Published in final edited form as:

Int J Gynaecol Obstet. 2013 February ; 120(2): 144–147. doi:10.1016/j.ijgo.2012.08.017.

Institutional prevention policies and rates of Group B *Streptococcus* infection among HIV-infected pregnant women and their infants in Latin America

Esaú Joao^{a,*}, Maria I. Gouvea^{a,b}, Laura Freimanis-Hance^c, Rachel A. Cohen^c, Jennifer S. Read^{d,e}, Victor Melo^f, Geraldo Duarte^g, Silvina Ivalo^h, Daisy M. Machadoⁱ, Jose Pilotto^{j,k}, and George K. Siberry^{d,1} for the NISDI/LILAC Protocol

^aServiço de Doenças Infecciosas e Parasitárias, Hospital Federal dos Servidores do Estado Rio de Janeiro, Rio de Janeiro, Brazil

^bInstituto de Pesquisa Clínica Evandro Chagas – IPEC/FIOCRUZ, Rio de Janeiro, Brazil

^cWestat, Rockville, USA

^dPediatric, Adolescent, and Maternal AIDS Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, Bethesda, USA

^eNational Vaccine Program Office/Office of the Assistant Secretary of Health/Office of the Secretary/Department of Health and Human Services, Washington, USA

^fFaculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

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*Corresponding author: Esaú Joao Serviço de Doenças Infecciosas e Parasitárias, Hospital Federal dos Servidores do Estado Rio de Janeiro, Anexo IV 4º Andar Rua Sacadura Cabral, 178 Saude, Rio de Janeiro, CEP 20221-903 Brazil. Tel.: +55 21 22330018; fax: +55 21 22331551. esaujoao@gmail.com.

¹Principal investigators, co-principal investigators, study coordinators, coordinating center representatives, and NICHD staff include: **Argentina: Buenos Aires:** Marcelo H. Losso, Irene Foradori, Alejandro Hakim, Erica Stankievich, Silvina Ivalo (Hospital General de Agudos José María Ramos Mejía); **Brazil: Belo Horizonte:** Jorge A. Pinto, Victor H. Melo, Fabiana Kakehasi, Beatriz M. Andrade (Universidade Federal de Minas Gerais); **Caxias do Sul:** Rosa Dea Sperhacke, Nicole Golin, Sílvia Mariani Costamilan (Universidade de Caxias do Sul/Serviço Municipal de Infectologia); **Nova Iguaçu:** Jose Pilotto, Luis Eduardo Fernandes, Gisely Falco (Hospital Geral Nova de Iguaçu - HIV Family Care Clinic); **Porto Alegre:** Rosa Dea Sperhacke, Breno Riegel Santos, Rita de Cassia Alves Lira (Universidade de Caxias do Sul/Hospital Conceição); Rosa Dea Sperhacke, Mario Ferreira Peixoto, Elizabete Teles (Universidade de Caxias do Sul/Hospital Fêmeina); Regis Kreitchmann, Luis Carlos Ribeiro, Fabrizio Motta, Debora Fernandes Coelho (Irmandade da Santa Casa de Misericórdia de Porto Alegre); **Ribeirão Preto:** Marisa M. Mussi-Pinhata, Geraldo Duarte, Adriana A. Tiraboschi Bárbaro, Conrado Milani Coutinho, Fabiana Rezende Amaral, Anderson Sanches de Melo (Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo); **Rio de Janeiro:** Ricardo Hugo S. Oliveira, Elizabeth S. Machado, Maria C. Chermont Sapia (Instituto de Puericultura e Pediatria Martagão Gesteira); **Esau Custodio Joao**, Leon Claude Sidi, Maria Leticia Santos Cruz, Maria Isabel Gouvêa, Mariza Curto Saavedra, Clarisse Bressan, Fernanda Cavalcanti A. Jundi (Hospital Federal dos Servidores do Estado); **São Paulo:** Regina Celia de Menezes Succì, Prescilla Chow (Escola Paulista de Medicina- Universidade Federal de São Paulo); **Peru: Lima:** Jorge O. Alarcón Villaverde (Instituto de Medicina Tropical “Daniel Alcides Carrion”- Sección de Epidemiología, UNMSM), Carlos Velásquez Vásquez (Instituto Nacional Materno Perinatal), César Gutiérrez Villafuerte (Instituto de Medicina Tropical “Daniel Alcides Carrion”- Sección de Epidemiología, UNMSM); **Data Management and Statistical Center:** Yolanda Bertucci, Rachel Cohen, Laura Freimanis Hance, René Gonin, D. Robert Harris, Roslyn Hennessey, James Korelitz, Margot Krauss, Sue Li, Karen Megazzini, Orlando Ortega, Sharon Sothem de Sanchez, Sonia K. Stoszek, Qilu Yu (Westat, Rockville, MD, USA); **NICHD:** George K. Siberry, Rohan Hazra, Lynne M. Mofenson, Jennifer S. Read, Heather Watts (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland, USA).

Conflict of interest

The authors have no conflicts of interest.

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^gDepartment of Gynecology and Obstetrics, Hospital das Clinicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, São Paulo, Brazil

^hHospital General de Agudos Jose Maria Ramos Mejia, Buenos Aires, Argentina

ⁱEscola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil

^jHIV Family Care Clinic, Hospital Geral Nova de Iguaçu, Nova Iguaçu, Brazil

^kAIDS and Molecular Immunology Laboratory/Instituto Oswaldo Cruz/FIOCRUZ, Rio de Janeiro, Brazil

Abstract

Objective—To describe Group B *Streptococcus* (GBS) prevention policies at 12 Latin American sites participating in the NICHD (Eunice Kennedy Shriver National Institute of Child Health and Human Development) International Site Development Initiative (NISDI) Longitudinal Study in Latin American Countries (LILAC) and to determine rates of rectovaginal colonization and GBS-related disease among HIV-infected pregnant women and their infants.

Methods—Site surveys were used to assess prevention policies and practices administered cross-sectionally during 2010. Data collected in NISDI from 2008 to 2010 regarding HIV-infected pregnant women were used to determine rates of colonization and GBS-related disease.

Results—Of the 9 sites with a GBS prevention policy, 7 performed routine rectovaginal screening for GBS. Of the 401 women included in the NISDI study, 56.9% were at sites that screened. The GBS colonization rate was 8.3% (19/228 women; 95% confidence interval [CI], 5.1%–12.7%). Disease related to GBS occurred in 0.5% of the participants (2/401 women; 95% CI, 0.1%–1.8%); however, no GBS-related disease was reported among the 398 infants (95% CI, 0.0%–0.9%).

Conclusion—Improved efforts to implement prevention policies and continued surveillance for GBS are needed to understand the impact of GBS among HIV-infected pregnant women and their infants in Latin America.

Keywords

Group B *Streptococcus*; Infection rates; Institutional policy; Maternal HIV; Pregnancy

1. Introduction

The incidence of neonatal disease related to infection with Group B *Streptococcus* (GBS) during delivery has markedly decreased in many high-income countries during the past 15 years, mainly as the result of implementation of prevention strategies. In the USA, for example, the incidence of neonatal GBS disease decreased from 1.7 cases per 1000 live births in the early 1990s to 0.34–0.37 cases per 1000 live births in 2003 [1]. Nevertheless, GBS continues to be a key infectious cause of neonatal disease.

Rectovaginal colonization, which is present among 10%–30% of all pregnant women, is implicated in mother-to-child transmission of GBS [1]. Approximately 50% of mothers colonized with GBS transmit the infection to their infants; of those infants who acquire GBS from their mothers, 1%–2% will develop invasive disease [1]. Two newborn syndromes are recognized: early-onset disease and late-onset disease. Early-onset disease occurs before 7 days of life and typically presents as sepsis with or without meningitis. By contrast, late-onset disease occurs 7–90 days after birth and usually presents with bacteremia, meningitis, otitis media, cellulitis, arthritis, endocarditis, or osteomyelitis. Intrapartum antibiotic

prophylaxis (IAP) prevents early-onset disease but has little or no impact on late-onset disease [2].

Rectovaginal colonization with GBS may be more frequent among HIV-infected pregnant women than their counterparts without HIV infection; furthermore, HIV-exposed but uninfected infants seem to be at higher risk of neonatal GBS-related disease than infants of HIV-negative mothers [3–6]. Little information is available, however, regarding institutional policies that aim to address prevention of neonatal GBS infection among infants of HIV-infected pregnant women in Latin American countries. The rates of maternal GBS colonization and GBS-related maternal and neonatal disease are also not well characterized in this population.

The aim of the present study was to describe the neonatal GBS prevention policies and practices at Latin American clinical sites participating in the NICHD (Eunice Kennedy Shriver National Institute of Child Health and Human Development) International Site Development Initiative (NISDI) Longitudinal Study in Latin American Countries (LILAC) and to determine the frequency of maternal rectovaginal GBS colonization and rates of GBS-related disease among HIV-infected pregnant women and their infants.

2. Materials and methods

The NISDI/LILAC protocol has been described in detail previously [7]. Briefly, 12 sites in 3 Latin American countries (Argentina, Brazil, and Peru) enrolled 401 HIV-infected women during pregnancy. Enrollment began in October 2008 and was ongoing, with data used up to December 2010. Eligibility criteria included confirmed HIV infection and prenatal care at an NISDI/LILAC site. Participants were enrolled at any time between a gestational age of 22 weeks and delivery. Study visits occurred during pregnancy (1–2 prepartum visits and 1 visit at delivery, depending upon gestational age at enrollment); at hospital discharge; at 6–12 weeks and 6 months postpartum; and every 6 months thereafter up to a maximum of 5 years. Infants were followed on the same schedule as their mothers, beginning with the delivery visit. At each study visit, current and interim medications, diagnoses (including infection and colonization with GBS), hospitalizations, and laboratory results (including hematology, biochemistry, HIV testing, and flow cytometry) were recorded using standardized case report forms.

For the present analysis, a standardized structured questionnaire was adapted from the Centers for Disease Control and Prevention (CDC) Survey of Hospital Obstetric Program Policies on the Prevention of Neonatal Group B *Streptococcus* Disease [8]. The principal investigator at each of the 12 sites participating in NISDI/LILAC completed the survey. Characteristics assessed included whether or not the institution had a GBS prevention policy; the year in which the GBS prevention policy was established; criteria, timing, and methods for prenatal GBS screening; criteria for the use of IAP, including information about antibiotic susceptibility testing; and modification of GBS prevention policies specifically for HIV-infected patients. Each respondent was also asked to provide the total number of live births and deliveries per year in his or her institution. For the purposes of the present study, a consensus screening-based policy was defined as routine rectovaginal culture for GBS at 35–37 weeks of gestation with IAP administered to all GBS carriers, women with unknown GBS status who delivered a preterm infant, women with GBS bacteriuria in the current pregnancy, and women whose previous infant had GBS-related disease. A consensus risk-based policy was defined as no routine provision of rectovaginal GBS screening, but instead administering IAP to all women with preterm delivery, duration of membrane rupture of at least 18 hours, intrapartum fever, GBS bacteriuria, and whose previous infant had GBS disease. The protocol was approved by the ethical review boards of each clinical site, the

sponsoring institution (NICHHD), the data management and statistics center (Westat), and the Brazilian National Ethics Committee. Informed consent was obtained from all participants.

Data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC, USA). Basic descriptive statistics were used to express the data at both the site and the individual level. Proportions were estimated and exact 95% confidence intervals (CI) were calculated.

3. Results

The characteristics of the neonatal GBS prevention policies and practices at the 12 NISDI/LILAC sites are shown in Table 1. The mean number of live births per year at these sites was 4261 (median, 2641; range, 943–18 371). All 12 centers indicated that they had access to an on-site clinical microbiology laboratory.

In all, 9 of the 12 study sites had GBS prevention policies in place, of which 8 were provided in writing (Table 1). A total of 285 participants (71.0%) were enrolled at a site with a GBS prevention policy. Consensus screening-based policies were used at 6 sites, whereas consensus risk-based policies were used at 2 sites. The remaining site reported the use of a hybrid policy that included routine rectovaginal screening for GBS, while initiation of IAP was based on the presence of intrapartum fever, GBS urinary infection, or previous infant infection with GBS. Policies were developed between 1998 and 2009; 8 sites (88.9%) based their policies on the 2002 CDC guidelines [1] and 1 site (11.1%) based its policy on UK guidelines [9].

Prevention was applied both to the general population of pregnant women and to HIV-infected women at all 9 sites where GBS policies were in place. Training sessions for physicians were provided by 5 (55.6%) sites, while 4 (44.4%) sites monitored provider compliance with the policy (Table 1).

At 7 (77.8%) of the 9 sites, policies specified that the appropriate specimen for GBS screening was a microbiologic culture obtained from swabbing the vagina and rectum (1 or 2 swabs per patient) at 35–37 weeks of gestation. Of the 7 sites where policies provided guidance on the management of women with GBS-positive rectovaginal cultures during pregnancy, 6 sites recommended the use of IAP for all patients with positive test results (Table 1). At the remaining site, IAP was recommended only if an additional risk factor was present.

All 9 policies included recommendations regarding antibiotic choice for IAP (Table 1). The first-line antibiotic for IAP was penicillin or ampicillin at 7 (77.8) and 2 (22.2%) sites, respectively. For patients allergic to penicillin, 8 (88.8%) sites recommended the use of cefazolin (4 sites) or clindamycin (4 sites); 1 (11.1%) site recommended erythromycin.

Of the 401 women enrolled at the 12 clinical sites, 19 (4.7%) had rectovaginal colonization with GBS. All 19 women attended 4 of the 7 sites with a GBS prevention policy in place that included routine screening for the presence of GBS. When limited to the 7 sites with a policy that included routine screening for GBS colonization, the colonization rate was 8.3% (19 of 228 women; 95% CI, 5.1%–12.7%). Urinary tract infection related to GBS was recorded for 2 participants (0.5%; 95% CI, 0.1%–1.8%); both women attended sites with a GBS prevention policy. No cases of GBS-related disease were recorded among the 398 infants (95% CI, 0.0%–0.9%).

Three of the 12 sites in the present study did not have policies directed at preventing neonatal GBS-related disease, resulting in 116 of 401 (28.9%) HIV-infected pregnant women giving birth at an institution where no GBS prevention policy was in place.

Additionally, among all live births recorded in 2009 at the 12 sites surveyed, 118 of 398 (29.6%) infants were born at an institution where no GBS prevention policy was in place. No cases of GBS were reported among the infants in the cohort.

4. Discussion

Most of the Latin American sites participating in the NISDI/LILAC HIV cohort study had specific policies addressing prevention of neonatal GBS-related disease. The rate of rectovaginal colonization reported among HIV-infected pregnant women attending 4 of the 7 sites where GBS screening was routinely performed was only 8.3%. Furthermore, on the basis of data collected from all 12 sites, the rate of maternal GBS-related disease was found to be extremely low (0.5%) in the study cohort, while no cases were reported among their infants.

The GBS colonization rate of 8.3% observed in the present study is lower than the rate of 20%–31% reported in previous studies of HIV-infected pregnant women in Brazil [3,5], though the CIs for the prevalence estimates overlap between the present study and that of El Beitune et al. [3]. Previous studies have shown that GBS colonization rates can vary widely among pregnant women in different settings and that the rates are not consistently higher among HIV-infected women than their non-infected peers [10–12]. In Zimbabwe, the rate of GBS colonization among HIV-infected pregnant women was 37% (35/95), a value not significantly different from the rate of 40% (110/274) reported among women without HIV infection [10]. Similarly, the 32% rate of GBS colonization among HIV-infected pregnant women in the USA was higher than that detected in the present study, but not significantly different from the 26% rate observed among women without HIV infection [11].

A neonatal GBS-related disease rate of 1.55% was reported for a cohort of HIV-infected pregnant women in Europe [4]. If this rate is applied to the present cohort of 398 infants, approximately 6 newborns might be expected to present with GBS-related disease; however, no cases of neonatal GBS-related disease were observed. It seems unlikely that prospective data collection with infant study visits at birth and at 6–12 weeks of age would miss an episode of neonatal GBS-related disease, whether or not the site screened for maternal GBS colonization during pregnancy or at delivery. The low rate of neonatal GBS-related disease, therefore, suggests that the true rate of maternal GBS colonization observed in the present study may be lower than that reported in other studies and not falsely low owing to under-ascertainment of colonization.

Three sites did not have policies directed at preventing neonatal GBS-related disease, resulting in 28.9% of HIV-infected pregnant women delivering at an institution with no GBS prevention policy. Furthermore, 29.6% of infants were born at an institution with no GBS prevention policy. In 2010, GBS-related disease was the foremost cause of early-onset neonatal sepsis in the USA [1,13]. The CDC-reviewed guidelines (endorsed by the American Academy of Pediatrics and published in 2011) recommend that a prevention strategy be focused on universal prenatal screening and the provision of IAP for women with a positive microbiologic culture result and risk factors for GBS [13]. However, some international guidelines still target only high-risk women in their GBS prevention policies [9].

The present study had certain limitations that might have had influenced the point estimate of GBS colonization. Although the prospective data collection methods used in the present study are a major strength, the GBS screening practice and procedures were not dictated by the study protocol. Colonization with GBS might not have been fully ascertained and so the rates could be under-reported.

Since 2008, almost all NISDI/LILAC sites have been following international guidelines as a model for their policies. However, in many countries this practice has not yet been implemented, and in several subsets of the population GBS-related disease still occurs at elevated rates. Improved efforts to implement GBS prevention policies and continued surveillance for GBS-related disease are required to fully appreciate the burden of GBS and the impact of GBS prevention policies among HIV-infected pregnant women and their infants in Latin America.

Acknowledgments

The present work was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Contract # HHSN267200800001C (NICHD Control # N01-HD-8-0001; 2007–2012).

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Synopsis

Consistent prenatal screening policies are required in Latin America to understand the impact of Group B *Streptococcus* infection on HIV-positive pregnant women and their infants.

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Table 1

Characteristics of Group B *Streptococcus* disease prevention policies and practices at 12 NISDI/LILAC sites in Latin America^a

Characteristic	Subgroup	Distribution
GBS prevention policy in place	Yes	9 (75.0)
	No	3 (25.0)
Among sites with a GBS policy (n=9)		
Written GBS policy in place	Yes	8 (88.9)
	No	1 (11.1)
Type of policy	Screening-based	6 (66.7)
	Risk-based	2 (22.2)
	Other	1 (11.1) ^b
Physician training sessions part of the policy	Yes	5 (62.5)
	No	3 (37.5)
	Unknown ^c	1
Among sites with physician training as part of the policy (n=5)		
Institutional monitoring of provider compliance with the policy	Yes	4 (80.0)
	No	1 (20.0)
Among sites performing routine GBS screening by microbiologic culture (n=7)		
Management of women testing positive for rectovaginal GBS during pregnancy with IV antibiotics in labor	Yes	6 (85.7)
	No	1 (14.3) ^d
Among sites with a GBS policy (n=9)		
Penicillin class used as the first-line antibiotic	Yes	9 (100.0) ^e
	No	0 (0.0)

Abbreviations: GBS, Group B *Streptococcus*; IV, intravenous; NA, not applicable; NISDI/LILAC, Eunice Kennedy Shriver National Institute of Child Health and Human Development International Site Development Initiative/Longitudinal Study in Latin American Countries.

^aValues are given as number (percentage).

^bThis site performed GBS screening but based the use of intrapartum antibiotic prophylaxis on intrapartum fever, GBS urinary infection, or previous infant infection with GBS.

^cNot included in the percentage calculation.

^dIntravenous antibiotics used only if an additional risk factor was present.

^eAmpicillin or penicillin.