



# Extrapulmonary tuberculosis in Kabul, Afghanistan: A hospital-based retrospective review

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## KEYWORDS

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Pathology;  
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## Summary

**Objectives:** The purpose of this study is to amplify the knowledge base of the epidemiology, symptoms, and signs of extrapulmonary tuberculosis (EPTB) in Afghanistan.

**Methods:** This is a retrospective review of EPTB diagnosed at CURE International Hospital and CURE Family Health Center (FHC) in Kabul, Afghanistan during a recent 20-month period.

**Results:** One hundred eighteen cases were identified from patients presenting to the hospital and FHC. This group represents the spectrum of EPTB seen at a single referral center in Kabul. The ratio of females to males was 2.03:1. Lymph node tuberculosis comprised the greatest number of EPTB cases (37.3%,  $n = 44$ ). The central nervous system was the next most frequent site of EPTB involvement (20.3%,  $n = 24$ ), followed in descending order by skeletal, pleural, abdominal, cutaneous, genitourinary, pericardial, miliary, and breast tuberculosis.

**Conclusions:** The 2:1 ratio of female to male EPTB cases coincides with the unusual epidemiologic pattern seen in smear-positive pulmonary TB in Afghanistan. As the first epidemiological report of EPTB from Afghanistan, this study illustrates the varied presentations of EPTB that should be known by healthcare workers throughout the country.

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## Introduction

More than two decades of conflict, from the Soviet invasion in 1979 to the fall of the Taliban in 2001, devastated the health infrastructure of Afghanistan. In 2002 the Afghan Ministry of Public Health (MOPH) began to build a new health system

using an innovative structure in which the government and international donors jointly contracted non-governmental organizations (NGOs) to provide a basic package of health services for the nation's entire population.<sup>1</sup> Afghanistan's Basic Package of Health Services (BPHS) was published in March 2003 with a subsequent revision in 2005.<sup>2,3</sup> The MOPH adopted the balanced scorecard (BSC) as a tool to measure the performance of the NGOs in their delivery of the BPHS. Baseline studies were done in 2004. The results of comparison studies completed in 2005 and 2006 demonstrated substantial improvement in the delivery of health services.<sup>4–6</sup>

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The recent history of tuberculosis (TB) control in Afghanistan reflects the wider process of healthcare reconstruction in the country. Control of communicable diseases is one of the seven core elements of the BPHS, and TB is one of three communicable diseases highlighted.<sup>3</sup> The BPHS integrates TB control throughout all four levels of the health system, from the village health post to the district hospital. Under the Taliban, the coverage rate of directly observed therapy short-course (DOTS) hovered around 12%.<sup>7</sup> In 2001, the year the Taliban regime fell, high morbidity and mortality rates of TB were documented in the country.<sup>8</sup> Since 2002, the DOTS coverage rate has increased steadily through the implementation of the BPHS. By 2006, DOTS coverage across the country had reached 97%. Detection, notification, and treatment success rates showed similar trends.<sup>7,9</sup>

It was noted after the fall of the Taliban, that communicable diseases posed a distinct threat to Afghanistan because risk factors such as overcrowding and internally displaced persons can be compounded in a post-conflict setting.<sup>10,11</sup> Among communicable diseases worldwide, TB is the second leading cause of death after HIV/AIDS.<sup>12,13</sup> TB kills nearly 2 million people per year, most of whom live in the lowest income countries. TB control is critical for the development of Afghanistan, which has been designated as one of twenty-two high burden countries that collectively account for 80% of TB globally.<sup>14,15</sup> The rate of multidrug-resistant TB was reported at 3.4% in 2006,<sup>7</sup> a statistic that makes TB control all the more urgent.

Extrapulmonary tuberculosis (EPTB) accounts for 13–21% of TB cases in areas of low HIV prevalence;<sup>7,16–19</sup> Kabul represents an area of low HIV prevalence.<sup>20</sup> In Afghanistan EPTB represents one fifth of all diagnosed cases of TB.<sup>7</sup> This study is a hospital-based retrospective analysis of all EPTB cases diagnosed at CURE International Hospital Kabul and its associated Family Health Center (FHC) in Kabul during a recent 20-month period. The city of Kabul is divided into 18 civil/geographical districts. The hospital and FHC are both located in the southeast of Kabul in District 6. A 2005 census reported that District 6 had 211 400 residents, 8.5% of the city's total population.<sup>21</sup> Women made up 48% of the district population and each household had approximately 5.8 members.<sup>21</sup> It is difficult to ascertain the exact origins of the patients presenting to the hospital and FHC. Approximately three quarters of all hospital inpatients report that they are from Kabul, the remainder report that they come from provinces around Afghanistan. However the population of Kabul has swollen in recent years. A 1986 Kabul census reported a population of 152 218 in District 6, 11.7% of the city's population at that time.<sup>22</sup> Although the majority of our patients report that they are from Kabul, it is possible that they are recent immigrants to the city. Within the city limits families are exposed to indoor cooking/heating fires, home childbirth is still practiced, and water is not always obtained from city pumps. Even among Kabul residents, the distinction between urban and rural lifestyles can be blurred.

CURE International, founded in 1996, is an NGO. It currently operates hospitals in eleven countries, and health worker education is among its core values. More information about CURE can be found on its website.<sup>23</sup> The CURE hospital in Kabul has surgical, medical, pediatric, obstetric, and neonatal services. X-ray, ultrasonography, electrocardiography, as well as basic blood and fluid analysis (total

lymphocyte count, differential, protein, glucose, Gram stain) can be performed at the hospital. Microbiology cultures are not available at the facility. Computed tomography (CT) or magnetic resonance imaging (MRI) scans are not available at the CURE hospital, but they can be obtained by patients in Kabul who can afford the \$100 to \$200 out-of-pocket expense. CURE hospital has the only pathology laboratory available to the civilian population in the country. This is the first research article to use data from a civilian pathology laboratory in Afghanistan in 30 years.<sup>24</sup> This report adds to the local knowledge base by describing the epidemiology of EPTB in Afghanistan and thus represents another step forward in the process of reconstructing a healthcare system in a post-conflict country.

## Methods

We conducted a retrospective review of EPTB diagnosed at CURE International Hospital and the CURE FHC in Kabul, Afghanistan between November 2006 and July 2008. Cases of EPTB were identified from the electronic tissue pathology database at CURE International Hospital, from a review of the CURE Hospital discharge logbooks, and from the Kabul District 6 TB register. In accordance with diagnostic criteria established by the World Health Organization,<sup>25</sup> a case of EPTB was defined as TB of organs other than the lungs, e.g., pleura, pericardium, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, meninges. Diagnosis of EPTB in patients presenting to CURE facilities was based on: (1) typical histological findings consistent with TB in tissue from an extrapulmonary site, or (2) strong clinical evidence consistent with active EPTB.

Clinical evidence was defined as the patient's presenting symptoms and signs as well as radiographic or body fluid analysis supporting the diagnosis of EPTB. Tuberculous meningitis (TBM) was diagnosed based on a clinical presentation consistent with TBM and a cerebrospinal fluid (CSF) analysis. CSF with a moderately elevated protein, low glucose, and elevated white blood cell count with a lymphocyte predominance was considered consistent with TBM.<sup>26,27</sup> Clinical evidence for pleural and abdominal TB was defined as body fluid analysis showing elevated protein, low glucose, and elevated white blood cells with lymphocyte predominance with a supporting clinical history. Spinal TB (Pott's disease) was diagnosed based on clinical and radiographic evidence typical for spinal TB. Miliary TB was diagnosed based on clinical presentation consistent with miliary TB and a chest X-ray typical for miliary TB.

All cases were exclusively EPTB. If at the time of presentation a patient was symptomatic for pulmonary TB (cough, hemoptysis, or constitutional symptoms),<sup>28</sup> a chest radiograph and sputum samples were obtained. A chest radiograph was not routinely performed on patients thought to have EPTB but not expressing pulmonary symptoms, due to the cost burden that would place on the patient and the fact that it would not alter the decision to initiate anti-TB therapy. Patients found to have concurrent pulmonary and extrapulmonary TB were excluded from our sample.

In all cases a clinician made the decision to treat the patient with a full course of anti-TB treatment. At the point of diagnosis the patient was referred back to a government run TB treatment facility. The closest facility during the time

of this study was the District 6 TB treatment facility, although some patients may have chosen to seek treatment at facilities closer to their homes. Treatment was carried out at those facilities in accordance with the guidelines of the National Tuberculosis Control Program (NTP) for Afghanistan.<sup>29</sup> Evaluating a patient's response to anti-TB therapy was not an aim of this study. Culture confirmation was not used as part of the diagnostic criteria in this study. To our knowledge, culture confirmation for TB is not available for the civilian population in Afghanistan. Acid-fast bacillus (AFB) staining was not used as a confirmatory test because we lack the reagent. Gram staining was performed on all body fluid samples. Additional stains for granulomatous diseases (e.g., fungal, *Actinomyces*, syphilis) were not performed by the CURE pathology lab due to the lack of reagents. Purified protein derivative (PPD) skin testing was not used for diagnostic evaluation in individuals over five years of age because it is not part of the NTP diagnostic guidelines.<sup>29</sup> PPD was not used in children because we chose to use the patient's limited resources on other diagnostic modalities.

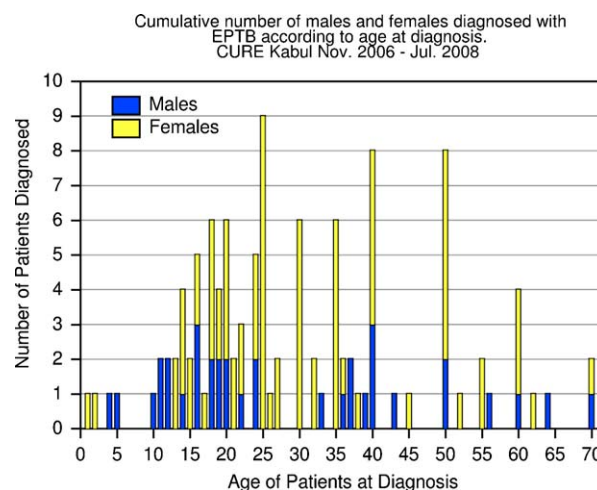
We analyzed cases according to gender, age, site of infection, presenting complaints, and symptom duration prior to diagnosis using Microsoft Excel. Due to the limitations of our record keeping, a complete set of demographic and clinical data was not available for every patient. Therefore we calculated averages and ranges using only the demographic and laboratory data that were available. The sample sizes used to make calculations are noted in the results section. A secondary aim of this study was to determine the relative frequency of pathologic diagnoses seen in lymph node specimens received by the pathology laboratory during this time period. The Afghan Ministry of Public Health Institutional Review Board has given CURE International Hospital the approval to conduct this research and disseminate the results.

## Results

Between November 2006 and July 2008, 118 cases of EPTB were diagnosed in patients presenting to CURE International Hospital and the CURE FHC. Sixty-one percent ( $n = 72$ ) of the patients presenting to CURE were diagnosed with the aid of tissue pathology analysis. The remainder were diagnosed through clinical symptoms and signs as well as radiographic or body fluid analysis. Fifty-nine (50%) of the 118 patients diagnosed at the CURE facilities were also listed in the TB register, having reported for treatment at the District 6 facility.

Females were more likely to be diagnosed with EPTB than males by a ratio of 2.03:1 (Figure 1). The average age of all patients with EPTB at the time of diagnosis was  $31.5 \pm 17.77$  years ( $n = 116$ ). The average age of males at the time of diagnosis was  $32.2 \pm 21.80$  years ( $n = 39$ ). Females had an average age of  $31.1 \pm 15.59$  years at diagnosis ( $n = 77$ ). There were seventeen (14.4%) patients at the time of diagnosis aged 15 years and younger. Nine of these children were female.

Among the 118 cases who presented to CURE Hospital, we have records for the duration of symptoms prior to diagnosis for 90 (76.3%) patients. The average duration of symptoms before presentation was 14.8 months for men ( $n = 31$ ) and 18.0 months for women ( $n = 59$ ). Twenty-four women reported symptoms lasting one year or longer compared to



**Figure 1** Cumulative number of males and females diagnosed with extrapulmonary tuberculosis according to age at diagnosis. CURE, Kabul, November 2006–July 2008.

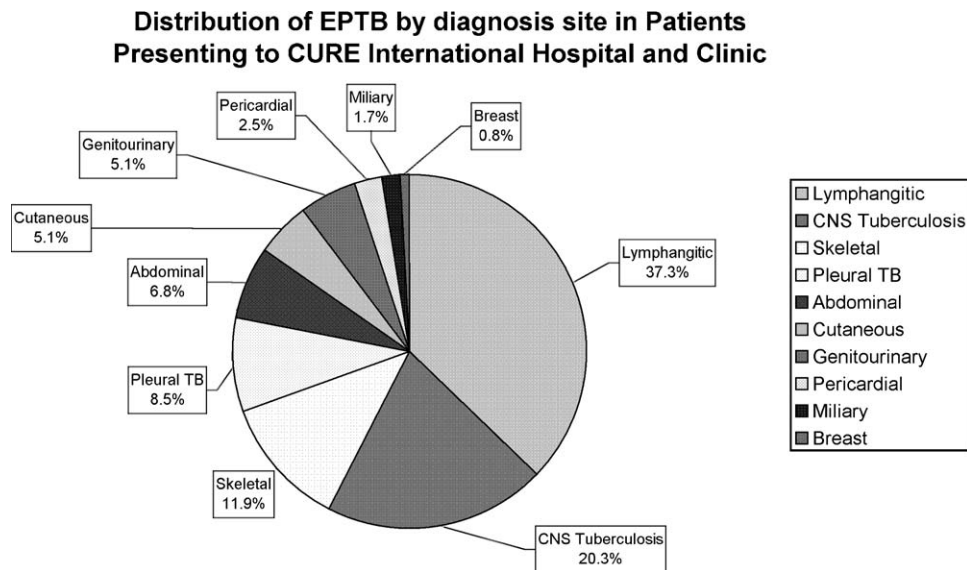
10 men. When we removed 22 cases of TBM from the analysis, the average duration of symptoms before presentation was 23.0 months for men ( $n = 19$ ) and 18.9 months for women ( $n = 49$ ).

Lymph node TB (LNTB) comprised the greatest number of EPTB cases (37.3%,  $n = 44$ ) (Figure 2, Table 1). The average age at the time of diagnosis was  $25.1 \pm 11.84$  years ( $n = 42$ ). Among children aged 15 years and younger, nine (52.9%) were diagnosed with LNTB. Cervical lymph nodes were the most common site of infection (81.8%,  $n = 36$ ), followed by axillary lymph nodes (13.6%,  $n = 6$ ). Symptoms were present for an average of 1.76 years prior to presentation ( $n = 30$ ). The most common symptoms of lymph node TB were swelling of the affected area (90.9%,  $n = 40$ ), fever (52.3%,  $n = 23$ ), and weight loss (36.4%,  $n = 16$ ). Five patients (11.4%) reported painful lymph nodes at the time of presentation.

During the 20-month period of this study the CURE pathology department examined 257 lymph node specimens. Twenty-five percent of lymph nodes examined by the pathology department at CURE were histologically compatible with TB. Other lymph node diagnoses included lymphoma (29.6%), carcinoma (8.9%), reactive hyperplasia (8.6%), and histiocytosis (5.1%).

The central nervous system was the next most frequent site of EPTB involvement (20.3%,  $n = 24$ ). Twenty-three cases were diagnosed as TBM. One patient was found to have an intracranial tuberculoma by CT scan. The most common symptoms for TBM at presentation were headache (69.6%,  $n = 16$ ), fever (60.9%,  $n = 14$ ), and vomiting (60.9%,  $n = 14$ ). Five patients (21.7%) were unconscious at the time of presentation to the hospital or health center. The average duration of symptoms was  $2.7 \pm 3.27$  months ( $n = 22$ ) prior to presentation. Six patients (26.1%) had neck stiffness at the time of physical examination. Data concerning permanent neurologic sequelae from TBM were not recorded. A summary of CSF findings can be found in Table 2.

Skeletal TB ( $n = 14$ ) was found in the spine, elbow, knee, and forearm. Fifty percent ( $n = 7$ ) of cases were spinal TB. Six spinal TB cases had radiographic evidence (X-ray, CT, or MRI) for TB. One case of spinal TB was confirmed through



**Figure 2** Percentage of cases of extrapulmonary tuberculosis diagnosed from patients presenting to CURE International Hospital and the CURE FHC in Kabul. Cases are grouped according to site of diagnosis.

histologic examination. Common symptoms of spinal TB included fever (100%,  $n = 7$ ), progressive lower extremity weakness or paraplegia (71.4%,  $n = 5$ ), and back pain (57.1%,  $n = 4$ ). The most common complaint in non-spinal

skeletal TB was swelling of the affected joint ( $n = 4$ ); in three of the four cases this was painful swelling.

Pleural TB accounted for 8.5% of cases ( $n = 10$ ). In four cases the diagnosis relied on pleural biopsy samples, the

**Table 1** Cases by site of diagnosis including numbers of females and males and average ages at time of diagnosis

Type	Cases (n)	Percentage of total cases	Female (n)	Female aged <30 years (n)	Average age female, years	Male (n)	Male aged <30 years (n)	Average age male, years
Lymphangitic	44	37.3%	31	31	25.69 <sup>a</sup>	13	8	23.58 <sup>b</sup>
CNS	24	20.3%	12	7	28.0	12	9	24.4
Skeletal	14	11.9%	8	1	46.0	6	2	54.2
Pleural	10	8.5%	6	1	41.0	4	0	49.8
Abdominal	8	6.8%	8	4	29.3	0	N/A	N/A
Cutaneous	6	5.1%	3	2	34.0	3	0	37.3
Genitourinary	6	5.1%	5	3	27.6	1	1	12.0
Pericardial	3	2.5%	3	1	45.0	0	N/A	N/A
Miliary	2	1.7%	2	0	42.5	0	N/A	N/A
Breast	1	0.8%	1	1	15.0	0	N/A	N/A
Total	118	100%	79			39		

N/A, not applicable; CNS, central nervous system.

<sup>a</sup>  $n = 30$ .

<sup>b</sup>  $n = 12$ .

**Table 2** Analysis of fluid samples from selected body sites

	Cerebrospinal fluid	Pleural fluid	Ascitic fluid
Range of total WBC count	10–600 × 10 <sup>6</sup> cells/l ( $n = 23$ )	63–1800 × 10 <sup>6</sup> cells/l ( $n = 6$ )	55–1600 × 10 <sup>6</sup> cells/l ( $n = 4$ )
Lymphocytosis	20 of 21 CSF samples demonstrated lymphocytosis	4 of 6 pleural fluid aspirates demonstrated lymphocytosis	3 of 4 peritoneal fluid aspirates demonstrated lymphocytosis
Protein (range)	3–2000 mg% Average = 95.8 mg% ( $n = 14$ )	2800–26 300 mg% Average = 11 300 mg% ( $n = 3$ )	34 000 mg% ( $n = 1$ )
Glucose (range)	8–113 mg% Average = 37.6 mg% ( $n = 20$ )	26–196 mg% Average = 116.8 mg% ( $n = 3$ )	64–82 mg% Average = 73.0 mg% ( $n = 2$ )

WBC, white blood cell; CSF, cerebrospinal fluid.

remainder relied on pleural fluid aspirate. Common symptoms were shortness of breath (50%,  $n = 5$ ) and cough (50%,  $n = 5$ ). A summary of the pleural fluid analysis can be found in Table 2.

Four of the eight cases of abdominal TB were peritonitis diagnosed by clinical examination and analysis of ascitic fluid obtained by paracentesis (see Table 2). The other four cases of intra-abdominal TB were diagnosed from biopsy specimens of the small intestine, mesentery, or peritoneum. Reported symptoms of gastrointestinal TB at presentation included weight loss (75%,  $n = 6$ ), fever (50%,  $n = 4$ ), and abdominal distention (37.5%,  $n = 3$ ).

Sites of cutaneous TB included ear, forehead, the gluteal area, wrist, and flank.

Six patients during this time period were diagnosed with genitourinary TB (GUTB). Five were women with an average age of 27.6 years. Three of the five women with GUTB had TB of the endometrium and two of these presented because of infertility.

During the 20-month time period, three patients (2.5%) presented with pericardial TB. All patients were found to have a pericardial effusion. Two of the patients with pericardial TB presented with shortness of breath.

Two cases of miliary TB and one case of breast TB were diagnosed. Patients with miliary TB were found to have constitutional symptoms (fevers, chills, sweats) and a chest X-ray typical for miliary TB. One case of breast TB was diagnosed in a 15-year-old female who reported six months of a gradually increasing painful breast mass.

## Discussion

In 2006, 21% of new cases of TB reported in Afghanistan were extrapulmonary.<sup>7</sup> In the 20-month period of our study, the District 6 TB register (the DOTS register for the area of Kabul we work in) showed 214 cases of extrapulmonary tubercular disease out of 390 recorded TB cases. This high percentage of EPTB (54.9%) is thought to be an over-representation and therefore not comparable to other reports. The reason for this is that patients in Kabul will often travel to our hospital to receive a copy of their pathologic diagnosis regardless of the origin of the tissue specimen. If diagnosed with EPTB the patient will then be referred to an NTP treatment facility. The closest one to the hospital during the time of our study was the District 6 facility. The fact that only 50% of cases diagnosed at our facility were found in the District 6 register raises questions about our TB reporting. It is possible that

patients were referred to the District 6 TB clinic but chose to seek care at a clinic closer to their home. Because we are the only civilian facility providing pathologic diagnosis, it is conceivable that patients are returning to their home provinces or one of the other 18 Kabul districts for TB treatment. It is also possible that the patients, once diagnosed with TB, are choosing not to seek treatment.

The cause of the long delay in diagnosis of EPTB is probably multifactorial. The delay could be due to the indolent nature of EPTB. It could reflect health-seeking behaviors of the population. It could also represent a failure of health providers to recognize EPTB. It is important for healthcare providers in areas of high TB prevalence, such as Afghanistan, to consider EPTB as a diagnostic possibility in order to make a prompt diagnosis and to prevent unnecessary invasive procedures. Common clinical symptoms and signs that should increase a primary care provider's suspicion of EPTB in Afghanistan are listed in Table 3. This country-specific information could be distributed throughout the healthcare system, from the health post to the district hospital, in order to increase recognition and thus control of TB.

Health-seeking behavior is likely to affect the time between symptom onset and diagnosis in Afghanistan. In 2002, women at health centers in Kabul were asked a series of questions about their healthcare knowledge and behaviors. Ninety-three percent reported needing authorization from their husband or a male relative before seeking professional health care.<sup>30</sup> House staff at our hospital report anecdotally that there is a stigma among both male and female patients associated with the diagnosis of TB. Reports of stigma related to the diagnosis of TB have been documented elsewhere in the developing world.<sup>31–33</sup> Stigma associated with the diagnosis may cause a delay in seeking care. A better understanding of these relationships in Afghanistan could help inform public health education programs.

The female to male ratio of EPTB cases in this study was 2.03:1. In 2006 the female to male ratio for all cases of newly diagnosed smear positive (ss + ) pulmonary TB cases in Afghanistan was 2.13:1.<sup>7</sup> In a recent study from southeastern Iran, all forms of newly diagnosed TB had a female to male ratio of 1.46:1.<sup>34</sup> Afghanistan and Iran reflect an unusual epidemiologic pattern in that the majority of pulmonary TB patients are women. In other areas of the world, pulmonary TB is predominantly a disease of males.<sup>17,19</sup> In series from South America, Nepal, and Turkey, males were also more frequently diagnosed with EPTB.<sup>35–38</sup> However, reports from Hong Kong and Germany have noted a female majority in cases of

**Table 3** Signs and symptoms of extrapulmonary tuberculosis in Kabul, Afghanistan

Lymph node	Indolent usually painless, lymph node swelling, which may be associated with fever or weight loss
Meningeal	Prolonged headache, fever and vomiting, often with altered mental status, usually without a stiff neck. CSF typically shows moderate elevation of white blood cells with a lymphocyte predominance, elevated protein, and low glucose
Spinal	Localized back pain and lower extremity weakness. Vertebral tenderness and deformity, often associated with fever
Pleural	Cough, shortness of breath and signs of a pleural effusion by physical examination, X-ray or ultrasound
Abdominal	Weight loss, fever and abdominal distention
Endometrial	Infertility in a reproductive age female
Pericardial	Shortness of breath and signs of pericardial effusion



EPTB.<sup>17,19</sup> Further investigation is needed to identify the cause behind the higher incidence of TB infection in females in this region.

Vitamin D is one modifiable risk factor that may play a role in the high female prevalence of TB in Afghanistan. Low serum vitamin D levels have been associated with a higher risk of active TB.<sup>39–43</sup> A cellular explanation for the association between vitamin D and TB has been proposed.<sup>44–46</sup> Important determinants of vitamin D deficiency are skin type, sex, clothing, nutrition, food fortification, use of supplements, high body mass index, and degree of urbanization.<sup>47</sup> Vitamin D deficiency (defined as serum vitamin D <25 nmol/l) has been demonstrated in both men and women in Jordan, Lebanon, and Iran, countries which share a number of similar geographic and cultural characteristics with Afghanistan.<sup>47,48</sup> In Iran, females between the ages of 20 and 39 years had significantly lower levels of serum vitamin D than other groups.<sup>49</sup> In Jordan and Lebanon it appears that a higher percentage of women are vitamin D deficient compared to men.<sup>47</sup> Unpublished data from our facility revealed a vitamin D deficiency in pregnant women in Kabul.<sup>50</sup> The causes of these discrepancies between the sexes have not been fully elucidated. Demonstrating a relationship between vitamin D deficiency and TB in Afghanistan would have important public health implications. Vitamin D supplementation has already been shown to be beneficial in patients with active TB,<sup>51</sup> but has not yet been studied as a low cost preventive agent. It is possible that the prevalence of active TB could be reduced by vitamin D fortification of food, or by providing vitamin D supplementation to targeted populations at risk for TB.

The lymph nodes were the most common site of EPTB in our study (37.3%), and LNTB was more frequent among reproductive age females. The most frequent site of EPTB in children aged 15 years and under was the lymph nodes, accounting for the majority (52.9%) of cases in children. These findings are consistent with previous reports from the developing world.<sup>16</sup> Tuberculous meningitis (20.3%) was the second most common form of EPTB in our series. This finding represents an unusual epidemiologic pattern. In other reports TBM has accounted for approximately 5% of EPTB cases.<sup>16</sup> We do not know the reason for this distribution. Referral bias may be partly responsible for our larger percentage of diagnosed TBM cases. Our facility's ability to perform lumbar puncture and analyze CSF enhances our ability to diagnose the disease. AFB staining would further increase the diagnostic accuracy. Most patients self-refer in our environment, and our ability to provide better diagnostics may mean we receive patients who have not responded to treatment by other providers. There are many possible risk factors for TB infection in Afghanistan. Any number of these factors, or an unrecognized risk factor, could also contribute to the higher percentage of TBM in our series. The rate of permanent neurologic sequelae from TBM has been reported at between 4% and 21%.<sup>52–55</sup> Due to difficulties with follow-up we are not able to present data on neurologic sequelae in our TBM patients. In a high burden area such as Afghanistan, primary healthcare workers should have a high level of suspicion for this potentially devastating illness in order to diagnose and treat it promptly.

Risk factors for TB infection relevant to Afghanistan include living in a high prevalence region, internally displaced persons,

poverty,<sup>56</sup> crowded living conditions,<sup>57</sup> undernutrition,<sup>58</sup> low levels of education,<sup>59</sup> use of glucocorticoids,<sup>60–62</sup> malignancy,<sup>63</sup> celiac disease,<sup>64</sup> cigarette smoking,<sup>65</sup> genetic predisposition,<sup>66</sup> drinking unpasteurized milk,<sup>67,68</sup> and vitamin D deficiency.<sup>43</sup> It is not yet clear which of these factors, if any, had an influence in the high percentage of TBM seen in our series.

The ingestion of raw milk is one of the known risk factors for TB infection.<sup>68</sup> Many Afghans, particularly in rural areas, consume unpasteurized milk from goats, cows, or sheep. These animals are susceptible hosts for *Mycobacterium bovis*.<sup>69</sup> It is impossible clinically or pathologically to distinguish the different species of mycobacteria. It is only possible with expensive laboratory equipment that is not currently available in this setting.<sup>67</sup> In our series the species of mycobacteria causing abdominal infection is unknown and it is possible that some cases of active disease could have been caused by species other than *Mycobacterium tuberculosis*. Regardless of mycobacterial species the diagnosis of abdominal TB can be difficult. Intra-abdominal TB can mimic conditions such as intra-abdominal malignancy or inflammatory bowel disease, and thus presents a diagnostic challenge. Tissue pathology provides a powerful tool to assess for granulomas and differentiate between other causes of intra-abdominal disease.

HIV infection is unlikely to be a significant risk factor for TB in Afghanistan at this time. In a recent series, Todd et al. found that 0.2% of patients undergoing treatment at a TB clinic in Kabul were co-infected with HIV.<sup>20</sup> The World Health Organization defines HIV-prevalent settings as an area where HIV prevalence among TB patients is  $\geq 5\%$ .<sup>70</sup> For this reason, and because of cost constraints, we did not screen our patients for HIV disease. As the prevalence of HIV in Afghanistan increases, it will be more important to screen TB patients for HIV. Since HIV is more common in EPTB patients,<sup>27,71</sup> this group should be watched more closely.

Infertility has been reported as the most common complaint of women with TB endometritis.<sup>72,73</sup> Women with infertility should be screened for symptoms of GUTB, especially abnormal uterine bleeding and lower abdominal pain. An endometrial biopsy is a simple procedure that can lead to the diagnosis and treatment of GUTB, and resolution of infertility.

In our study 6 of 72 diagnoses (8.3%) made in the pathology laboratory were done with tissue obtained through fine needle aspiration. Fine needle aspiration cytology (FNAC) is a safe, cost-effective, and minimally invasive means to diagnose EPTB.<sup>74</sup> It has been shown to be effective in diagnosing TB of the lymph node, breast, and testis.<sup>75–79</sup> Diagnosis by FNAC can avoid an unnecessary mastectomy or orchiectomy. FNAC is particularly useful to distinguish TB lymphadenitis from other disease in a TB endemic country with limited resources. Because this is a cost-effective and safe technology there may be a role for using FNAC in the more peripheral parts of the Afghan healthcare system.

There are weaknesses in this study. Many Afghans do not know their true age. Ages obtained may represent estimates by patients or physicians. Medical records were at times incomplete. The lack of AFB stain and the absence of culture for confirmation are also a weakness. An experienced pathologist can often diagnose a tissue specimen based on its morphological characteristics. We are fortunate to have

telepathology consultation for difficult cases. However, because of atypical presentations it is recommended to define an etiological agent by special stains or cultures.<sup>80</sup> While a civilian pathology laboratory adds greatly to the diagnostic tools available to clinicians in Afghanistan, the lack of special stains and cultures are among the limitations of our laboratory capabilities. There are no data on the relative frequency of granulomatous disease in Afghanistan. Data from Pakistan and Oman suggest that syphilis is seen much less frequently than TB, and brucellosis is slightly more common.<sup>81,82</sup> Following the patient's response to treatment would have been useful for clinicians given the diagnostic limitations. However, because the patients are followed at NTP TB clinics we do not possess the data regarding treatment outcomes. This represents another weakness. These weaknesses point to challenges in obtaining new knowledge within a post-conflict health system.

Medical research is a helpful component in rebuilding a healthcare system in a country devastated by conflict. In fact 'making evidence-based decisions' is one of the seven principles of the BPHS.<sup>3</sup> Policy makers realize the benefit of population-specific information in order to guide sound policy decisions. Protocols for disease management are often based on the results of research done in the developed world. It is not always possible or advisable to generalize those conclusions to the developing world.<sup>83</sup> Building local research capacity is needed to inform cost-effective clinical decision-making in settings with limited resources. The information presented within this paper is intended to amplify the clinician's knowledge base at all levels of the health system about EPTB in the Afghan population.

**Ethical approval:** This study was approved by the ethics panel at CURE Hospital Kabul. We also received approval for conducting the study and disseminating the results from the Ministry of Public Health of the Islamic Republic of Afghanistan.

**Conflict of interest statement:** All authors report no financial or personal relationships with individuals or organizations that would inappropriately influence the work.

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