell types, including epithelial cells and immune cells. It also contains mucous, saliva, and potentially pathological agents (viruses, fungi, and bacteria).[10] Droplets vary in size and content depending on where and how they are generated. Droplets bigger than five micrometer (μm) mostly get trapped in the upper respiratory tract (oropharynx — nose and throat), whereas droplets smaller or equal to five μm have the potential to be inhaled into the lower respiratory tract (the bronchi and alveoli of the lungs). Droplets bigger than five μm are subjected to gravity and fall to the ground rapidly, leading to a limited transmission distance of less than one meter. Droplets smaller or equal to five μm remain in the air for significant periods and have a transmission distance of more than one meter. Pathogenic TB particles are smaller or equal to five μm, which contributes to its infectiousness.[10] During intra-thoracic TB infection, there is a variable increase in the production of bio-aerosols of one to five μm. This variation in aerosol production can relate to the degree of infectivity and the risk of TB transmission.[11] The size of droplets is primarily due to the generation process and the environmental conditions, whereas the actual size of distribution depends on parameters such as exhaled air velocity, the viscosity of fluid, and the flow path (nose, mouth, or both).[10]

When looking at preventing the nosocomial spread of pulmonary tuberculosis (PTB), the framework of primary, secondary, and tertiary prevention should be implemented. The three primary preventative measures include administrative control measures, environmental control measures, and personal protection measures.[10] Administrative control measures include the routine screening of patients attending any hospital or health care clinic in SA for symptoms of active TB. It should be recognized that TB does not always present with the typical symptoms in immunocompromised patients, for example, HIV-infected patients.[12] All patients with a positive symptom screening test should be sent for TB sputum tests and be notified as indicated by South African TB guidelines. Screening is often neglected, in urgent or emergent cases, especially in patients who need to go to the theatre for emergency surgery. Environmental /engineering control measures such as proper ventilation of the theatres need to be implemented to improve airborne infection control.[10] Personal protection equipment accounts for the third and least overall effective level of TB infection control and includes wearing N95 masks. Secondary TB prevention includes the screening and rapid treatment of affected patients and HCW, aiming to keep HCW unimpaired and non-infectious.[13] Tuberculosis-infected HCW should be granted

special sick leave and adequate time for rehabilitation.[13] Secondary TB prevention includes medical care to HCW who contracted occupational TB disease. In low incidence TB countries, HCW should also be screened and treated for latent TB either with a skin test, TST, or blood test, Interferon-γ release assays (IGRA).[14]

The WHO conceptualized assessment and strengthening health systems by focusing on six inter-related aspects: governance and leadership, information, health financing, health workforce, services, and improving technology.[13] Each of these aspects needs to be implemented for TB prevention programs to be successful. In 2019, the WHO updated its recommendations on TB infection prevention and control (IPC).[15] The integrated package included seven primary interventions. These interventions included: Triage of people with TB signs and symptoms or with TB disease, respiratory separation of TB infected/suspected patients, prompt initiation of effective TB treatment in people with TB disease, respiratory hygiene, upper-room germicidal ultraviolet (GUV) systems, ventilation systems, and particulate respirators.

The spread of TB to HCW and other patients is a specific concern in theatre, where the anesthetist is especially vulnerable due to the proximity with the patient's airway during airway management and intubation.[16] Health care workers are furthermore at higher risk of contracting TB during certain high-risk procedures. Although high-risk procedures are not clearly defined, intubation, cardiopulmonary resuscitation, bronchoscopy, airway suctioning, autopsy, and surgery using high-speed devices have been associated with an increased risk of transmission of airborne infections.[17]

The 2005 guidelines set by the American Society of Anesthesiologists (ASA) specify measures that can be taken to minimize exposure to theatre staff and patients in theatre to possible TB aerosols.[18] Such measures include: Elective surgery should be delayed until the patient is no longer infectious – according to the American Association of Anesthesiology, it is defined as being on treatment for two to three weeks, clinical improvement, and three negative TB sputum smear tests on three different days. In emergency cases, surgery should take place in a theatre with the recommended ventilatory controls. Patients with known PTB coming for elective surgery should be done last on the theatre slate. The staff members in the theatre should be kept at minimal numbers needed for the procedure, theatre doors should be kept closed, and infectious hazard signs should be visible outside of the theatre. The patient and all staff should wear N95

masks, and the patient should be transferred directly into the correct theatre. Specific anesthetic-related measures include adequate good muscle relaxant to prevent coughing and stopping of the gas flow for an hour after surgery to prevent transmission of TB via the anesthetic circuit.

Additionally, two bacterial filters (High-efficiency particulate air (HEPA) filters), should be used. One filter on the patient's airway and one on the expiratory limb of the circuit to prevent the passage of particles equal to or greater than 0.3 μm to the anesthetic machine. All circuits to a potential TB infected person using a dedicated anesthetic machine or ventilator should be sterilized after any operation.[18] Exhausted air should ideally be diverted away from the hospital to prevent transmission but can be recirculated if it is filtered through a HEPA filter. Patients should be allowed to recover in a private recovery room or in the theatre to prevent exposure of other patients to PTB.[18]

Adequate ventilation plays a crucial role in preventing airborne infections or the spreading of TB. The movement of air carries droplets floating on air. The entrainment of air influences them into neighboring spaces (by opening a door between two rooms or a room and a corridor). Managing the movement of air can be achieved with ventilation.[10] Two types of ventilation systems are implemented when designing a hospital, namely natural ventilation, and hybrid ventilation systems.[10] Designing natural ventilation depends on the on-site design, building design, and vent opening design. The on-site design involves integrating the building/hospital with the topographical environment and the surrounding buildings that include the type of building. The internal distribution of airspace includes natural ventilation strategies, including heating, air-conditioning, and humidity control. The vent opening design looks at the site, size, and number of vent openings. Six basic natural ventilation systems can be identified and classified according to their architectural design elements. These include single-side corridors, central corridors, courtyards, a wind tower, an atrium and chimney, and hybrid (mixed-mode) ventilation. When looking at hybrid ventilation, three basic principles are important, including switching between natural and mechanical ventilation, fan-assisted natural ventilation, and concurrent use of these types. These systems are combined according to the specific needs and different areas in a hospital.[10]

The typical layout of an operation theatre includes a reception patient area, an anesthetic room, the main operation rooms, sterile material rooms, scrub rooms, auxiliary rooms, and a recovery

room. When designing air-conditioning for a theatre, parameters of importance include space, temperature, humidity, ventilation, and hygiene.[19]

The design of theatre ventilation remains extremely important with total air changes varying between 25 (conventional) and 300 (laminar airflow) per hour. A minimum recommendation of twenty total air exchanges per hour indoor and four outdoor air exchanges per hour is advised.[20] The two main types of ventilation designs described are conventionally ventilated operation suits and ultraclean ventilated operation theatres.[19] Conventionally ventilated operation suits are most commonly used and it work with turbulent air flow on the principle of dilution of air contaminants and prevention of air contaminants from the environment. It is generally considered adequate for general surgery. The air is filtered using filters of 82,95% efficiency, removing airborne particles greater or equal to five µm.[19] Ultraclean ventilated theatres use ultraclean air formed by laminar flow where the air travels parallel carrying contaminants away at the same velocity, thus decreasing airborne infections.[20] Part of the laminar flow design includes moving particle-free air at a constant rate of 0,3 to 0,5 µm/second over the aseptic operating field. Laminar flow is mainly combined with a HEPA filter, which removes all particles larger than 0,3µm with a 99,97% efficiency. Ultraclean ventilation is used in theatres where minimal particles can have detrimental effects, such as the arthroplasty theatre. Mixed airflow systems are also used at times. In these systems, laminar flow is only used in the critical areas, e.g., around the operating field. The rest of the theatre will work on the turbulent flow pattern.[20]

Measures to prevent the spread of TB, should be consistent through the whole health care system. It should ensure testing of patients presenting to hospitals and appropriate health care facilities. However, a delay in the diagnosis of TB is still a significant concern in low- and middle-income settings.[21] Reasons for this include failure to follow-up caused by a lack of available transport, patients living in rural areas with no health care facility nearby, and the high incidence of co-existing HIV infection.[21]

FINANCIAL IMPLICATION OF OCCUPATIONAL TUBERCULOSIS

Health care workers exposed to *Mycobacterium tuberculosis* in the workplace that later develops TB, are presumed to have an occupational or compensable disease according to the internal circular, (H/34/2004 26 March 2004), of the Department of Health (DOH), Provincial Government of the Western Cape. The circular is entitled 'Compensation for Occupational Injuries and Diseases Act (COIDA)', 1993 (Act No. 130 of 1993: 'Reporting of tuberculosis of the lungs in health care workers').[22] These HCW have a progressive benefit according to COIDA, which covers an occupation with a particular risk of contracting an infectious or parasitic disease. The benefits of claims made due to occupational or compensated TB are occupational leave (not deducted from sick leave) with a salary of 75% of the regular wage, reimbursement of medical expenses that were not covered by the HCW medical aid (up to 24 months from date of diagnosis) and payments for temporary (up to 24 months from date of diagnosis) or permanent disablement, based on the percentage of impairment. It also includes death benefits with reasonable burial expenses and widow's and dependents pensions if the patient is demised from occupational TB.[22] Unfortunately, many reported cases showed no record of the claim status on the Compensation Fund website leading to poor progression of claims. Poor communication regarding progression is also a problem.[22] All these factors contribute to the financial burden TB places on HCW and the health care system.

PSYCHOLOGICAL IMPACT OF OCCUPATIONAL TUBERCULOSIS

Chronic disease is frequently associated with psychological changes. Certain studies indicated that drug-resistant TB (DR-TB) had a higher incidence of psychiatric comorbidities and that the duration and severity of the disease correlated well with the prevalence of depression.[23] After TB, other psychiatric conditions acquired included adjustment disorders, mood disorders, anxiety disorders, somatoform disorders, delirium, cognitive disorders, and personality changes.[23]

In patients with occupational acquired TB, there are often feelings of decreased self-worth and a loss of dignity. The loss of identity due to getting ill, losing a job, and being dependent on the health care system rather than providing health care, is a major psychological hurdle that needs to be overcome. If all the above factors are not addressed timely, it can lead to a downward spiral

of anxiety, anger, depression, and frustration, amplified by the stresses of the illness itself, loss of income, and purpose.[24]

GAPS IDENTIFIED

There is also minimal data available on the exposure of theatre personnel specifically to PTB and its impact on the health care system. There are no statistics regarding which theatre personnel is at higher risk and more likely to contract occupational TB.

The psychological impact of working in a high-risk environment and being exposed to multiple occupational hazards such as TB, has not been evaluated in theatre personnel.

There is currently no South African or international research on the prevalence of TB in patients undergoing either emergency or elective surgery. Therefore, theatre personnel and other patients may still be at risk of contracting TB from patients diagnosed with TB before surgery. These risks can be minimized by implementing protective measurements, as stipulated by the ASA guidelines.[18] Unfortunately, these measures are not practically possible to implement in undiagnosed cases.

Establishing the prevalence of patients with undiagnosed TB in Pelonomi Tertiary Hospital preoperatively can assist in evaluating the quality and effectiveness of preoperative TB screening and assist in decreasing the exposure of health care personnel to occupational TB. Therefore, such a study can assist in decreasing the burden on the health care system and the financial and psychological burden associated with occupational TB.

AIM OF THE STUDY

The study aimed to estimate how frequently patients with undiagnosed/unreported pulmonary tuberculosis underwent surgery at Pelonomi Tertiary Hospital theatres.

OBJECTIVE

To extract the data of all the patients over the age of thirteen years, who underwent surgery in all the theatres at Pelonomi Tertiary Hospital during November 2019 including the data on the date and the type of surgery, emergency or scheduled, from the hospital theatre record books.

To compare the patient data collected from Pelonomi Tertiary Hospital theatre lists with the data from NHLS Corporate Data Warehouse (NHLS CDW), TrakCare, for three months before and three months after the patients' date of surgery and assess how many patients had positive Xpert® Ultra TB tests during that period.

To assess how many patients underwent surgery during November 2019 at Pelonomi Tertiary Hospital, with a positive Xpert® Ultra TB test and assess the exposure of theatre staff to undiagnosed/unreported PTB.

HYPOTHESIS

Health care workers are being exposed to patients with undiagnosed PTB booked for emergency or elective surgery at Pelonomi Tertiary Hospital, increasing their risk of developing occupational PTB.

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CHAPTER 2 (Publishable Manuscript)

ABSTRACT

Background: Tuberculosis (TB) is one of the major causes of death in South Africa (SA), resulting in a massive financial burden on the economy. Furthermore, delayed diagnosis is a problem in low and middle-income countries and can lead to unintentional exposure of Health care Workers (HCW) and patients. The study aimed to determine the number of undiagnosed pulmonary TB (PTB) amongst patients tested for PTB prior to receiving surgery.

Method: This was a retrospective descriptive study investigating patients older than thirteen, that underwent surgery at Pelonomi Tertiary Hospital during November 2019. Any patient with a documented positive TB laboratory test result three months before or three months after their surgery and not on TB treatment for at least two weeks, was considered potentially infectious.

Results: A total of 583 patients underwent surgery during the study period. Twenty-one patients (3,6%) had a TB test done during the six months of data included in the study. No pharmacy records were collected. Of the 21, only one patient with signs and symptoms of a lower respiratory tract infection was tested for pulmonary TB (PTB) preoperatively on the day of surgery, 12/11/2019. The Xpert® MTB/RIF Ultra test was reported positive on 13/11/2019. Unfortunately, the positive patient, was not managed as a TB infected patient during surgery, and the necessary precautions were not taken, leading to possible exposure to PTB of the theatre staff and other patients, stressing the need for increased infection control measures to be implemented.

Conclusion: The proportion of undiagnosed TB infection under patients perioperatively tested for TB was (1/21) 4,8%. However, since only patients admitted to ICU or patients showing respiratory symptoms were tested for TB before surgery, this study could not determine the prevalence of TB in patients receiving surgery.

INTRODUCTION

Pulmonary tuberculosis (PTB) is one of the top 10 causes of death worldwide, with South Africa being one of the eight countries contributing to 66% of the cases.[1] Along with the high incidence of PTB, the incidence of Rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB), and extensive drug-resistant TB (XDR-TB) is still high with a survival rate of only 56% with second line treatment globally.[1] Although the World Health Organization approved the molecular Xpert® MTB/RIF Ultra (Xpert® Ultra) test for rapid diagnosis of PTB with results available within four hours, delays in making the diagnosis of PTB is still of great concern in low- and middle-income settings. Reasons for this includes among others the failure to follow-up patients with positive test results due to lack of available transport, patients living in rural areas with no health care facility nearby, and the high incidence of co-existing HIV infection.[1,2] Therefore, health care workers (HCW) are at high risk of developing latent or active TB through nosocomial transmission, especially from undiagnosed patients not yet on treatment.[3] The World Health Organization's Global Tuberculosis Report in 2016 showed that almost 10 000 HCW in the world contracted TB at that time.[4] The annual incidence of latent TB infection (LTBI), diagnosed with a positive tuberculin skin test (TST), ranged between 33% to 79% in HCW.[5]

Despite the high TB burden and risk of transmission to HCW and patients, implementing infection control measures is still lacking in many health care facilities.[6] This is particularly true in the operating theatre environment, where the theatre personnel and especially the anesthetist work near the patient in a confined space, specifically, during airway management and intubation.[7]

To minimize exposure to theatre staff and other patients in theatre, the American Society of Anesthesiologists (ASA) guidelines of 2005 suggested specific patient handling, theatre ventilation and personal protection measures to be implemented.[8,9] Unfortunately, these practices are only implemented when patients are known to have contracted PTB or have been recently diagnosed with PTB. Thus, when a patient with undiagnosed PTB is admitted to hospital for surgery, they can potentially threaten the health of the HCW and other patients in the theatre, and the wards. Even the environments can be a source of infection where patients might be transported for any specific interventions or treatment when they expel infectious droplets into the air during breathing and coughing.[8,9]

When patients are known to or suspected of having active PTB and are in need of urgent surgery with no available PTB results, recommendations suggest that they should be done last on the theatre list.[8] The ASA guidelines of 2005 further state that staff members in the theatre should be kept at the minimal number needed for the procedure, with closed theatre doors and infectious hazard signs visible outside of the theatre to prevent staff from entering unnecessarily.[8] The patient should wear at least a surgical mask and staff should wear N95 masks to avoid airborne transmission pre- and post-induction of anesthesia.[8] The airway equipment used on these patients needs to be thoroughly cleaned with extra precautions to prevent transmitting TB to other users. The patient should be transferred directly into the correct theatre. Recovery must happen in an isolated or separate recovery room or the theatre used for the surgery to minimize the exposure of the other patients. These patients also need to be operated in theatres equipped with special high-efficiency particulate air (HEPA) filters and laminar airflow to minimize the time that TB bacilli remain in the air and to minimize the transmission distance.[8]

AIM OF THE STUDY

The study aimed to estimate how frequently patients with undiagnosed/unreported pulmonary tuberculosis underwent surgery at Pelonomi Tertiary Hospital theatres.

OBJECTIVE

To extract the data of all the patients over the age of thirteen years, who underwent surgery in all the theatres at Pelonomi Tertiary Hospital during November 2019, including the data on the date and the type of surgery, emergency or scheduled, from the hospital theatre record books.

To compare the patient data collected from Pelonomi Tertiary Hospital theatre lists with the data from NHLS Corporate Data Warehouse (NHLS CDW), TrakCare, for three months before and three months after the patients' date of surgery and assess how many patients had positive Xpert® Ultra TB tests during that period.

To assess how many patients underwent surgery during November 2019 at Pelonomi Tertiary Hospital, with a positive Xpert® MTB/RIF Ultra (Xpert® Ultra) TB test and assess the exposure of theatre staff to undiagnosed/unreported PTB.

METHODS

Study design:

A retrospective descriptive study design.

Study participants:

All patients over the age of thirteen years who underwent surgery of any kind, emergency, and elective, at any of the five theatres at Pelonomi Tertiary Hospital during November 2019 were included in the study.

Inclusion Criteria:

All patients over the age of thirteen who underwent surgery at Pelonomi Tertiary Hospital during November 2019.

Exclusion Criteria:

Children under the age of thirteen years were excluded from the study.

Patients for whom records could not be found.

Patients living outside of the Free State (as we did not have access to their TB records).

Measurements:

The name, date of birth, age, gender, and date of surgery of all patients over thirteen years who underwent surgery, elective and emergency, at Pelonomi Tertiary Hospital during November 2019 were collected from the theatre record books. The data was inserted into an Excel spreadsheet.

The patient data on Xpert® Ultra TB tests from the Pelonomi Tertiary Hospital were received from the NHLS CDW, TrakCare, for the above patients for three months before and three months after their date of surgery and was compared to the patient surgery data. In addition, the date of the negative or positive Xpert® Ultra TB test, and resistance/sensitivity to the anti-bacterial drug Rifampicin were recorded.

The number of patients that received surgery without a Xpert® Ultra TB test done were determined. If the diagnosis of tuberculosis was made three months before or three months after the documented surgery date, the patient was recorded as a potential case of undiagnosed PTB at the time of surgery.

Pilot study:

A pilot study was done at Pelonomi Tertiary Hospital theatres on five surgical patients to determine if there would be any problems with the proposed data collection system. No issues were identified, and the results of those five patients were included in the main study.

Methodological and measurement errors:

Electronic data capturing was complex, and faults could have occurred due to wrong entries of patients' dates of birth, wrong spelling of names and incomplete theatre records.

Patients were only included as potentially having PTB by using Xpert® Ultra TB tests results. The fact that a Xpert® Ultra TB test might not be routinely done and might cause the inability to determine prevalence was not considered. No other laboratory tests results were included nor

was any screening done for clinical signs or symptoms of PTB and no chest x-ray findings were looked at.

ANALYSIS

Data were analyzed using categorical variables. The data were expressed as frequencies, percentages, means, medians, and ranges. The Department of Biostatistics assisted with the analysis of the data collected.

ETHICAL CONSIDERATIONS

Ethics approval was obtained from the Health Sciences Research Ethics Committee (HSREC**)** of the Faculty of Health Sciences, University of the Free State. A change of study period application was applied for and approved by HSREC. Study Approval Number: UFS-HSD2019/2017/2502

Approval was sought and received by the Free State Department of Health (Health Research Committee). Study Approval Number: FS_201911_012.

RESULTS

The study was done for one month, from 1 November 2019 to 30 November 2019, at Pelonomi Tertiary Hospital. The first five patients that received surgery (1 November 2019) were part of the pilot study. The pilot study results included two patients who received previous TB tests**,** whose tests were done more than three months before their surgery. The other three patients did not have any TB test results on the system. The data of the study population from 1 November 2019 to 30 November 2019 are presented in (Figure 1). Of the patients, 583 met the inclusion criteria for the study, of which 230 cases were emergency surgery, and 412 were female. The patients had a median age of 33 years (range 14 – 88 y; IQR 27-41y). Of the 583 patients included in the study, 31 had TB test results, according to TrakCare. Of the 31 patients, 21 patients received their test three months prior to or three months after their surgery. The other ten patients had their TB tests done outside of the study period (Figure 1).

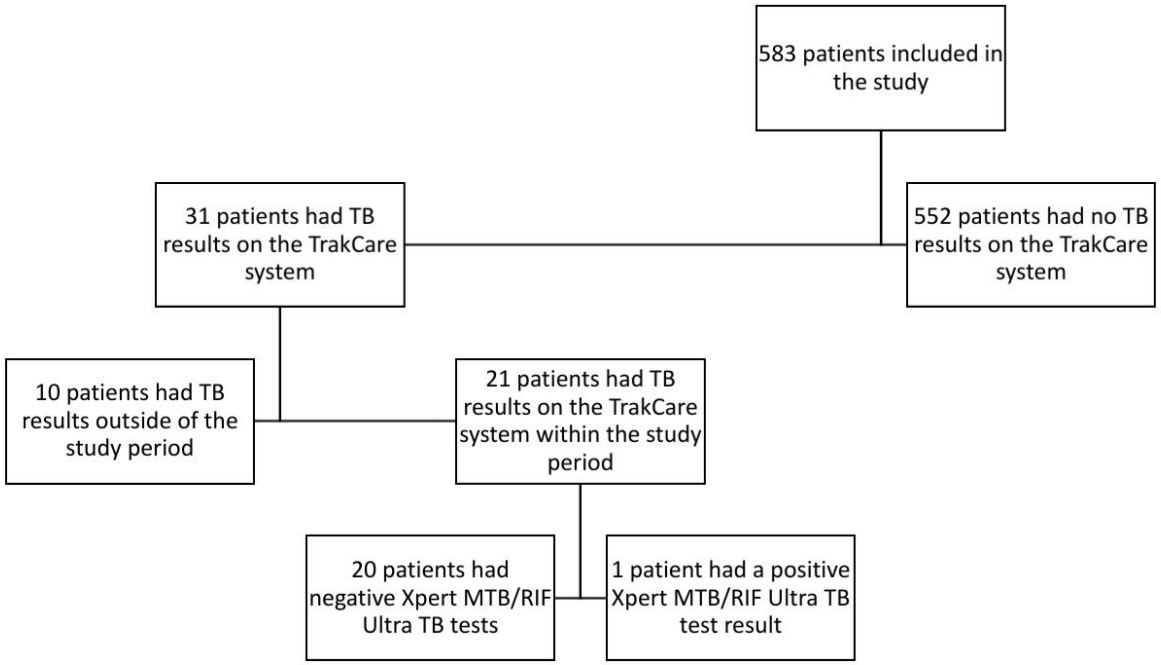

Figure 1: Flow diagram of the study population

Of these 21 patients, eight were tested preoperatively, seven on the same day of surgery, and six were tested postoperatively, and one of the latter was TB-positive, as illustrated in Table 1. Furthermore, of these 21 patients, eight were female, and the rest were male.

Table 1: TB diagnosis during the study period

TUBERCULOSIS		
TB DIAGNOSIS	FREQUENCY	PERCENTAGE
NEGATIVE	20	95,2
POSITIVE	1	4,8

Table 2: Date of TB testing and date of surgery

DATE OF TB TESTING AND DATE OF SURGERY			
DATE OF SURGERY	DATE OF TB TESTING	RESULT OF TEST	GENDER
1/11/2019	1/11/2019	Negative	Male
3/11/2019	3/9/2019	Negative	Female
3/11/2019	13/11/2019	Negative	Male
10/11/2019	26/9/2019	Negative	Male
11/11/2019	7/11/2019	Negative	Male
12/11/2019	13/11/2019	Positive	Male
12/11/2019	20/8/2019	Negative	Female
13/11/2019	14/10/2019	Negative	Female
14/11/2019	22/11/2019	Negative	Male
17/11/2019	27/11/2019	Negative	Male
18/11/2019	13/11/2019	Negative	Male
19/11/2019	19/11/2019	Negative	Female
20/11/2019	27/11/2019	Negative	Male

21/11/2019	21/11/2019	Negative	Male
21/11/2019	21/11/2019	Negative	Female
21/11/2019	21/11/2019	Negative	Male
21/11/2019	21/11/2019	Negative	Female
21/11/2019	19/12/2019 9/1/2020	Negative Negative	Male
21/11/2019	22/11/2019	Negative	Female
28/11/2019	13/11/2019	Negative	Male
30/11/2019	30/11/2019	Negative	Female

Comparing the date of the TB diagnostic test with the date of surgery in the 21 patients tested for PTB (Table 2) during the study period, eight patients received their testing on the same day as the surgery, and four of the eight patients were booked for emergency surgery. These four patients were transferred to the Intensive Care Unit (ICU) directly postoperatively. They were intubated on admission to ICU and, as part of the routine ICU admission investigations, received a sputum Xpert® Ultra, microscopy, culture, and sensitivity test for TB. All four of these patients had negative tests. Two of the other four patients had septic surgery (drainage of a liver abscess and chronic osteitis with non-union of a tibia fracture). The specimen forms sent to Microbiology did not specify if the Xpert® Ultra was done on the sputum or samples from the patients' wounds. The last two patients who received their TB testing on the same day as their surgery did not have any documentation stating why they received TB testing. These patients were not managed as possibly PTB intraoperatively.

One of the 21 patients tested TB-positive during the study period while having HIV and receiving first line antiretroviral treatment. The patient further had signs and symptoms of lower respiratory tract infection, and tests for TB (Xpert Ultra), Gram stain, bacterial, and mycology culture were requested only on 12/11/2019. However, an elective open L4 biopsy was booked for the same day. The operation was performed due to possible infective spondylolysis. The sputum Xpert® Ultra test results were reported as TB positive and sensitive to Rifampicin on 13/11/2019. On admission to the theatre, the patient was assumed to have a bacterial lower respiratory tract infection and was subsequently not managed as a TB infected patient. The patient received a general anesthetic with a supraglottic airway device, and the surgeon did local infiltration of the wound with a local anesthetic. The duration of the surgery was 40 min. The case was subsequently (13/11/2019) reported to the authorities as per South African guidelines, and the patient started on the correct treatment. The theatre staff was also informed of their exposure after the results were confirmed.

DISCUSSION

Assessing the frequency of undiagnosed perioperative and postoperative TB during one month, 1st to 30th November 2019, showed that 1 out of 21 patients tested perioperatively (three months before to three months post-surgery) had undiagnosed PTB when receiving surgery. This resulted in a PTB proportion of 4,8% amongst the 21 perioperative/postoperative patients tested for PTB during the study period, with the study unable to comment on the real exposure risk to potential active undiagnosed TB of theatre staff and or other patients.

This study was a retrospective study using theatre records. Of 583 patients receiving surgery during the mentioned month 552 never had a Xpert® Ultra TB test performed that was recorded and for ten patients the recorded test fell outside the criteria for inclusion of the study. Therefore, 562/583 (96,4%) of patients receiving surgery during the study period did not have TB screening or tests done. Different spellings of names and surnames and poor record-keeping could have contributed to records not being found. Two hundred and thirty cases were emergencies, and therefore no previous test would have been done preoperatively without TB symptoms. Masked PTB or abnormal presentations of potential PTB due to patients having other comorbidities, e.g., HIV or having additional pathology, e.g., bacterial lower respiratory tract infection, could also

have contributed to the potential under presentation of true PTB infections.[10]

The END TB strategy places great emphasis on early screening and diagnosis of TB.[4] The Xpert® Ultra has superior sensitivity over smear microscopy in the diagnosis of TB, but its routine use in the perioperative setting is not recommended due to increase in cost and increased waiting time for test results.[11]

Thirty-one patients had TB tests done according to TrakCare, of which 21 tests were done perioperatively. Most of the perioperative TB tests were done as part of routine PTB screening before admission to ICU and not due to symptomatic screening of patients for active TB or radiological suspicion of PTB, potentially further explaining the high prevalence of negative Xpert® Ultra tests in this study.

The main theatres at Pelonomi Tertiary Hospital primarily use mechanical ventilation systems and have no Upper-room germicidal ultraviolet (GUV) systems. Three of the five theatres, including the emergency, general surgery, and orthopedic theatres, have laminar flow, and the other two, maternity and gynecology, have turbulent flow. All the theatres have central heating by steam from boilers and central cooling from chillers. Pelonomi Tertiary Hospital uses three different air filters: washable filters, pocket filters, and HEPA filters. All the theatres have four supply diffusers and one extraction grill to aid in ventilation. Thus, Pelonomi Tertiary Hospital is complying with the WHO Guidelines of infection control in theatre.[9,12]

The PTB-positive patient described in this study was done as an elective orthopedic case done in a theatre with the necessary flow and ventilation that would have led to minimal exposure if the correct protocols were followed regarding personal protection, pre-and postoperative isolation.

SHORTCOMINGS OF THE STUDY

- During the pilot study two of five patients had TB tests more than three months before surgery and the other three did not have TB test results found. However, as the finding of test results was expected to be a challenge, the type of/lack of results were not noticed, indicating a major limitation of this study and resulted in a limited number of cases that were relevant.

- Limitation to one site and one theatre complex.
- Limited differentiation between elective and emergency surgery.
- Not considering patients who might have been on TB treatment, although this would not have changed the results of the one positive patient since the patient only had a positive TB test result which was done within 24 hours of the operation date. This patient, therefore, had not yet been on adequate TB treatment and was thus most likely potentially infectious.
- Patients with asymptomatic TB, mainly HIV-positive patients, could not be accounted for.
- Routine perioperative screening for symptomatic tuberculosis was not done.
- Missed laboratory results might be possible because of potential errors in patient identification.
- Selection bias is a real potential.

RECOMMENDATIONS

- A prospective study comparing the effectiveness of routine TB screening preoperatively with the result of Xpert® Ultra testing.
- A prospective study where all patients who were going for surgery has a TB Xpert® Ultra test done preoperatively to quantify the exposure of theatre personnel to PTB.
- Implementing the standard questionnaire for symptomatic TB screening as available and suggested by the health department for all patients admitted to hospital during the preoperative evaluation.

CONCLUSION

Most patients who underwent surgery at Pelonomi Tertiary Hospital did not get any form of TB screening preoperatively, due to inadequate or neglected practices. Although three of the five

theatres at Pelonomi Tertiary Hospital are equipped to prevent TB infection, implementation of universal TB infection control precautions in all theatres, even in a high TB endemic region, might still be impractical even though very important.

In this study a very small number of patients was tested for TB perioperatively. The few patients who were tested perioperatively mainly had negative laboratory TB test results, except for one patient. This study is unable to comment on the prevalence or the real exposure risk to active undiagnosed PTB of either theatre staff or other persons in the hospital environment. However, although the study indicated limited thread due to the small number, it might suggest a need for perioperative testing and in cases of emergency surgery, the use of TB preventative protocols.

Routine screening of all patients for TB symptoms on admission for surgery will most likely increase the number of undiagnosed patients with potential active PTB. This might be more practical since routine screening with either chest x-rays or laboratory testing is not feasible. A practical implementable approach for improving theatre safety in terms of TB transmission needs further research.

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A - Letter of Approval from Research Ethics Committee

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

05-Feb-2020

Dear **Dr Anna Botha**

Ethics Clearance: **The prevalence of patients with undiagnosed pulmonary tuberculosis, undergoing surgery at Pelonomi Tertiary Hospital.**

Principal Investigator: **Dr Anna Botha**

Department: **Anaesthesiology Department (Bloemfontein Campus)**

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2019/2017/2502**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
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B – Permission from HOD

Department of Anaesthesia
University of the Free State

1 July 2019

Dr. E. Turton
Head of Department Anaesthesia
University of the Free State
Bloemfontein

Re: Permission for research study.

I, AM Botha, am a registrar in anaesthesia. As part of my training I plan to do a study to determine the incidence of patients with undiagnosed pulmonary tuberculosis undergoing surgery at Pelonomi Tertiary Hospital and Universitas Academic Hospital.

I hereby request permission to use the information of patients that underwent surgery at Pelonomi Tertiary Hospital and Universitas Academic Hospital theatre in 2018 to compare it with patients that were newly diagnosed with pulmonary tuberculosis in the Free State in 2018.

Data analysis will be done by me, the researcher.

Regards

Dr. AM Botha
Registrar Anaesthesia

Dr. D. Steyn
Consultant in Infective Diseases
Department Internal Medicine

EW Turton HOD Anaesthesiology
1 July 2019

C - Copy of the research protocol approved by the HSREC

D – Forms for collecting data

Research numbe	Date of surgery	Name	Surname	Date of birth	Age	Gender	TB diagnosis	Rifampicin resistant	Date of diagnosis	Type of Surgery	Elective or Emergency surgery
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											

E – Full author guidelines for the South African Journal of Analgesia and Anesthesia (SAJAA)

F – A summary report compiled in the Turnitin Plagiarism Search Engine