

Pulmonary tuberculosis in a cohort of forensic autopsies: a preliminary study from Saudi Arabia

Journal of International Medical Research

48(2) 1–6

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DOI: 10.1177/0300060519896434

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Abstract

Aims: The purpose of this study was to identify any cases of previously undiagnosed pulmonary tuberculosis during autopsy.

Methods: This prospective study investigated a cohort of deceased individuals that underwent a full external and internal postmortem examination at the Forensic Medicine Centre, Dammam, Saudi Arabia. Gross pathology, histopathology and molecular pathology were used to identify pulmonary tuberculosis in forensic autopsy samples from the lungs.

Results: A total of 82 cases autopsied were included in the study. The mean \pm SD age of the study cohort was 35.5 ± 10.3 years (range, 20–80 years). Males ($n = 70$; 85.37%) outnumbered females. The deceased were from 15 different countries. The number of Saudis was 16 (19.51%). The maximum number of non-Saudis was from India with 26 cases (31.71%). There were no cases of undiagnosed pulmonary tuberculosis detected for the first time at autopsy.

Conclusions: Although the prevalence of pulmonary tuberculosis in forensic autopsy cases in this preliminary study was nil, we recommend further studies to be conducted on a larger scale and in different autopsy centres throughout Saudi Arabia to get an insight into the burden of clinically undiagnosed tuberculosis in the entire country.

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Keywords

Pulmonary tuberculosis, autopsy, Saudi Arabia

Date received: 25 May 2019; accepted: 2 December 2019

Introduction

Tuberculosis is a major infectious disease that causes morbidity and mortality in millions of people worldwide.¹ It is a chronic necrotizing granulomatous infection caused by *Mycobacterium tuberculosis*. A nation-wide community survey of tuberculosis epidemiology in Saudi Arabia demonstrated that Saudi Arabia is an intermediate prevalence area for tuberculosis despite high standards of living and free health care facilities.² An estimated 1000 deaths due to tuberculosis occur in Saudi Arabia per year.³ A recent study published in 2013 revealed that tuberculosis continues to be a cause of death among both Saudis and non-Saudis living in Saudi Arabia.⁴

Missed or delayed diagnosis of tuberculosis is not uncommon in Saudi Arabia due to non-specific clinical presentation or unusual chest X-ray findings.⁵ In a cohort of 80 patients, the diagnosis of tuberculosis was missed in nine patients until the patient's condition deteriorated so as to require admission to an intensive care unit.⁵ Moreover, studies from different regions of the world have reported that clinically undiagnosed or unrecognized cases may only be diagnosed or recognized to be cases of tuberculosis at autopsy.⁶⁻¹¹ A literature review reveals that autopsies on people undiagnosed during life remain a potential health hazard to the autopsy surgeons, technicians, support-staff working in the autopsy room and medical students attending such autopsies.¹²

Autopsy studies have been conducted in countries such as India, Turkey, Ireland and New Zealand to find the prevalence

of previously undiagnosed cases of pulmonary tuberculosis.^{6,9-11} However, there is a lacuna in literature reported from Saudi Arabia regarding cases of tuberculosis identified for the first time during postmortem examination and therefore the present prospective, preliminary study was conducted.

Patients and methods

Study population

This prospective study enrolled deceased individuals that had undergone autopsies at the Forensic Medicine Centre, Dammam, Eastern Province, Saudi Arabia between January 2014 and December 2015. Basic demographic data (including age, sex, ethnic origin and immigrant status), past medical history and information relating to the circumstances of death were obtained from the forensic autopsy reports and the related police reports. The Forensic Medicine Centre serves one million people. The present cohort of deceased individuals was selected based on convenience.

This research was approved by the Institutional Review Board at Imam Abdulrahman Bin Faisal University (formerly, University of Dammam), Dammam, Saudi Arabia (IRB-2014-01-013). The families of the deceased were not required to provide written or verbal informed consent because in most cases of foreign nationals the families were not available. However, wherever applicable a courtesy verbal informed consent was obtained and in cases where the families were available but did not consent, lung specimens were not collected.

Autopsy examinations and histopathology

During the autopsy procedure, following a gross examination of the external surfaces, the cut-surfaces of the lungs and examination of the pleural cavities, samples of lung tissue from the apical regions of both the lungs, middle lobe of the right lung, including grossly abnormal areas if found anywhere in the lungs were preserved for further microscopic and molecular examinations at the Department of Pathology, College of Medicine, King Fahd Hospital of the University, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia.

Lung specimens for light microscopy were fixed by immersion in 10% neutral buffered formalin for 24–48 h, dehydrated in a graded isopropanol series and embedded in paraffin wax. Paraffin sections of 4 µm thickness were stained with haematoxylin and eosin (H&E) stain and Zeihl–Neelsen (ZN) stain and examined using an Olympus BX51TF light microscope (Olympus Corporation, Tokyo, Japan). H&E-stained sections of the lung tissue were examined for multi-nucleated giant cells and other granulomatous inflammatory findings compatible with tuberculosis. ZN-stained sections of the lung tissue were examined for acid fast bacilli.

DNA probe analysis for *Mycobacterium tuberculosis*

A DNA probe using polymerase chain reaction (PCR) was used in the identification of *M. tuberculosis*. Sections (5 µm thick) were cut from each paraffin block. Two sections were taken from each lung specimen for DNA extraction. DNA extraction from formalin-fixed, paraffin-embedded (FFPE) lung tissue samples was achieved by using a QIAamp DNA FFPE Tissue Kit (Qiagen, Valencia, CA, USA). This was followed by checking the concentration and the quality of DNA using a NanoDrop™ 2000

spectrophotometer (Thermo Fisher Scientific, Rockford, IL, USA). An *M. tuberculosis* PCR kit from Abbott Laboratories (Abbott Park, IL, USA) was used to investigate the *M. tuberculosis* DNA sequence in the current samples. This ready-to-use kit is able to detect all members of the *M. tuberculosis* complex and is sensitive enough to identify very small copy numbers of the microorganism.

Statistical analyses

All statistical analyses were performed using the SPSS® statistical package, version 16.0 (SPSS Inc., Chicago, IL, USA) for Windows®. All data are presented as mean ± SD or *n* of patients (%).

Results

A total of 523 bodies were subjected to a postmortem examination at the Forensic Medicine Centre, Dammam, Saudi Arabia between January 2014 and December 2015. Of these, 236 bodies were subjected to a complete autopsy including external and internal postmortem examinations. The remaining bodies (*n* = 287) were subjected to an external postmortem examination only. Lung specimens were collected from a cohort of 82 deceased individuals where the autopsy included external and internal postmortem examinations; all of which were forensic/medico-legal autopsies. This cohort did not include any previously diagnosed cases of tuberculosis. The mean ± SD age of the study cohort was 35.5 ± 10.3 years (range, 20–80 years). Most of the cases (*n* = 62; 75.60%) were in the age group of 20–40 years. Males (*n* = 70; 85.37%) outnumbered females (*n* = 12; 14.63%). The deceased were from 15 different countries. The number of Saudis was 16 (19.51%). The maximum number of non-Saudis was from India with 26 cases (31.71%). The other nationalities (*n* = 40;

48.78%) included Pakistan, Bangladesh, Nepal and Sri Lanka from the Indian sub-continent; Philippines and Indonesia from Southeast Asia; and Yemen, Qatar, Egypt and Sudan from the Arab world. Ethiopia, Spain and Ukraine completed the list of nationalities of the deceased.

The manner of death in the study cohort was suicide ($n=44$; 53.66%), homicide ($n=23$; 28.05%), natural ($n=7$; 8.54%) and accident ($n=6$; 7.32%). Two cases are still under investigation. The natural causes of death included coronary artery disease and bronchopneumonia, while accidents included fall from a height and drug overdose. The cause of death for the suicides was mostly hanging (38 of 44; 86.36%). Cut-throat injury and poisoning formed the rest of the suicides. The cause of death was head injury, stab injury, firearm injury and strangulation in the homicides.

In all cases, no evidence of pulmonary tuberculosis was noted on gross examination of the lungs at autopsy. Fibrous thickening and pus secretions suspicious of tuberculosis were noted in one case. Laboratory investigations including histopathology (Figures 1 and 2) and molecular

pathology did not reveal any positive cases of tuberculosis.

Discussion

Clinically diagnosed cases of tuberculosis are not uncommon in Saudi Arabia.^{13–16} The decrease in tuberculosis incidence rates in Saudi Arabia from 15.80/100 000 population in 2005 to 13.16/100 000 population in 2012 can potentially be attributed to the national tuberculosis programme.¹⁶ The present study is the first of its kind to be conducted in Saudi Arabia that attempts to provide data on previously clinically undiagnosed cases of tuberculosis diagnosed at postmortem. In this preliminary study conducted in the Eastern Province of Saudi Arabia, no positive cases of pulmonary tuberculosis were detected. Since the study revealed no new cases of tuberculosis, it could be assumed with caution that the health policies, planning and management in relation to antemortem diagnosis of tuberculosis in the Dammam region of the Eastern Province of Saudi Arabia are perhaps appropriate to a certain extent at least.

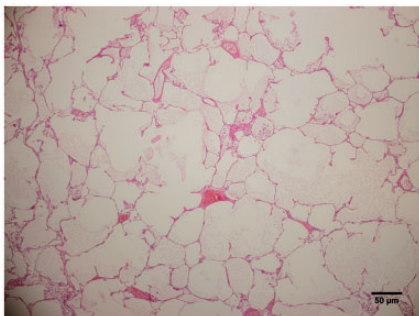


Figure 1. Representative photomicrograph of postmortem lung tissue showing no evidence of infection with *Mycobacterium tuberculosis*. Haematoxylin and eosin stain. Scale bar 50 μm . The colour version of this figure is available at: <http://imr.sagepub.com>.

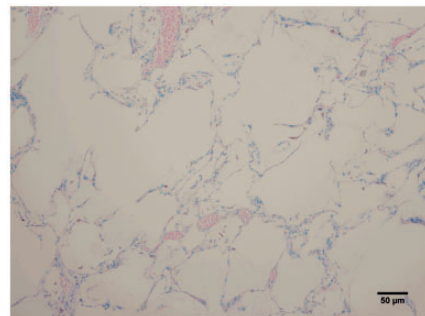


Figure 2. Representative photomicrograph of postmortem lung tissue showing no evidence of infection with acid fast bacilli such as *Mycobacterium tuberculosis*. Zeihl–Neelsen stain. Scale bar 50 μm . The colour version of this figure is available at: <http://imr.sagepub.com>.

In a similar study conducted in Chandigarh, North India, 33 cases of tuberculosis were diagnosed for the first time at autopsy accounting for 4.3% of the total number of autopsies ($n=768$) over the study period from 2004 to 2009.⁶ Previously undiagnosed cases of tuberculosis were also identified for the first time in the South Indian city of Mangalore.^{7,8} The three cases of tuberculosis diagnosed at autopsy in Ankara, Turkey accounted for nearly 1% of the total number of 302 randomly studied cases.⁹ A study conducted in Dublin, Ireland in a 14-year period from 1991 to 2004, during which 4930 autopsies were conducted, reported 10 cases of unsuspected tuberculosis diagnosed at autopsy.¹⁰ Twenty one cases of tuberculosis diagnosed at autopsy were undiagnosed before death in a cohort of 13866 autopsies performed during the period January 1994 to June 2004 in Auckland, New Zealand.¹¹ By identifying the previously undiagnosed cases of tuberculosis, autopsy plays a significant role in ensuring contact screening in the interest of the community at large.¹⁷ Moreover, the results of similar studies^{6,9-11} conducted in India, Turkey, Ireland and New Zealand raise an alarm in those unknowingly exposed to such infectious diseases in the autopsy room to be reasonably careful while conducting postmortem examinations by always adhering to biosafety precautions for airborne pathogens as a protocol to be routinely followed in order to reduce the risk of exposure to infections such as *M. tuberculosis* that are readily aerosolized by autopsy procedures.

This current preliminary study had several limitations. First, a small sample size that was selected on the basis of convenience was a limitation. A complete autopsy is not always the norm in Saudi Arabia. Death investigations in unnatural mannered deaths is usually based only on an external postmortem examination and/or a needle blood sample toxicological

examination. Nevertheless, a complete autopsy is performed when indicated despite religious beliefs and social customs.¹⁸⁻²⁰ Considering the fact that a complete autopsy is not done in all forensic or medico-legal deaths, the present study is a good beginning in the direction of identifying previously undiagnosed cases of pulmonary tuberculosis. Secondly, another limitation is related to the potential risk of false negative results in low quantity FFPE DNA due to scarcity of amplifiable templates.

In conclusion, although the prevalence of pulmonary tuberculosis in forensic autopsy cases in this preliminary study conducted in a cohort from the Dammam region of the Eastern Province of Saudi Arabia was nil, we recommend multicentre studies to be conducted on a larger scale in different autopsy centres throughout Saudi Arabia to get an insight into the burden of clinically undiagnosed tuberculosis in the entire country. This would offer a better understanding of the burden of clinically undiagnosed disease to those involved in providing healthcare policies, planning and management in Saudi Arabia to bring about any necessary amendments.

Acknowledgements

The authors express their sincere thanks to the Deanship of Scientific Research at Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia for providing a grant to conduct this research and to Shakir Ahmed for his role as research assistant.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

Funding

This research was funded by the Deanship of Scientific Research at Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia.

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