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Sex disparities in tuberculosis suspect evaluation: a cross-sectional analysis in rural Uganda

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SUMMARY

SETTING—Six primary health care centers in rural Uganda.

OBJECTIVE—To compare the quality of tuberculosis (TB) evaluation for men and women presenting to primary health care facilities in high-burden settings.

DESIGN—Cross-sectional study using indicators derived from the International Standards of Tuberculosis Care (ISTC) to compare the quality of TB evaluation services provided to men and women.

RESULTS—Of 161 230 patient visits between January 2009 and December 2010, 112 329 (69.7%) were women. We considered 3308 (2.1%) patients with cough \geq 2 weeks as TB suspects, of whom 1871 (56.6%) were women. Female TB suspects were less likely to be referred for sputum smear examination (45.9% vs. 61.6%, $P < 0.001$), to complete sputum smear examination if referred (73.7% vs. 78.3%, $P = 0.024$) and to receive comprehensive evaluation and care as defined by the ISTC (33.0% vs. 45.6%, $P < 0.001$). After adjusting for age, clinic site and visit date, women remained less likely to be referred for sputum smear examination (risk ratio [RR] 0.81, 95% CI 0.74–0.89, $P < 0.001$) and to receive ISTC-recommended care (RR 0.79, 95% CI 0.72–0.86, $P < 0.001$).

CONCLUSION—Strategies to ensure that women receive appropriate TB evaluation could provide a valuable opportunity for increasing case detection while also promoting equitable and universal access to care.

Keywords

operational research; TB diagnostics; women; equity; access

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TUBERCULOSIS (TB) is a major cause of morbidity and mortality for women globally, with 3.2 million incident cases and at least 320 000 deaths reported to the World Health Organization (WHO) in 2010. Although TB represents the third leading cause of death among women aged 15–44 years, women account for just 36% of TB cases reported worldwide.^{1,2} Social and biological factors may account for part of this difference in incidence,^{3,4} but the potential contribution of sex disparities in health care delivery requires further study.

Most studies examining gender and TB case detection in high-burden countries have focused on social and economic barriers that women face in accessing health care services, as evidenced by lower rates of self-referral to health clinics and longer delays between the onset of symptoms and the decision to seek care.^{5–7} However, sex differences in TB case detection may also result from disparities in the quality of TB evaluation provided to men and women after they present to health centers. Although the Stop TB Strategy emphasizes equitable and universal access to care,⁸ few studies have systematically assessed sex disparities in TB services provided in routine primary health settings in high-burden countries.^{9,10} To our knowledge, none have been conducted in sub-Saharan Africa, the region with the world's lowest case detection rates.

We previously reported substantial increases in case detection associated with improved adherence to evidence-based TB suspect evaluation practices recommended by the International Standards for Tuberculosis Care (ISTC)¹¹ at primary health care clinics in rural Uganda.¹² The ISTC, an evidence-based set of recommendations developed by the Tuberculosis Coalition for Technical Assistance in partnership with many national and international partners, describes the accepted standard of care worldwide for managing patients who are suspected of having or have TB. With respect to TB suspect evaluation, the ISTC states that:

All persons with otherwise unexplained productive cough lasting 2–3 weeks or more should be evaluated for tuberculosis (Standard 1),

All patients . . . suspected of having pulmonary tuberculosis should have at least two sputum specimens submitted for microscopic examination (Standard 2), and

All patients [testing positive for TB] . . . should receive an internationally accepted first-line treatment regimen (Standard 8).

In the present study, we extend our analysis to assess the influence of patient sex on the level of ISTC adherence in TB suspect evaluation to identify where in the diagnostic process sex disparities, if present, might be occurring.

METHODS

Study design and setting

We conducted a cross-sectional study to assess for sex differences in the quality of TB diagnostic and treatment services. We collected data on all adults (aged ≥ 15 years) undergoing evaluation for any reason at six primary health care centers located in six rural districts across Uganda from January 2009 to December 2010. Each health center serves a population of approximately 100 000, and offers basic TB evaluation and treatment services. All six health centers participate in the Uganda Tuberculosis Surveillance Project (UTBSP), one component of an ongoing infectious disease surveillance network that was first established in 2001 to monitor malaria case management in primary care centers throughout Uganda. TB surveillance activities were added in 2006 to evaluate and improve the management of patients with suspected pulmonary TB.¹²

Data collection and management

The scope, methods and operations of the surveillance project, including data collection and validation, have been described previously.^{12–15} Briefly, at each health center, clinical officers use a standardized clinical encounter form to capture demographic and clinical characteristics, including the presence or absence of cough of ≥ 2 weeks' duration, referral for and results of sputum acid-fast bacilli (AFB) smear examination and referral for anti-tuberculosis treatment. Data are transferred electronically to a central server, analyzed by UTBSP staff and uploaded monthly to a publicly available website (www.mu-ucsf.org/tb/).

Outcomes

To assess the quality of TB suspect evaluation, we defined and measured three quality-of-care indicators, each representing a key step in TB care as recommended in the ISTC:¹¹ 1) the proportion of patients with cough ≥ 2 weeks (i.e., TB suspects) referred for sputum examination, 2) the proportion of TB suspects who completed sputum examination (i.e., at least one positive or two negative results) if referred, and 3) the proportion of AFB smear-positive TB suspects prescribed anti-tuberculosis treatment. In addition, we defined a summary indicator to measure the proportion of TB suspects who received all ISTC-recommended care (i.e., TB suspects referred for sputum examination and found to have ≥ 1 positive AFB smear result and prescribed treatment, or TB suspects with at least two negative AFB smear results).

Data analysis

We compared the proportions of male and female TB suspects receiving appropriate care as measured by each quality indicator using *t*-tests. We then calculated risk ratios (RRs) and their 95% confidence intervals (CIs) for the association between sex and each of the quality indicators using a Poisson model with a log link and robust standard errors, adjusting for age and date of clinic visit and accounting for clustering within health centers.¹⁶ We performed all analyses using STATA 11.0 (Stata Corporation, College Station, TX, USA).

Human subjects

The Makerere University Faculty of Medicine Research and Ethics Committee and the University of California San Francisco Committee on Human Research approved the study protocol and waived the requirement for informed patient consent. Some of these patients were included in previously published studies.¹²

RESULTS

Patient characteristics

A total of 169 500 adult patient encounters occurred during the study period, including 351 visits to refill TB medications for previously diagnosed disease and 7919 encounters with missing data on sex or history of cough, which were excluded. Of the 161 230 patient encounters included in this analysis, 112 329 (69.7%) were with women. The median age was 29 years (interquartile range [IQR] 21–40), differing slightly by sex (28 years for women vs. 30 years for men, $P < 0.001$). The number of patients seen per site varied based on the size of the clinics and their surrounding population, ranging from 15 394 (9.6% of total) to 42 838 (26.6% of total) patient encounters. Data on human immunodeficiency virus (HIV) status were not available, but HIV prevalence in Uganda is estimated at 6.5%,¹⁷ varying from 5.3% to 8.5% in the districts where the clinic sites are located.¹⁸

Compared to men, women were less likely to report having cough of ≥ 2 weeks' duration (1.7% of female patients vs. 2.9% of male patients, $P < 0.001$). However, due to the

predominance of female patients overall, the majority of the patients reporting cough of 2 weeks' duration (i.e., TB suspects) were female (1871/3308, 56.6%). Female TB suspects were younger than their male counterparts (median age 32 years, IQR 24–46 vs. 38 years, IQR 27–51, $P < 0.001$; Table 1).

Quality indicators, by sex

Clinicians referred a lower proportion of women than men with cough for sputum AFB examination (45.9% vs. 61.6%, difference 15.7%, 95%CI 12.3–19.1, $P < 0.001$). Women were also less likely to complete sputum AFB examination if referred (73.7% vs. 78.3%, difference 4.6%, 95%CI 0.6–8.6, $P = 0.024$) and to be found AFB smear-positive (9.5% vs. 22.2%, difference 12.7%, 95%CI 8.8–16.7, $P < 0.001$). However, there were no significant differences in the proportions of smear-positive women and men referred for anti-tuberculosis treatment (73.3% vs. 75.3%, difference 2.0%, 95%CI –11.1–15.1, $P = 0.76$). Overall, women were substantially less likely to receive ISTC-recommended care compared to men (33.0% vs. 45.6%, difference 12.6%, 95%CI 9.3–15.9, $P < 0.001$). Older age was associated with an increased likelihood of being referred for sputum AFB examination for both women and men and of receiving ISTC-recommended care overall ($P < 0.001$ for both outcomes for both sexes). However, age did not significantly modify the association between sex and either outcome. Results were similar when data were analyzed by individual site, but did not reach statistical significance in most cases (Table 2).

Multivariate analysis

In adjusted analyses (Table 3), clinicians remained less likely to refer female TB suspects for sputum AFB examination (RR 0.81, 95%CI 0.74–0.89, $P < 0.001$). However, women were as likely as men to complete sputum AFB examination if referred (RR 0.94, 95%CI 0.87–1.02, $P = 0.14$), and to be referred for anti-tuberculosis treatment if found to be AFB smear-positive (RR 0.96, 95%CI 0.73–1.27, $P = 0.80$). Overall, women had a 21% lower likelihood (RR 0.79, 95%CI 0.72–0.86, $P < 0.001$) of receiving ISTC-adherent care.

DISCUSSION

In this multi-center study of primary health care clinics in Uganda, we found significant sex disparities in the quality of TB suspect evaluation. Specifically, women with cough of 2 weeks' duration were less likely than men to be referred for TB testing, and only one third of female TB suspects received care in accordance with internationally recommended practices. These findings suggest that, in addition to possible biological differences in TB susceptibility and social differences in access to care, sex disparities in TB suspect evaluation likely contribute to the differences in TB case notification rates between women and men,^{4,19–21} and that women may be an important group to target for programs seeking to increase case detection.

Few studies have evaluated the quality of TB care received by women presenting to routine health care settings in high-burden countries. One study in Bangladesh found a lower likelihood of women displaying symptoms of TB to be referred for sputum smear examination as compared to men,⁹ and a study in Thailand found that female patients had a lower probability of receiving diagnostic care adherent to national guidelines.¹⁰ These similar results indicate that sex disparities may be a generalized phenomenon in the provision of TB services at primary health care centers in high-burden countries.

Although our study was not designed to evaluate reasons for the observed sex disparities, several factors may account for the lower likelihood of women receiving ISTC-recommended TB care than men. First, as TB case notification rates are lower among

women than men, clinicians may be conditioned to have a lower suspicion of TB among women. Even in our setting, the yield of smear examination was higher in men than in women (22.2% vs. 9.5%). Second, efforts to diagnose TB in women may be hindered, as standard TB diagnostic methods can be less sensitive among women, which may insidiously reduce suspicion of TB in women even further. Studies from Pakistan and Bangladesh have reported that women produce sputum less often and of lower quality and volume than men.^{9,22} Moreover, sputum smear microscopy has been shown to be less sensitive in women, even when specimens are of adequate quality.²³ Sputum smear microscopy is also less sensitive in HIV- infected patients,²⁴ and women are disproportionately infected with HIV compared to men in sub-Saharan Africa.¹⁷ Finally, in many high-burden countries, women are less likely to seek care for TB symptoms than men,^{6,25} and even when they do seek care, women infected with TB may present with a different constellation of symptoms from men.²⁶ These factors likely contribute to reduced case detection rates among women in high-burden settings, although studies suggest that these differences can be reduced with simple interventions. For example, Khan et al. and Alisjahbana et al. have both shown that improved patient instructions for sputum sample submission can improve TB diagnosis overall,²² and can help reduce discrepancies in case detection between male and female patients.²⁷ Further studies employing qualitative methods are needed to elicit reasons for sex disparities in TB suspect evaluation and to identify potential interventions to eliminate or reduce such disparities.

The importance of identifying and addressing sex disparities can be viewed from human rights, patient care and public health perspectives. To advance human rights, there is a moral imperative to address sex-based inequities in health care delivery. The United Nations Convention on the Elimination of All Forms of Discrimination against Women calls on all states to ‘eliminate discrimination against women in the field of health care in order to ensure, on a basis of equality of men and women, access to health care services’.²⁸ More recently, the United States Agency for International Development has called for a ‘focus on women, girls, and gender equality’ in the first principle of its Global Health Initiative.²⁹ Delivering high-quality care to every individual is also a fundamental principle espoused in the WHO Stop TB Strategy prioritization of ‘universal access to high-quality diagnosis and patient-centered treatment’.⁸ From a public health perspective, women are particularly important allies in the effort to strengthen existing health systems when implementing new diagnostic interventions, given their central position in the household and their importance in helping to identify and treat pediatric TB cases. Reducing the prevalence of TB among women should also reduce transmission to children, who are at high risk of severe morbidity and mortality from TB, and who can constitute up to 40% of the TB caseload in high-burden settings.³⁰ In addition, given the high rates of treatment adherence and treatment success among women,³¹ appropriate evaluation and treatment of women is likely to yield large dividends in reducing prevalent TB in the community.

Our analysis has several strengths. First, we examined TB suspect evaluation in a highly relevant setting for TB control: the rural primary care clinics that serve as first-line TB diagnostic units in most countries in sub-Saharan Africa. Second, we collected data over an extended period of time from over 160 000 patient encounters in multiple, geographically distributed clinics using a comprehensive monitoring and evaluation system. Finally, the sex disparities observed were consistent over time. These factors strengthen both the internal and external validity of our findings. However, the relatively low prevalence of smear-positive TB in rural, primary care settings—even in a high-burden country—limited our ability to detect a significant difference in the proportions of smear-positive men and women referred for anti-tuberculosis treatment. Furthermore, as the data come from a disease surveillance project, the amount of data for each patient encounter is small, limiting our ability to explore the effects of individual clinical characteristics or to identify repeat patient

encounters. Finally, the reasons for the difference in smear positivity between male and female TB suspects are not clear, as it could be due to a true difference in incidence, a difference in the quality of sputum submitted or a difference in clinician referral patterns for sputum smear evaluation between male and female patients. Given these limitations, our findings highlight the need for better local data collection systems to identify sex and other disparities in TB care, and for local capacity to analyze data, recognize problems and develop and implement solutions.

In conclusion, the sex disparities observed in this study represent a critical inequity in access to TB diagnostic and treatment services that limits the efficiency of case detection in settings utilizing clinician referral and smear microscopy for TB diagnosis. Although women may have lower biologic susceptibility to TB, strategies to identify and address sex disparities within health facilities in high-burden countries may improve case notification in women and will prove vital to ensuring that the WHO's objective of universal access to TB care is fulfilled.

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Table 1

Bivariate analysis of tuberculosis quality-of-care indicators

| Characteristic | All patients (N = 161 230) n (%) | Women (n = 112 329) n (%) | Men (n = 48 901) n (%) | P value |
|--|--|---------------------------------|------------------------------|---------|
| Age, years, median [IQR] | 29 [21–40] | 28 [21–39] | 30 [21– 43] | <0.001 |
| Clinic site | | | | |
| Aduku | 23 359 (14.5) | 17 112 (15.2) | 6 247 (12.8) | <0.001 |
| Kamwezi | 33 019 (20.5) | 21 766 (19.4) | 11 253 (23.0) | |
| Kasambya | 15 394 (9.6) | 9 639 (8.6) | 5 755 (11.8) | |
| Kihihi | 22 844 (14.2) | 16 014 (14.3) | 6 830 (14.0) | |
| Nagongera | 23 776 (14.8) | 16 886 (15.0) | 6 890 (14.1) | |
| Walukuba | 42 838 (26.6) | 30 912 (27.5) | 11 926 (24.4) | |
| Cough < 2 weeks (among all patient encounters) | 3 308 (2.1) | 1 871 (1.7) | 1 437 (2.9) | <0.001 |
| Sputum AFB ordered (among patients with cough < 2 weeks) | 1 744 (52.7) | 859 (45.9) | 885 (61.6) | <0.001 |
| Sputum AFB completed (among patients with AFB examination ordered) | 1 326 (76.0) | 633 (73.7) | 693 (78.3) | 0.024 |
| AFB-positive (among patients with AFB examination completed) | 214 (16.1) | 60 (9.5) | 154 (22.2) | <0.001 |
| Referred for anti-tuberculosis treatment (among patients found AFB-positive) | 160 (74.8) | 44 (73.3) | 116 (75.3) | 0.76 |
| Received ISTC-adherent care overall (among patients with cough < 2 weeks) | 1 272 (38.5) | 617 (33.0) | 655 (45.6) | <0.001 |

IQR = interquartile range; AFB = acid-fast bacilli; ISTC = International Standards of Tuberculosis Care.¹¹

Table 2

Site-specific analysis of selected tuberculosis quality-of-care indicators by sex

| Characteristic | Women n (%) | Men n (%) | P value | Unadjusted RR (95%CI) | P value | Adjusted RR (95%CI)* | P value |
|--|----------------|--------------|---------|--------------------------|---------|-------------------------|---------|
| Sputum AFB ordered (among patients with cough of > 2 weeks) | | | | | | | |
| Total | 859 (45.9) | 885 (61.6) | <0.001 | 0.75 (0.70–0.79) | <0.001 | 0.81 (0.74–0.89) | <0.001 |
| Aduku | 160 (53.5) | 151 (66.5) | 0.003 | 0.80 (0.70–0.93) | 0.002 | 0.88 (0.78–0.98) | 0.026 |
| Kamwezi | 44 (12.5) | 87 (33.6) | <0.001 | 0.37 (0.27–0.52) | <0.001 | 0.56 (0.42–0.74) | <0.001 |
| Kasambya | 154 (81.9) | 206 (91.6) | 0.004 | 0.89 (0.83–0.97) | 0.005 | 0.91 (0.84–0.98) | 0.010 |
| Kihhi | 110 (38.9) | 141 (58.8) | <0.001 | 0.66 (0.55–0.79) | <0.001 | 0.72 (0.60–0.85) | <0.001 |
| Nagongera | 207 (47.9) | 170 (57.1) | 0.015 | 0.84 (0.73–0.97) | 0.014 | 0.88 (0.76–1.00) | 0.059 |
| Walukuba | 184 (57.9) | 130 (69.2) | 0.011 | 0.84 (0.73–0.96) | 0.009 | 0.88 (0.77–1.00) | 0.55 |
| Received ISTC-adherent care overall (among patients with cough of > 2 weeks) | | | | | | | |
| Total | 617 (33.0) | 655 (45.6) | <0.001 | 0.72 (0.66–0.78) | <0.001 | 0.79 (0.72–0.86) | <0.001 |
| Aduku | 117 (39.1) | 120 (52.9) | 0.002 | 0.74 (0.61–0.89) | 0.002 | 0.81 (0.68–0.96) | 0.016 |
| Kamwezi | 40 (11.4) | 63 (24.3) | <0.001 | 0.47 (0.33–0.67) | <0.001 | 0.73 (0.53–1.00) | 0.049 |
| Kasambya | 142 (75.5) | 187 (83.1) | 0.057 | 0.91 (0.82–1.00) | 0.062 | 0.92 (0.83–1.02) | 0.099 |
| Kihhi | 91 (32.2) | 118 (49.2) | <0.001 | 0.65 (0.53–0.81) | <0.001 | 0.71 (0.58–0.87) | 0.001 |
| Nagongera | 140 (32.4) | 99 (33.2) | 0.818 | 0.98 (0.79–1.20) | 0.818 | 1.01 (0.81–1.24) | 0.956 |
| Walukuba | 87 (27.3) | 68 (36.2) | 0.038 | 0.76 (0.58–0.98) | 0.036 | 0.79 (0.61–1.02) | 0.077 |

* Adjusted for age, site and date of clinical encounter; reference is male sex.

RR = relative risk; AFB = acid-fast bacilli; ISTC = International Standards of Tuberculosis Care. 11

Table 3

Multivariate analysis of tuberculosis quality of care indicators

| Outcome | Unadjusted RR | P value | Adjusted RR* | P value |
|--|------------------|---------|------------------|---------|
| Sputum AFB ordered | 0.75 (0.70–0.79) | <0.001 | 0.81 (0.74–0.89) | <0.001 |
| Sputum AFB completed | 0.94 (0.89–0.99) | 0.02 | 0.94 (0.87–1.02) | 0.14 |
| Referred for anti-tuberculosis treatment | 0.97 (0.82–1.16) | 0.77 | 0.96 (0.73–1.27) | 0.80 |
| Received ISTC-adherent care overall | 0.72 (0.66–0.78) | <0.001 | 0.79 (0.72–0.86) | <0.001 |

* Adjusted for age, site and date of clinical encounter; reference is male sex.

RR = relative risk; AFB = acid-fast bacilli; ISTC = International Standards of Tuberculosis Care.¹¹