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Dynamics of tuberculosis in Wau, South Sudan during a period of armed conflict

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ABSTRACT

Background: South Sudan has endured decades of armed conflict, with the most recent in 2016. This has left the health system and infrastructure overstretched by a myriad of infectious diseases like tuberculosis. Our study aimed at quantitatively and qualitatively documenting TB dynamics and challenges with access to health care during a period of civil unrest in Wau.

Materials & Methods: A cross sectional study was carried out between January and February 2016 at Wau Teaching Hospital (WTH). Sputum was randomly collected from 207 of the 1035 TB suspects and analyzed using Ziehl-Neelsen (ZN) and Fluorescent Microscopy (FM), Culture, Capilia MTBC Neo, and DST. The laboratory results and questionnaire metadata were used for descriptive statistics, logistic regression in R version 3.4.2. These results were presented along with results from a qualitative assessment of the situation at WTH.

Results: Of 207 TB suspects, 39 (18.8%) were positive on FM with bacilli growth on culture, later confirmed as *Mycobacterium tuberculosis* complex. Only 5.4% of the cases were resistant to Isoniazid. Age; 20–45 OR = 13 (95%CI = 2.4–25.6, p = 0.011), > 46 OR = 3 (95%CI = 0.5–58, p = 0.005) and raw milk consumption OR = 2.2 (95%CI = 0.37–42.48, p = 0.005) were associated with being TB positive. The qualitative evaluation reveals that gunfights in the surroundings of Wau influenced the number of patients attending WTH, with some travelling up to 545 km to seek medical attention.

Conclusion: We report a high prevalence of tuberculosis among patients who presented at WTH, with approximately 1 out of 5 individuals testing positive for tuberculosis. This is likely an underestimation given the challenges patients had to endure as they sought medical attention. Tuberculosis epidemiology is likely to be driven by individual and household factors, but further investigations are needed to fully understand the risk profile. The tools in use were adequate for TB diagnostics and we observed a remarkably low prevalence of drug resistance, a statistic that is worth preserving. We therefore call for action from all stakeholders.

1. Background

Tuberculosis (TB) is an infectious and chronic inflammatory disease caused by members of *Mycobacterium tuberculosis* complex (MTBC) [1,2]. TB caused by *Mycobacterium tuberculosis* is the 9th leading cause of death globally and in addition, the leading cause from a single infectious agent ranking above HIV/AIDS [2]. This disease accounts for about 9.6 million new cases and 1.5 million deaths annually, majority of who were from Africa, Asia and the former Soviet Union [2]. Factors such as: population density, poverty, malnutrition, armed conflict and imprisonment have for long been linked to the increased incidence of tuberculosis [3-5]. For example, some reports have suggested that armed conflict is most likely responsible for the current TB epidemic in Ukraine [4,6]. Indeed, a recent report using high definition molecular

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tools has revealed the legacy of armed conflict on tuberculosis spread [7]. A *Mycobacterium tuberculosis* strain which evolved in Afghanistan and then into the former Soviet Union has spread throughout Northern and Western Europe [7]. The protracted armed conflict in South Sudan is likely to present the same scenario for the Great Lakes region of Africa. The current World Health Organization (WHO) TB estimate for all forms of tuberculosis in South Sudan stands at 140 cases per 100,000 persons, and it is apparent that lack of data has made regular estimates for this country difficult [3,8]. In this case, data generation in such an unstable setting requires that the National Tuberculosis Program (NTP) remains fully functional. Countries like Afghanistan, whose NTP has remained functional during periods of armed conflict have demonstrated that it is possible to meet internationally set TB control targets [9]. Like Afghanistan, South Sudan is currently experiencing high levels of migrations [10]. Wau region is surrounded by three Internally Displaced Persons (IDP) camps within the United Nations Mission sites, “Unity” to the North East, Western Equatorial to the South West and the Lakes IDP camp, each accommodating ~ 0.55, 0.120 and 0.128 million, internally displaced persons respectively [11]. This mass migration has not only led to a complex humanitarian challenge exacerbated by famine [3], but it is most likely to give rise to a tuberculosis epidemic in the region [3]. In order to address this eminent public health problem, there is dire need to document the current dynamics of the disease and identify context specific challenges to its control. This study was therefore aimed at documenting the routine diagnostic capacity, drug susceptibility of isolated *Mycobacterium tuberculosis*, and identify potential drivers of TB. Furthermore, we qualitatively assessed the challenges of accessing TB management facilities in this area.

2. Materials and method

2.1. Study site

The city of Wau is located in the Northwestern part of South Sudan and is home to approximately 151,120 people. This population grew by 20% in the four years after its separation from Sudan [11]; the area is inhabited by the Balanda, Ndogo, Jur Chol, Dinka and Fellata Mbororo who are primarily agro- pastoralists [11,12].

The education, health and economic infra-structure is poor, and has further crumbled due to the recent armed conflict [11]. In fact, this city has been at the center of conflict for sometime and for this reason, it has been referred to as a garrison town acting as a base for Khartoum forces during the second Sudanese civil war in 1998 [11]. Wau Teaching Hospital is a 500-bed health facility, and it's the only hospital of this size in a 350-km radius serving approximately 3 million people [13] (Fig. 1 & S1A-B). The hospital has had a critical shortage of professional health cadres since only about 1.5 physicians and 2 Nurses/Midwifes are available for every 100,000 citizens [14]. The clinicians in this hospital deal mostly with common diseases such as: gastro-intestinal infection, malaria, and HIV/AIDS and tuberculosis [13].

2.2. Study design

This was a cross sectional study conducted at Wau Teaching Hospital between January and February 2016 at the peak of the current armed conflict in South Sudan. The study targeted suspected TB cases, defined as; “Any individual who had a persistent cough for at least two weeks and presented at the tuberculosis unit at the Wau Teaching Hospital” . We used both qualitative and quantitative methods to allow for metric-based analysis linked to nuanced social dynamics of tuberculosis in Wau. In this regard, a structured questionnaire was used to collect quantitative data from the randomly selected patients.

2.3. Sample size estimation

The sample size estimation of suspected tuberculosis cases at the Wau Teaching Hospital was computed based on 0.08–0.46% national average tuberculosis prevalence estimate reported [3,15]. However, we recognize that the regional average although unknown, would more likely be higher than the national average for some areas. Therefore, we assumed a range of 5–19% as reported in pastoral systems with similar settings [16]. With these assumptions, we expected to detect a minimum of 5 cases and a maximum of 19 cases if we randomly sampled 100 suspected TB cases at Wau Teaching Hospital. Here, we collected a sample from a sequence of five (from every fifth) suspected tuberculosis case at Wau teaching hospital. In addition to clinical history and biodata, a questionnaire was administered to each of the sampled suspected TB cases. Given the instability in the region at the time, we utilized a two months window to collect 207 samples from approximately 1035 suspected TB patients.

2.4. Sample collection and transportation

It is note worthy that some of the TB suspects had previously been on medication even in the absence of a confirmatory diagnosis. Three sputum samples (spot-morning-spot) were consecutively collected from 207 suspected TB cases. These included among others routine and referred suspected cases of TB from various areas in Greater Bahr El Ghazal. On the initial hospital visit, the patient was provided with a sterile wide-neck sputum container (see Figure S1) to provide a sputum specimen. The suspected TB case was also given another sputum container and instructed basing on standard early-morning sputum specimen collection for the next day's visit to the clinic [17].

The third specimen was collected when the early-morning specimen was delivered to the laboratory. Here, fluorescent microscopy was done as described below, and the positive samples were kept at - 20 °C in the EPI (Expand Programme on Immunization Unit) refrigerators at Wau Teaching Hospital. Each tube was then packaged in a three-layer receptacle (zip lock sterile bags), maintained at least at 0 °C in an ice box, and transported by road and air transport to the Central Diagnostic Laboratory (CDL), College of Veterinary Medicine, Animal Resources and Biosecurity (COVAB), Makerere University. These were then stored at −80 °C before being delivered to World Health Organization Supranational Tuberculosis Reference Laboratory in Wandegaya, Kampala. The sample transportation by road and air from Southern Sudan was done in compliance with the Southern Sudanese public health Act on transportation of biological material and International Air Transport Association regulations www.iata.org/ads/issg.htm (IATA) respectively.

2.5. Fluorescent microscopy in Wau, South Sudan

Once samples were collected at the teaching hospital, they were then submitted to the in-house diagnostic laboratory for acid-fast microscopic testing (Figure S1C & S1D). A thin smear of the processed sputum material was heat fixed on the slide by the flaming of a Bunsen burner. This was then flooded with Auramine O-Rhodamine B solution and allowed to stand for 15 minutes. This was then followed by a 2-3-minute chlorine free water rinse until there was no more dye leaving the fixed slide. The slide was then flooded for a further 2 minutes with acid alcohol to remove any redundant stain, followed by rinsing with distilled water and then air-drying. At this point, potassium permanganate was added for 2 minutes followed by rinsing and air-drying [18,19]. Presence or absence of acid-fast bodies was determined by use of a fluorescent microscope at 20X, 40X objective magnification for field selection, and later using 100X oil immersion objective to observe the morphology of fluorescing organisms. Bacillary load was graded using standard acid-fast bacillus (AFB) scoring system according to the International Union against Tuberculosis and Lung Disease (IUATLD) and the WHO smear grading scale [17].