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DISEASE BURDEN

Estimating disease burden of maternal syphilis and associated adverse pregnancy outcomes in India, Nigeria, and Zambia in 2012

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ABSTRACT

Objective: To estimate maternal syphilis and its associated adverse pregnancy outcomes in India, Nigeria, and Zambia. *Methods:* An online estimation tool was used to generate point estimates and uncertainty ranges of maternal syphilis and adverse pregnancy outcomes due to mother-to-child transmission (MTCT). The most recent data (2010–2012) on antenatal care coverage, syphilis seroprevalence, and syphilis screening and treatment coverage at the subnational level in India, Nigeria, and Zambia were used to estimate disease burden for 2012. Sensitivity analysis was conducted for three screening and treatment scenarios (current coverages, current coverages minus 20%, and ideal coverages consistent with WHO targets for eliminating MTCT of syphilis). *Results:* A total of 103 960, 74 798, and 9072 pregnant women with probable active syphilis were estimated to occur in India, Nigeria, and Zambia, resulting in 53 187, 37 045, and 2973 adverse outcomes, respectively; approximately 1.6%, 4.8%, and 37.0% of these were averted under the current service coverages in India, Nigeria, and Zambia. The disease burden varied significantly in its subnational distribution within India and Nigeria, but was distributed evenly across Zambia. *Conclusions:* The obtained results suggest an ongoing, unaverted high burden of maternal syphilis and associated adverse outcomes in India, Nigeria, and Zambia. Screening and treatment for syphilis must be scaled-up significantly in these countries to achieve elimination of MTCT of syphilis.

1. Background

Syphilis remains a major social and public health burden globally despite its relatively simple prevention and treatment. It is of particular concern in pregnancy given the risk of mother-to-child transmission (MTCT) [1,2], which causes significant perinatal morbidity and mortality, particularly in low-resource countries [2]. Untreated maternal syphilis can result in a significant reproductive health burden and contributes to syphilis-associated adverse pregnancy outcomes, including stillbirth and late fetal loss, neonatal death, premature and low birth weight infants, and congenital syphilis [3].

In 2007, the WHO launched the global initiative to eliminate congenital syphilis [1]. Three regions (Americas, Asia-Pacific, and Africa) have initiated local efforts focusing on the dual elimination of MTCT (EMTCT) of HIV and syphilis [4–6], thus striving to improve maternal and child health and contribute to the achievement of Millennium Development Goals 4, 5, and 6 [7].

Routine reporting and periodic estimation of maternal syphilis and its associated adverse outcomes facilitate monitoring of disease burden and assessment of the impact of initiatives at a global or regional level and of EMTCT programs at the national or subnational level. The WHO recently reported global and regional estimates of the burden of maternal syphilis and related adverse outcomes for 2008 [8]. These estimates

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suggest that, globally, nearly 1.4 million pregnant women are infected with probable active syphilis (PAS), accounting for approximately 1% of all pregnancies worldwide. Africa and Asia are regions with high disease burden, representing 39.3% and 44.3% of the global estimate, respectively. Nevertheless, despite their use, global and regional estimates may not exemplify the status quo at the national or subnational level, which may be more useful for programmatic purposes.

In 2013, the Bill and Melinda Gates Foundation, along with WHO and PATH, selected India, Nigeria, and Zambia to participate in the Dual Testing to Eliminate Congenital Syphilis (DTECS) project, which explores the feasibility of achieving the EMTCT of syphilis within existing prevention of MTCT of HIV programs. As part of the DTECS project, the present study estimates subnational and national disease burdens of maternal syphilis and related adverse outcomes based on the available national data sources for 2012 in India, Nigeria, and Zambia.

2. Material and methods

2.1. Estimation process

Estimation in each country was conducted through consultative processes involving key stakeholders, including the National AIDS Control Organization under the Ministry of Health and Family Welfare in India, the National AIDS/STI Control Program of the Federal Ministry of Health in Nigeria, and the Ministry of Community Development, Mother, and Child Health and the Ministry of Health in Zambia.

Presentation of the estimation methods, including the data needed and the assumptions proposed, was provided by an expert from WHO, followed by an intensive discussion to explore available data from different sources among national program managers and WHO country officers in each of the three countries. Consensus on the data and assumptions used for estimation was agreed prior to each estimation exercise. Draft estimates were reviewed by key stakeholders, who provided comments and any necessary improvements before finalization of the estimates.

2.2. Estimation model and tool

A health service delivery model involving calculation of the number of pregnant women with PAS infection and the number of adverse pregnancy outcomes associated with syphilis was developed by WHO and reviewed and approved by the Child Health Epidemiology Reference Group. Details of the model have been reported elsewhere [8]. In this model, PAS infection was defined as seropositivity on both treponemal and non-treponemal tests. Adverse pregnancy outcomes included stillbirth/early fetal death, neonatal death, prematurity/low birth weight, and congenital syphilis. Stillbirth was defined as death of a fetus of at least 28 weeks of gestation or at least 1000 g weight, and early fetal death as fetal death occurring from 22 − 28 weeks of gestation (i.e. second and early third trimester) [9].

The number of women with PAS infection was calculated as the product of the number of pregnant women and prevalence of seropositive women with both treponemal and non-treponemal syphilis test positivity. A correction factor was used to adjust the prevalence if only one test type was used to determine seropositivity. The number of adverse pregnancy outcomes in pregnant women with PAS infection was calculated as the product of the number of infected pregnant women and the probability of those women having a syphilis-related adverse outcome without treatment.

The probabilities of syphilis-related adverse outcomes occurring without effective treatment were 0.21 for stillbirth/early fetal death, 0.09 for neonatal death, 0.06 for prematurity/low birth weight, 0.16 for congenital syphilis, and 0.52 for any adverse outcome [3]. The effectiveness of screening and treatment with penicillin in averting adverse outcomes was 0.82 for stillbirth/early fetal death, 0.80 for neonatal death, 0.64 for prematurity/low birth weight, 0.97 for congenital syphilis, and 0.84 for any adverse outcome [10].

An Excel spreadsheet tool (Microsoft, Redmond WA, USA) based on the 2008 estimation model was developed by WHO [11]; the estimation was centered upon a health service delivery model involving four estimation steps [8]. By entering the background data (number of pregnant women, seroprevalence of syphilis, and antenatal care (ANC), syphilis screening, and treatment coverage rates) at subnational level and the corresponding assumptions described above (namely, probability to develop adverse outcomes without effective interventions and probability to avert these with effective treatment), the spreadsheet automatically generated estimates of the number of pregnant women with PAS infection who did or did not attend ANC, as well as the incidence of each syphilis-related adverse pregnancy outcome. The national estimate was calculated as a sum of the subnational estimates. An approximate uncertainty at subnational level for the estimate of pregnant women with PAS was calculated using the delta method and a 5% relative error for seroprevalence of syphilis, the number of pregnancies, and the correction factor for the estimated proportion of women with PAS. The subnational uncertainties were summed to obtain the national uncertainty.

The estimation covered all subnational regions in each of the three countries. Based on data available at subnational level, subnational estimations were conducted in 35 units at state level (Andhra Pradesh, Arunachal Pradesh, Assam, Bihar, Chhattisgarh, Goa, Gujarat, Haryana, Himachal Pradesh, Jammu and Kashmir, Jharkhand, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Mizoram, Nagaland, Odisha, Punjab, Rajasthan, Sikkim, Tamil Nadu, Tripura, Uttar Pradesh, Uttarakhand, and West Bengal) or union territory level (Andaman and Nicobar, Chandigarh, Dadra and Nagar Haveli, Daman and Diu, Lakshadweep, National Capital, and Puducherry) in India, six subnational units at regional level (North Central, consisting of Benue, Federal Capital Territory, Kogi, Kwara, Nasarawa, Niger, and Plateau; North East, consisting of Adamawa, Bauchi, Borno, Gombe, Taraba, and Yobe; North West, consisting of Jigawa, Kaduna, Kano, Katsina, Kebbi, Sokoto, and Zamfara; South East, consisting of Abia, Anambra, Ebonyi, Enugu, and Imo; South South, consisting of Akwa Ibom, Bayelsa, Cross River, Delta, Edo, and Rivers; and South West, consisting of Ekiti, Lagos, Ogun, Ondo, Osun, and Oyo) in Nigeria, and 10 subnational units at province level (Central, Copperbelt, Eastern, Lusaka, Luapula, Muchinga, Northern, North Western, Southern, and Western) in Zambia.

2.3. Data sources

2.3.1. Number of pregnant women

The estimated number of pregnancies in India was obtained primarily from the National Health Management Information System (HMIS) [12]. Since a functional system to register either pregnancies or live births is not available at primary health care centers in Nigeria or Zambia, the number of pregnant women was calculated according to local practice and estimated as 5% of the projected 2012 population size based on 2006 census data for Nigeria and 5.2% of the most recent census population size for Zambia [13].

2.3.2. Syphilis seroprevalence

Syphilis seroprevalence was calculated by dividing the total number of pregnant women seropositive for syphilis by the total number of pregnant women screened. Prevalence data were obtained from the HIV Sentinel Surveillance System in India, the General Antenatal Register (GAR) in Nigeria, and the HMIS in Zambia.

Non-treponemal tests (venereal disease research laboratory test [VDRL] or rapid plasma reagin [RPR]) were recommended by the national guidelines and used in sentinel surveillance programs in India [14]. VDRL tests were used in ANC services in Nigeria to identify and report seropositivity for syphilis [15], while treponemal tests, including rapid syphilis tests, were applied in Zambia. Based on the correction