Is routine antenatal screening for syphilis in Nigeria still justified clinically and economically?

Mohammed Bukar, FWACS, FMCOG, *Bala M. Audu,* MSc, FMCOG, *Usman I. Takai,* MBBS, AFMCOG,
Bamidele B. Ajayi, MHPM, FMLSCN, *Abubakar A. Kullima,* MBBS, FWACS.

ABSTRACT

الأهداف: تحديد إصابة المصل وأثر التكلفة لفحص السفلس ما قبل الولادة بمستشفى جامعة مايدوغوري UMTH– مايدوغوري – نيجيريا.

الطريقة: أجريت دراسة استطلاعية لتحليل نتائج مختبر أبحاث الأمراض التناسلية (VDRL) عند النساء الحوامل بجامعة UMTH – مايدوغوري – نيجيريا خلال فترة العشر سنوات من 1 يناير 1999 حتى 31 ديسمبر 2008.

النتائج: تم تسجيل 18,712 امرأة لمتابعة ما قبل الولادة خلال مدة الدراسة. ومن بين هؤلاء خضع 18,101 للفحص المصلي للسفلس. ظهر مصل إيجابي لدى 12 من 18,101 بواسطة VDRL. تم تأكيد إصابة 9 75% بواسطة اختبار التراص الدموي للولبية الشاحبة (TPHA)، وإعطائهن معدل إصابة مصل بقدر 0.05%. وظهر فحص إيجابي خاطئ عند 3 25%. يتراوح عمر الذروة للإصابة في 0.02% في مجموعة تتراوح أعمارهم 20–24 عام. لم تظهر أي إصابة في مجموعات التي تتراوح أعمارهم 15–19 و <40 عام. لم توجد أي إصابة خلقية لسفلس. تقدر تكلفة اختبار VDRL للمريض في جامعة مايدوغوري US$2. تقدر التكلفة الإجمالية للمال المنفق لاختبارات VDRL خلال مدة الدراسة أعلى من US$37,424.

خاتمة: إن معدل إصابة المصل بالسفلس منخفضة في هذه الدراسة. وهذا ما يدعو إلى مراجعة سياسة فحص الأمصال الروتيني لما قبل الولادة لسفلس في مايدوغوري – نيجيريا.

Objectives: To determine the seroprevalence and cost effectiveness of antenatal syphilis screening at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Nigeria.

Methods: A retrospective chart analysis of venereal disease research laboratory (VDRL) results among pregnant women at the UMTH, Maiduguri, Nigeria, during a 10-year period (from 1st January 1999 to 31st December 2008) was undertaken.

Results: A total of 18,712 women registered for antenatal care during the study period. Of these, 18,101 had serological screening for syphilis. Only 12 of the 18,101 screened were seropositive by VDRL, 9 (75%) were confirmed by *Treponema pallidum* hemagglutination assay (TPHA), giving a seroprevalence rate of 0.05%. Three (25%) were biological false-positive. The peak age-specific incidence of 0.02% was in the 20-24 year-age group. There was zero prevalence in the age groups 15-19 and >40 years. There was no case of congenital syphilis seen. The cost for VDRL testing per patient in UMTH is US$2. The total amount of money spent on VDRL tests over the study period was US$37,424.

Conclusion: The seroprevalence rate of syphilis is extremely low in this study. This calls for a review of the policy of routine antenatal serology screening for syphilis in Maiduguri, Nigeria.

Syphilis has a significant long-term morbidity for mothers, and can seriously complicate pregnancy, resulting in spontaneous abortion, preterm birth, stillbirth, non-immune hydrops, and congenital malformations. Syphilis remains an important sexually transmitted disease in many countries such as Africa,[1] Asia,[2] and Latin America,[3] including Venezuela.[4,5] In common with other bacterial sexually transmitted infections (STIs), it is more common in poor populations who lack access to treatment, and in those with many sexual partners.[1] The World Health

Organization estimates that there are approximately 12 million new cases of syphilis worldwide each year, and many of these occur in developing countries.[6] An increase in the number of cases of congenital syphilis from 277 in 1980 to 1,700 cases in 1989 has been reported.[6] This was attributed to maternal drug abuse particularly crack cocaine, poverty, prostitution, and lack of antenatal care. Congenital syphilis poses significant challenges for the clinicians because infants may be asymptomatic at birth, or present with a highly variable clinical picture.[4,5] Despite the clinical efficacy of penicillin in the treatment of pregnant patients with syphilis, infants with congenital syphilis are still encountered.[3,4] Although many studies have shown that the prevalence of maternal and congenital syphilis is on the decline,[7-11] a re-evaluation of the value of routine antenatal screening for syphilis in our population has received scant attention. The aim of this study therefore, is to determine the seroprevalence, and cost effectiveness of antenatal syphilis screening.

Methods. A retrospective chart analysis of the venereal disease research laboratory (VDRL) results among pregnant women at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Nigeria, from 1st January 1999 to 31st December 2008 was undertaken. The study was carried out after approval was obtained from the research and ethics committee of the hospital. Booking registers, and VDRL/ *Treponema pallidum* hemagglutination assay (TPHA) registers were obtained from the medical records department, and the serology section of the immunology department. The total annual antenatal booking and delivery rates were also obtained. We included all attendees who had antenatal serology test for syphilis, and those who had incomplete information for analysis were excluded from the study. Five milliliters of blood were collected from each patient and sent to the laboratory for analysis. The sera were analyzed for VDRL by using VDRL carbon antigen (a non-treponemal test). Tests that were reactive by showing flocculation were confirmed using TPHA, a treponemal test (New market Laboratories Limited, Kent Ford, UK and distributed by Bio-rad, Marnes-la-Coquette, France), according to the manufacturer's instructions with 100% concordant qualitative results. Those that were positive by TPHA were confirmed as positive.

The age, pregnancy outcome, congenital abnormality, and the results of the serology tests were recorded and analyzed using the Statistical Package for Social Sciences version 16 (SPSS Inc., Chicago, IL, USA). Chi-square was used to test for significance. A *p*-value of <0.05 was considered significant. The results were presented by simple statistical tables.

Results. Over the 10-year period, a total of 18,712 women had booked for antenatal care, out of which 18,101 had routine serology screening for syphilis, giving a screening rate of 96.7%. For no obvious reasons, 611 (3.3%) of the booked women had not been screened. Only 12 of those screened were found to be seropositive by VDRL; 9 (75%) out of the 12 were confirmed by TPHA, giving a seroprevalence rate of 0.05%. Three (25%) were biological false-positive. Some of those who were confirmed by TPHA were treated with intramuscular benzathine penicillin 2.4 megaunit weekly for 3 weeks, while in others, there was no documentation of treatment offered. **Table 1** shows the age-specific distribution of seropositivity of syphilis among the antenatal attendees. Most of those screened were in the 25-29 years age range (37.1%), while the least were in those >40 years (2.9%). The peak age specific incidence of 0.02% was among the 20-24 years age group, while the age groups 15-19, and >40 years old had zero prevalence. During the same period there were 19,944 deliveries with 19,539 live births, and 405 stillbirths (2%). There was no case of stillbirth among those who tested positive with TPHA, and no case of congenital syphilis was recorded during the study period (**Table 2**).

Discussion. In most parts of the developing world, screening for syphilis during pregnancy is carried out by VDRL test. When the test is positive, either the titer is estimated, or an antibody based-test is performed to confirm the result of the VDRL test.[12] The theory that syphilis is associated with adverse perinatal outcome is not new. Prevention, timely detection, and treatment will go a long way in reversing this ugly trend.[13] Syphilis is a systemic infection caused by the spirochete *Treponema pallidum*, which is transmitted by close mucosal contact, including oral, anal, and vaginal sex. Other spirochetal infections like Yaws, Bejel, and Pinta are serologically indistinguishable from syphilis, and is a cause of biological false positivity.[14]

Table 1 - Age distribution among the studied sample.

Age group (years)	Antenatal attendees n	Positive cases n
15-19	974	0
20-24	6419	3
25-29	6952	2
30-34	2566	2
35-39	1247	2
≥40	554	0
Total	18,712	9
χ^2 = 3542.82, *p*=0.000		

Table 2 - Yearly distribution and outcome of antenatal syphilis serology.

Year	+VDRL	-VDRL	Total	+TPHA	Live birth	Stillbirth	Total	CS	ANC B
1999	5	1647	**1652**	4	1803	63	**1866**	0	1697
2000	-	1948	**1948**	0	2052	34	**2086**	0	1975
2001	-	1704	**1704**	0	1865	58	**1923**	0	1764
2002	-	1849	**1849**	0	1969	29	**1998**	0	1897
2003	-	1751	**1751**	0	1863	39	**1902**	0	1781
2004	4	1839	**1843**	2	1989	47	**2036**	0	1899
2005	-	1619	**1619**	0	1786	30	**1816**	0	1709
2006	1	1890	**1891**	1	2042	42	**2084**	0	1957
2007	2	1964	**1966**	2	2112	36	**2148**	0	2033
2008	-	1878	**1878**	0	2058	27	**2085**	0	1988
Total	12	18,089	**18,101**	9	19,539	405	**19,944**	0	18,712

+: positive, -: negative, TPHA - *Treponema pallidum* hemagglutination assay, VDRL - venereal disease research laboratory, CS - congenital syphilis, ANC B - number of booked patients

Syphilis is common in the developing world with localized prevalence in pregnant women varying widely from 2.5% in Burkina Faso to 17.4% in Cameroon.[15] The prevalence from our study of 0.05% is approximately the lowest reported in the sub-Saharan Africa. Our prevalence is also lower than 0.125%, and 0.4% reported from the eastern part of Nigeria,[7,8] but fairly agrees with the 0.03% reported from Saudi Arabia.[16] The prevalence from our study is also lower than 4.3% reported in the same center 12 years ago,[11] suggesting a declining trend in syphilis over the study period. This reassuring trend could be associated partly with increasing over-the-counter use of antibiotics, awareness of pregnant women to health needs created during antenatal classes, increased public awareness through media, and safer sex practices. The decline in risky sexual behavior due to interventions to control the HIV pandemic, and the introduction of syndromic management of STIs in Nigeria, may also have contributed to the reduction in the prevalence of syphilis. The low proportion of booked women who were not screened (3.3%) is probably due to high acceptability of pregnant women to the routine investigations carried out at booking. Some of the physicians who do not see the need for routine screening probably had not requested for the screening in the first place, and secondly some of the attendees may fail to carry out the test for a variety of reasons.

The interpretation of serological tests for syphilis in the tropics is compounded by tropical illnesses like malaria and parasitic infestations that could lead to biological false-positive results.[17] This no doubt limits the usefulness of antigen-based screening for the detection of syphilis in the tropics. The 0.02% biological false-positive in this study attests to this fact. This is however, lower than the biological false-positive results of 0.26% and 0.7% reported from other studies.[18,19] While syphilis in Africa may be a major public health problem, its significance varies from one community to the other. Although we could not directly relate VDRL/TPHA positivity to stillbirths in this study, the absence of congenital syphilis over the study period implies that the contribution of primary or latent syphilis to perinatal mortality is likely to be insignificant. This calls to question the routine screening of all pregnant women for syphilis in a region, where the contribution of syphilis to perinatal outcome is extremely low. However, several studies have found screening of pregnant women for syphilis to be a highly cost-effective intervention, even if the prevalence of syphilis is low.[8,20,21]

Those in the 20-24 year age group had the highest prevalence of 0.02%. This could be attributed to the large number of women in this age group, and to the higher sexual activity of this group (most of our women marry at this age group, or even at younger ages), which therefore makes the group more vulnerable to risks of acquiring infection. Similarly, the zero prevalence in the age groups 15-19 and >40 could be due to the low number of the studied cases, coupled with reduced sexual activity, or indiscriminate exposure to penicillin for treatment of other diseases. However, the findings between the age of the patient and susceptibility to the disease in our study (p=0.0000), is in contrast to the findings of Brillman et al,[22] who stated that most new cases of syphilis occurred in both men and women of age 15-39 years, with the highest infection rates in persons of age 20-29 years, but fairly agrees with the CDC[23] studies, which reported some significant (p<0.05) relationship between the age group and the occurrence of disease.

To prevent congenital syphilis, it is imperative to screen for syphilis early in pregnancy, but this remains a challenge in most parts of the sub-Saharan Africa. We found that the median gestational age at booking in our center was 28.5 weeks. This suggests that most women book at a time that the effect of syphilis on the fetus would have occurred, and late detection of syphilis would have little effect on the overall outcome of the pregnancy. Early booking and screening is essential in preventing congenital syphilis.

More than one third of the population of Nigeria live in extreme poverty, defined by the World Bank as earnings of under $1 per day, while 9 out of 10 Nigerians live on less than $2 per day. The zones in the northern part of the country where this study was carried out present the highest vulnerability, with the highest proportion of households experiencing chronic poverty.[24]

The estimated cost for VDRL test per attendee in UMTH is US$2. On the other hand, the cost of prophylactic iron (60 mg elemental iron), folic acid (5 mg), and anti-malarial prophylaxis (sulfadoxine-pyrimethamine, 500 mg/25 mg) per attendee from booking to the end of puerperium is US$1.80. The total amount of money spent on VDRL tests over the study period was US$37,424. Over the same period, to provide prophylactic iron, folic acid, and sulfadoxine-pyrimethamine during pregnancy, the puerperium will cost US$33,681.60.The balance of US$3742.40 will provide iron, folic acid, and sulfadoxine-pyrimethamine for an additional 2,079 women during pregnancy and puerperium. Anemia and malaria in pregnancy have deleterious effect on both maternal and perinatal outcome, and iron supplementation and intermittent preventive therapy of malaria have been shown to reduce the untoward effects of these disease conditions.[25-29] The twin evil of anemia and malaria are unarguably more important reproductive health problems than syphilis in Maiduguri.

The limitation of this study lies in its retrospective nature with some information not readily available for analysis.

In conclusion, the continuing routine screening of a disease condition, which is not a significant cause of mortality with such a very low prevalence (0.05%) is difficult to justify. If the primary aim of screening for syphilis in the antenatal care setting is to prevent congenital syphilis, and over a 10-year period, no case of congenital syphilis was seen despite the colossal amount of money spent, then such a screening method cannot be said to be economically justifiable. In the future, selective screening, based on risk factors for syphilis may be more justifiable than routinely screening a population with extremely low prevalence.

References

1. Gichangi P, Renterghem LV, Karanja J, Bwayo J, Kiragu D, Temmerman M. Congenital syphilis in a Nairobi maternity hospital. *East Afr Med J* 2004; 81: 589-593.
2. Lim CT, Koh MT, Sivanesaratnam V. Early congenital syphilis- a continuing problem in Malaysia. *Med J Malaysia* 1995; 50: 131-135.
3. Valderrama J, Zacarías F, Mazin R. [Maternal syphilis and congenital syphilis in Latin America: big problem, simple solution] *Rev Panam Salud Publica* 2004; 16: 211-217. Spanish.
4. Sangtawesin V, Lertsutthiwong W, Kanjanapattanakul W, Khorana M, Horpaopan S. Outcome of maternal syphilis at Rajavithi Hospital on offsprings. *J Med Assoc Thai* 2005; 88: 1519-1525.
5. Vásquez-Manzanilla O, Dickson-Gonzalez SM, Salas JG, Rodriguez-Morales AJ, Arria M. Congenital syphilis in Valera, Venezuela. *J Trop Pediatr* 2007; 53: 274-277.
6. Cheesbrough M. District laboratory practice in tropical countries, part 2. Cambridge (UK): Cambridge University Press; 2000. p. 218-224.
7. Ikeme ACC, Okeke TC. The relevance of VDRL as routine test in pregnant women: a critical study. *Niger J Clin Pract* 2006; 9: 65-67.
8. Gharoro EP, Abedi HO. Is routine antenatal screening for syphilis useful? *Int J Gynaecol Obstet* 2000; 68: 55-57.
9. Obisesan KA, Ahmed Y. Routine antenatal syphilis screening-a case against. *Afr J Med Med Sci* 1999; 28: 185-187.
10. Imoru M, Kashibu E, Aminu B. Sero-prevalence of syphilis in pregnant women in Kano. *Borno Medical Journal* 2005; 2: 10-12.
11. Idrissa A, Agida ET, Moses AE. Antenatal screening for syphilis. *Nigerian Journal of Surgical Sciences* 1996; 6: 17-18.
12. Morse SA. Advances in diagnostic tests for bacterial STDs. *Salud Publica Mex* 2003; 45 (Supp 5): S698-S708.
13. Sethi S, Sharma K, Dhaliwal LK, Banga SS, Sharma M. Declining trends in syphilis prevalence among antenatal women in northern India: a 10-year analysis from a tertiary healthcare centre. *Sex Transm Infect* 2007; 83: 592.
14. Egglestone SI, Turner AJ. Serological diagnosis of syphilis. PHLS Syphilis Serology Working Group. *Commun Dis Public Health* 2000; 3: 158-162.
15. Chakraborty R, Luck S. Syphilis is on the increase: the implications for child health. *Arch Dis Child* 2008; 93: 105-109.
16. Shakoor Z. Antenatal screening for syphilis at a tertiary care hospital in Riyadh. *Ann Saudi Med* 2004; 24: 262-264.
17. Meheus A. Non-venereal trepanematoses. *Medicine* 2009; 33: 82-84.
18. Wolff T, Shelton E, Sessions C, Miller T. Screening for syphilis infection in pregnant women: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med* 2009; 150: 710-716.
19. Taiwo SS, Adesiji YO, Adekanle DA. Screening for syphilis during pregnancy in Nigeria: a practice that must continue. *Sex Transm Infect* 2007; 83: 357-358.

20. Mofenson LM, Centers for Disease Control and Prevention, U.S. Public Health Service Task Force. U.S. Public Health Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. *MMWR Recomm Rep* 2002; 51: 1-38.

21. Buvé A. Should all pregnant women be screened for syphilis? *Women's Health* 2007; 3: 547-555.

22. Brillman JC, Quenzer RW (eds). Infectious disease in emergency medicine. 2nd ed. Philadelphia (PA): Lippincott-Raven Publishers; 1998. p. 686-692.

23. Centre for disease control and prevention. Sexually transmitted diseases treatment guidelines. *MMWR* 2002; 51: 1-80.

24. The World Bank Group. Nigeria Country Brief. updated March 2009. Accessed 16th September 2009. Available at URL: http://go.worldbank.org/FII0T240KO

25. Bukar M, Audu BM, Yahaya UR, Melah GS. Anaemia in pregnancy at booking in Gombe, North-eastern Nigeria. *J Obstet Gynaecol* 2008; 28: 775-778.

26. Steketee RW, Wirima JJ, Hightower AW, Slutsker L, Heymann DL, Breman JG. The effect of malaria and malaria prevention in pregnancy on offspring birthweight, prematurity, and intrauterine growth retardation in rural Malawi. *Am J Trop Med Hyg* 1996; 55 (Suppl 1); S33-S41.

27. Achidi EA, Kuoh AJ, Minang JT, Ngum B, Achimbom BM, Motaze SC, et al. Malaria infection in pregnancy and its effects on haemoglobin levels in women from a malaria endemic area of Fako Division, South West Province, Cameroon. *J Obstet Gynaecol* 2005; 25: 235-240.

28. Idowu OA, Mafiana CF, Sotiloye D. Traditional birth home attendance and its implications for malaria control during pregnancy in Nigeria. *Trans R Soc Trop Med Hyg* 2008; 102: 679-684.

29. Mohamed K. Iron and folate supplementation in pregnancy (Cochrane Review). In: The Cochrane Library. Issue 1. Oxford (UK): Oxford University Press; 2000.

Illustrations, Figures, Photographs

Four copies of all figures or photographs should be included with the submitted manuscript. Figures submitted electronically should be in JPEG or TIFF format with a 300 dpi minimum resolution and in grayscale or CMYK (not RGB). Printed submissions should be on high-contrast glossy paper, and must be unmounted and untrimmed, with a preferred size between 4 x 5 inches and 5 x 7 inches (10 x 13 cm and 13 x 18 cm). The figure number, name of first author and an arrow indicating "top" should be typed on a gummed label and affixed to the back of each illustration. If arrows are used these should appear in a different color to the background color. Titles and detailed explanations belong in the legends, which should be submitted on a separate sheet, and not on the illustrations themselves. Written informed consent for publication must accompany any photograph in which the subject can be identified. Written copyright permission, from the publishers, must accompany any illustration that has been previously published. Photographs will be accepted at the discretion of the Editorial Board.