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RESEARCH

Assessment of the impact of rapid syphilis tests on syphilis screening and treatment of pregnant women in Zambia

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ABSTRACT

Objective: To evaluate the impact of rapid syphilis tests (RSTs) on syphilis testing and treatment in pregnant women in Kalomo District, Zambia. *Methods:* In March 2012, health workers at all 35 health facilities in Kalomo Distract were trained in RST use and penicillin treatment. In March 2013, data were retrospectively abstracted from 18 randomly selected health facilities and stratified into three time intervals: baseline (6 months prior to RST introduction), midline (0–6 months after RST introduction), and endline (7–12 months after RST introduction). *Results:* Data collected on 4154 pregnant women showed a syphilis-reactive seroprevalence of 2.7%. The proportion of women screened improved from baseline (140/1365, 10.6%) to midline (976/1446, 67.5%), finally decreasing at endline (752/1337, 56.3%) ($P < 0.001$). There was no significant difference in the proportion of syphilis-seroreactive pregnant women who received 1 dose of penicillin before (1/2, 50%) or after (5/48, 10.4%; $P = 0.199$) RST introduction with low treatment rates throughout. *Conclusion:* With RST scale-up in Zambia and other resource-limited settings, same-day test and treatment with penicillin should be prioritized to achieve the goal of eliminating congenital syphilis.

1. Background

Globally, it is estimated that approximately 1.4 million annual cases of syphilis occur during pregnancy [1]. A recent meta-analysis demonstrated that, among asymptomatic, untreated pregnant women with syphilis, fetal loss and stillbirth, neonatal deaths, and prematurity/low birth weight were 21%, 9.3%, and 5.8%, respectively, more frequent when compared with women without syphilis [2]. Treatment of syphilis-seroreactive pregnant women with 1 dose of intramuscular penicillin at least 30 days prior to delivery reduces the risk of adverse pregnancy outcomes to that of a non-infected mother, although full treatment of latent maternal syphilis requires three doses of intramuscular penicillin [3–5]. However, modeling data suggest that less than 10% of women with syphilis during pregnancy are screened and appropriately treated [1], despite the 2007 World Health Organization's Global Elimination of Congenital Syphilis initiative goals of testing more than 90% of pregnant women and of treating more than 90% of those who are seroreactive by 2015 [6].

Recently-developed rapid syphilis tests (RST; BIOLINE, Korea) have a high sensitivity (85.7% to 100%) and specificity (96% to 100%), and do not require the traditional laboratory infrastructure used for rapid plasma reagin (RPR) tests [7–9]. Previous studies have suggested increased syphilis screening post-RST implementation, but longer-term evaluation of screening rates after initial training is needed [10]. In March 2012, the Elizabeth Glaser Pediatric Aids Foundation completed RST training and implementation in accordance with the Zambian Ministry of Health (MOH) guidelines [11,12] for antenatal care (ANC) staff in Kalomo District, Zambia. The present study evaluates the performance of RSTs and treatment of seropositive women in ANC facilities 12 months after RST implementation and describes the impact of RST use on ANC and prevention of mother-to-child transmission (PMTCT) services.

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2. Methods

2.1. Study site selection and standard of care

Kalomo is a rural district with a population of 254 211 (2010 census) in an area of approximately 15 000 km^2 with one main tarmac road [13]. Prior to March 2012, RPR tests were used during ANC to screen for syphilis. In March 2012, 35 MOH staff from all 35 facilities in Kalomo received off-site training for RST and syphilis treatment, with intermittent on-site supervision at some facilities afterwards. Of these 35 facilities, 18 were selected by random-number generator, and included 1 urban district hospital, 2 urban health centers, and 15 rural health centers. All facilities provide antenatal PMTCT of HIV services, which at the time of the study included HIV testing, partner testing, and referral to antiretroviral therapy services, as well as under-five pediatric services, free of charge. The selected facilities had a mean of 39.3 first ANC visits per month (range, 8.5—70.3). The study population discussed herein included a random sample of pregnant women attending their first ANC visits at any of these 18 facilities.

2.2. Study design

The study followed a quasi-experimental evaluation design with baseline, midline, and endline comparisons. Data on pregnant women were retrospectively abstracted using facility registers from September 2011 to March 2013 and stratified into three intervals, namely baseline (6 months prior to introduction of RSTs), midline (0 to 6 months after introduction of RSTs), and endline (7 to 12 months after introduction of RSTs). The primary outcome was the proportion of pregnant women screened for syphilis at the first ANC visit. Secondary outcomes were: (1) the proportion of syphilis-seroreactive women treated with penicillin; (2) the proportion of women seroreactive for HIV and syphilis; and (3) the proportion of syphilis-seroreactive women with poor pregnancy outcomes (i.e. low birth weight (<2500 g), premature delivery (<37 weeks), stillbirth). For the purposes of the present study, stillbirth was defined as any birth outcome recorded by health facility staff as a stillbirth (fresh or macerated) in the Labor and Delivery register. The Zambian MOH training defines stillbirth as any fetus born at more than 28 weeks of gestation without a heartbeat [11].

2.3. Data collection

Ten data collectors from Kalomo District were trained and tested in research ethics, standardized data extraction, and management techniques prior to data collection. Data capture was done using TeleForms (Hewlett-Packard, Palo Alto, CA, USA) [14]. Pregnant women attending their first ANC visit during the observation period were randomly selected from the MOH-approved Safe Motherhood (SMH) register using a sequential skip pattern dependent on ANC volume at the facility. Facilities with less than 12 first ANC visits per month randomly sampled every other woman in the SMH register; all other facilities (with a range of 16—70 first ANC visits per month) randomly sampled every fourth woman in the SMH register across all three time periods. Women were identified by a unique SMH number and tracked across other MOH-approved, standardized registers, including the Integrated PMTCT register, the Labor and Delivery register, and facility RST logs. Abstracted data for analysis included information on (1) syphilis testing, (2) syphilis treatment, (3) HIV testing, and (4) delivery for mother/infant pairs. All women randomly selected from the SMH register were included in the analysis, even if they could not be traced to delivery. Stockout data for testing materials and penicillin were abstracted from facility pharmaceutical and supply logs. Baseline testing values were calculated using data from the 6 (33.3%) facilities that had RPR testing materials in stock. Twelve facilities (66.7%) were not performing antenatal syphilis screening prior to the introduction of RST and thus baseline data were not available for analysis. There was no documentation of any confirmatory RPR tests performed for any positive RSTs at the facility level. Verification and completeness of forms was done in the field by data supervisors. Forms were then sent to the central data processing office and scanned using TeleForm software, allowing for double-data entry compiled into a password-protected Microsoft Access (Microsoft, Redmond, WA, USA) database.

2.4. Data analysis

Differences in patient outcomes between index (baseline) and comparison groups (midline and endline) were calculated using Pearson's χ^2 test or Fisher exact test. A P value of less than 0.05 was considered statistically significant. SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) was used for all analyses.

2.5. Ethics

The protocol for the study was reviewed and approved by the Boston University Institutional Review Board, the ERES Converge Zambian Institutional Review Board, and the Centers for Disease Control and Prevention's Associate Director for Science.

3. Results

3.1. Demographic and ANC characteristics

ANC data from 4154 pregnant women presenting to any of the 18 selected ANC facilities during the observation period were collected and analyzed (Table 1). ANC demographic data were missing for 19 women across all three time periods. Median gestational age at first ANC visit was 22 weeks (range, 7—39) across the three time intervals. The median number of visits for the study population was 1 ANC visit across all time periods (median, 1; range, 1—6).

3.2. Performance of syphilis screening

At baseline, 10.3% (140/1365) of women were screened for syphilis at their first ANC visit by RPR testing (Table 2). Within the first 6 months following the introduction of RSTs, testing increased to 67.5% (976/1446) of women across all 18 facilities, finally dropping to 56.3% (752/1337) at endline (P <0.001 for both midline and endline compared with baseline).

3.3. Syphilis and HIV seropositivity

Syphilis seroreactivity prevalence in the study population was 2.7% (50/1868), with no significant differences across the three time periods. HIV seropositivity was 4.5%, with no significant differences across the three time periods. HIV testing data was available for all 4154 women included in the study.

3.4. Treatment and birth outcomes of syphilis-seroreactive women

In the baseline group, 1 of 2 syphilis-seroreactive women was treated with 1 dose of penicillin. During the first 6 months following RST introduction, only 13% (3/23) of seroreactive women received 1 dose of penicillin, and 7—12 months after RST introduction, 8% (2/25) of seroreactive women received 1 dose of penicillin (Table 2). Timing of treatment was not reliably recorded. Birth outcome data from Labor and Delivery registers were available for 19.3% (802/4154) of women in the study population, 1.5% (12) of whom had tested syphilis seroreactive at their first ANC visit; these 12 women had documented live births, but birth weight and gestational age data were not available in the Labor and Delivery register. Treatment with at least 1 dose of penicillin was documented for three women, but there was no