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Group B streptococcus and pregnancy : towards an optimal prevention strategy for neonatal Group B Streptococcal Disease

Valkenburg-van den Berg, A.W.

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Author: Valkenburg-van den Berg, Arijaantje Willemijntje (Arijaan)

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Chapter 2

Prevalence of colonization with Group B Streptococci in pregnant women of a multi-ethnic population in the Netherlands

2

Arijaan W. Valkenburg-van den Berg
Arwen J. Sprij
Paul M. Oostvogel
Johan A.E.M. Mutsaers
Wouter B. Renes
Frits R. Rosendaal
P. Joep Dörr

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ABSTRACT

Objective This study was performed to determine the prevalence of GBS and to identify GBS colonization risk factors in a multicultural population of pregnant women in the Netherlands. We calculated predictive values of cultures in pregnancy for intrapartum GBS carriage.

Study Design From a total of 1702 women visiting several antenatal outpatient departments, rectovaginal swabs were collected at 35-37 weeks' gestation. In 761 women swabs were repeated at time of delivery. Carriage of GBS late in third trimester and at time of delivery was analysed in relation to age, parity, ethnicity and socio-economic status.

Results Twenty-one percent was GBS carrier late in pregnancy. Compared to Europeans, African women were at a higher risk (29%) and Asian women were at lower risk (13%) for GBS carriage. No differences in colonization were found between women with respect to age, parity or socio-economic background. Positive predictive value of GBS carriage at 35-37 weeks' gestation for carriage at time of parturition was 79% and negative predictive value was 93%.

Conclusions It is impossible to identify a group of pregnant women at high risk for GBS colonization. Predictive values of antenatal genital group B streptococci cultures at 35-37 weeks' gestation for intrapartum GBS carriage are lower than previously reported.

INTRODUCTION

Since the 1970s, Group B Streptococcus (GBS, *Streptococcus agalactiae*) has been recognized as the most important infectious cause of morbidity and mortality in newborn infants. Despite the decrease in mortality during the last decades, early-onset GBS disease remains a serious neonatal condition, which may cause severe neurological damage. In the Netherlands, the incidence of early-onset GBS disease in 1997-1998 was estimated at 1.9 per 1000 live births, with a case fatality rate of 5%(1). GBS transmission is vertical from mother to child. The gastrointestinal tract is the source of vaginal GBS colonization and many adults are colonized with GBS without showing symptoms. Approximately 10%-30% of women of childbearing age carries GBS in the rectovaginal compartment(2-4). The prevalence may vary due to differences in the culture technique, the location and number of sites cultured and the population studied(2). A role for ethnic or genetic factors is presumed, since Caribbean Hispanics and black women were reported to be GBS carriers more frequently(2;5;6).

Dutch data originate from studies by Gerards in 1985 and Adriaanse in 1995, in which overall carrier rates of 14% in the 16-20th week of pregnancy(7) and 20% at delivery(8) have been described.

In the United States, revised consensus guidelines regarding the management of GBS were published in 2002. These guidelines recommend screening of all pregnant women for GBS carriage at 35 to 37 weeks' gestation and intrapartum treatment of those women with positive cultures(9).

The Dutch Society of Obstetrics and Gynaecology and the Dutch Society of Pediatrics(10) recommend intrapartum maternal administration of antibiotics in women with intrapartum temperature > 38°C, in women with GBS bacteriuria during current pregnancy and in women who previously gave birth to an infant with early-onset GBS disease, irrespective to their GBS status. In women presenting with any of the other risk factors associated with early onset GBS disease, i.e. delivery at <37 weeks' gestation or rupture of membranes for more than 24 hrs, screening for GBS carriage is performed first, followed by chemoprophylaxis when the culture is positive. In case the delivery occurs before the result is available, the obstetrician should decide about antibiotic prophylaxis, based on the severity of the risk factor(11). The choice for this risk factor-based strategy was made in 1998, with the intention to reduce the number of women that receives prophylactic antibiotics(11), taking account of the Dutch organisation of obstetrical care with approximately 30% home deliveries. The disadvantages of this strategy are, that 30%-40% of neonatal early-onset GBS infections may occur in the absence of risk factors(1) and that in most cases delivery occurs before culture results are available.

The best preventive strategy maximises treatment in women who need it, and minimises treatment in women who do not need it. To be able to optimise the strategy it is essential to know the prevalence of GBS colonization of pregnant women in the Netherlands, which

may have changed due to recent changes in demographics, in particular with regard to ethnic background of women living in major cities. The aim of this study was to ascertain GBS carrier-rate late in pregnancy in a multicultural, urban population in the Netherlands, to find out if a group of high risk for GBS colonization could be identified and to calculate positive and negative predictive values for intrapartum carriage, based on results of the cultures at 35-37 weeks' gestation.

METHODS

In The Hague, approximately 8000 deliveries take place annually. Almost all hospitals and a part of midwifery practices joined this study. Between July 2000 and December 2002, physicians and midwives at their discretion non-selectively asked women at 35-37 weeks of pregnancy to participate in the study. All these women attended either the outpatient department of obstetrics and gynaecology at the Medisch Centrum Haaglanden, the Leyenburg Hospital, the Rode Kruis Hospital or one of the six participating midwifery practices in The Hague, the Netherlands.

After informed consent, the physician or midwife collected a rectovaginal swab for GBS culture by initially swabbing the vaginal introitus and thereafter the rectum (through the anal sphincter). Swabs were placed in a transport medium (Amies transport medium with charcoal) and sent to one of the participating laboratories. Inoculation took place at 35-37°C for 18-24 hours into a selective broth medium (Todd-Hewitt supplemented with gentamycin (8 micrograms/ml) and nalidixid acid (15 micrograms/ml)). The broth was subcultured onto a blood agar under anaerobic circumstances and GBS suspected colonies were then Gram-stained. A catalase reaction was performed for all Gram-positive cocci. On all catalase negative colonies, a streptococcus grouping latex agglutination test (PathoDx group B, Diagnostic Products Corporation, Los Angeles, USA) was performed to identify GBS. The results were reported to the participating antenatal clinics and midwifery practices. Colonized women received intrapartum antibiotics only when one or more of the risk factors associated with early onset GBS disease was present. The initial intention was to repeat GBS cultures during labour in all GBS positive women and in 400 of GBS negative women.

All women were asked to complete a questionnaire about ethnic, demographic and socio-economic factors and obstetric details. Age, parity, postal code and the country of birth of both the woman and her parents were registered. The participants were grouped into different demographic and socio-economic categories by using the classification systems of the Municipal Information Centre of The Hague and the Central Commission for Statistics in the Netherlands (Statistics Netherlands/CBS) and into different ethnic categories by using publications published by the Ministry of the Interior and Kingdom Relations (BZK) and information acquired from the United Nations. The country of birth was used to classify the

women into ethnic groups according to the Dutch standard identification method(12). These ethnic groups are Class A: Born in the Netherlands or coming from one of the developed countries; Class B: Coming from any less developed country (Table 2B).

A protocol was formulated to screen 2100 women from The Hague, classified into different ethnic and socio-economic groups:

Group 1: Class A and living in the inner city (lower socio-economic group),

Group 2: Class B and living in the inner city,

Group 3: Class A and living in the suburbs (higher socio-economic group) and

Group 4: Class B and living in the suburbs.

Although we initially planned to include 2100 women, we found that after 2 years and 5 months 1700 women were included, and that no additional information would be gained by continuation of the inclusion period.

We estimated the prevalence of positive cultures as the proportion of positive testing women over all women, with 95%-confidence intervals based on a binomial distribution. These calculations were performed for various subgroups, and prevalences were compared by calculating relative risks (prevalence ratios), with 95%-confidence intervals based on a Poisson distribution of the positive tests.

Positive and negative predictive values for intrapartum carriage, based on the results of the cultures collected at 35-37 weeks pregnancy, were calculated.

The medical ethics committees of the participating hospitals approved the protocol for this study.

RESULTS

During the study period, a total of 1702 pregnant women were enrolled. Mean age was 30.5 years, median was 31 years (range 14 to 45 years). Four hundred and sixty-six women were primigravida and 1225 women were multigravida, while data about parity were missing in 11 cases. Six hundred and ninety-two women were Dutch and had parents who were both born in the Netherlands, the remaining women had at least one parent born in a foreign country or were born in another country themselves. The ethnic origin of 53 women was unknown. Of the 1702 women, 365 (21%) had positive cultures for Group B Streptococcus at 35-37 weeks of gestation. There was no relationship between colonization and age, parity or miscarriages (Table 1). Table 2 shows the breakdown of women by classification in group A or B, living in the inner city or the suburbs and the percentage of GBS carriage found per group. The prevalence of GBS carriage in Classes A and B were identical: 21%. We then analysed whether the place where women lived (inner city or the suburbs) affected the prevalence of GBS colonization. Of the 1702 women, 657 lived in the inner city and 1032

Table 1 Age, parity, history of abortions and GBS culture results

Age	N	% GBS positive	95% CI
< 20	41	32	0.18-0.46
20-29	663	17	0.14-0.20
30-39	905	24	0.21-0.27
>= 40	92	25	0.16-0.34
Unknown	1	100	
Parity			
0	663	21	0.18-0.24
1	645	19	0.16-0.22
2	232	29	0.23-0.35
3 or more	181	22	0.16-0.28
Unknown	11	18	
History of Abortions			
0	1163	21	0.20-0.21
1 or 2	470	22	0.18-0.26
3 or more	58	22	0.11-0.33
Unknown	11	18	

Table 2A GBS carrier rates according to origin and where people lived in The Hague (The Netherlands)

		Rate	%	95% CI
Class A	Inner City	29/174	17	0.11-0.23
	Suburb	129/569	23	0.19-0.26
	Unknown	1/2		
	Total	159/745	21	0.18-0.24
Class B	Inner City	104/471	22	0.18-0.26
	Suburb	88/427	21	0.17-0.25
	Unknown	2/6		
	Total	194/904	21	0.18-0.24
Unknown	Inner City	1/12		
	Suburb	8/36		
	Unknown	3/5		
	Total	12/53		
Total	Inner City	134/657	20	0.17-0.23
	Suburb	225/1032	22	0.19-0.23
	Unknown	6/13		
	Total	365/1702	21	0.19-0.23

Table 2B Classification in Class A or B according to country of birth

	Country
Class A	Netherlands, Belgium, Canada, Denmark, Germany, Finland, France, Greenland, United Kingdom, Ireland, Iceland, Israel, Japan, Channel Islands, Liechtenstein, Luxembourg, Monaco, Dutch East Indies, Dutch Newguinea, Newfoundland, New-Zealand, Norway, Austria, United States of America, Sweden, Switzerland.
Class B	All other countries
Class A:	Women of Dutch origin or coming from one of the developed countries
Class B:	women coming from one of the other countries

lived in the suburbs. Prevalence in these groups was 20% and 22%, respectively. The place of residence of 13 women was unknown.

Participating women originated from 72 different countries. When using United Nations world region classifications to cluster these countries, differences in GBS carriage between the women of these various countries of birth become apparent. (Table 3). In women originating from countries in Europe and Latin America we found a colonization rate of 21% compared to colonization rates of 29% in African women and 13% in Asian women. Women born in Africa had an increased risk for colonization compared with European women (RR 1.4, CI 1.1 – 1.7), whereas Asian women had a reduced risk for GBS carriage compared to European women (RR 0.6, CI 0.4 - 0.8). In 173 of the 365 GBS positive women and in 588 of the 1337 GBS negative women, cultures were repeated at delivery. In 174 (23%) of these 761 women, cultures were positive at this time.

Table 4 shows the proportion of women with positive and negative intrapartum cultures in relation to the results of the first swab taken between 35 - 37 weeks' pregnancy. Of all the pairs of cultures, 136 of 173 women who were positive at 35-37 weeks gestation were also positive at delivery (Positive Predictive Value 79%) and 550 of 588 women who were initially negative, remained negative at delivery (Negative Predictive Value 93%). Thirty-eight women acquired GBS in the last weeks of pregnancy, whereas cultures in 37 previously positive women were negative at delivery.

COMMENT

In this study we show that in the multicultural, urban population of pregnant women in The Hague, the Netherlands, the GBS carrier rate is 21%. We showed differences between colonized and non-colonized women in ethnicity, but we could not demonstrate differences between colonized and non-colonized women with respect to age, parity or socio-economic background. Positive predictive value of GBS carriage at 35-37 weeks' gestation for carriage at time of parturition was 79% and negative predictive value was 93%.

Table 3 World regions and GBS culture results

Continent of Native Country	N	% GBS positive	95% CI
Africa	240	29	0.23-0.35
Asia	256	13	0.09-0.17
Latin America	245	22	0.17-0.27
Europe	907	21	0.18-0.24
Other	10	30	0.015-0.58
Unknown	44	27	0.14-0.40
Total	1702	27	

Table 4 Cultures at 35-37 weeks' gestation compared to intrapartum cultures*

Culture at 35-37 weeks	Intrapartum Positive	Intrapartum Negative	Total
Positive	136	37	173
Negative	38	550	588
Total	174	587	761

* In 761 of 1702 cases intrapartum GBS cultures were performed
PPV was 79%, NPV was 93%

Table 5 Studies with Rectovaginal GBS cultures on selective broth medium in third trimester of pregnancy

Author	Year	Country	N	Prevalence GBS
Dillon et al	1982	United States	754	28%
Easmon et al	1985	United Kingdom	895	19.8%
Sunna et al	1991	Jordan	500	30.4%
Yancey et al	1996	United States	826	26.5%
Grimwood et al	2002	New Zealand	240	22%
This study	2003	The Netherlands	1702	21%

The large number of women in our study distinguishes this study from other GBS prevalence studies. Table 5 presents other studies in which pregnant women were cultured rectovaginal at about 35-37 weeks' gestation with the use of selective broth media.

In previous studies, GBS carriage prevalences between 1,6% and 30,4% have been described(2-5;7;8;13-26). The differences in these prevalences can probably be explained by the different gestational ages at culturing, differences in culture site and in the use of different culture techniques.

Characteristics of the population studied can also explain differences in prevalence rates. Women of Caribbean origin and black women were previously reported to be at greater risk of colonization than those of Mexican origin and white women(2;5;6), which suggests a role for ethnic or genetic factors. However, other small studies(27-29) have reported no differences in group B streptococcal prevalence between any ethnic groups. The women in our study originated from 72 different countries. Differences were found in the prevalence rates between European, Asian and African women. These results are in accordance with the findings of others(2;5;6).

Differences in GBS carriage rates may also be explained by differences in the socio-economic status of the study group. A study in New Zealand women showed an increased risk for GBS carriage in the socially advantaged(3), whereas Regan et al(2) found GBS was less common among women with a higher education. In our study, we registered postal codes and related socio-economic status to the neighbourhood. Even when calculating prevalences for the poor and wealthy neighbourhoods separately and using different levels of income, we could not find any relation between socio-economic status and GBS carriage. An explanation for this might be that in our population the higher income group was quite small compared to the other groups.

Numerous studies have documented that the accuracy of prenatal screening cultures in identifying intrapartum colonization status can be enhanced by careful attention to the timing of cultures, the anatomic sites swabbed and the laboratory procedures used for culture and detection of the organisms(9). Swabbing both the lower vagina and the rectum (through the anal sphincter) substantially increases the yield compared with sampling only the cervix or sampling the vagina without swabbing the rectum(30). Isolation rates will be increased by approximately 10%-15% if the lower genital and anorectal areas are sampled rather than only the upper vagina and cervix(31).

Yow(14), Kubota(23) and others(15;25) performed only vaginal or cervicovaginal swabs and found prevalences between 6% and 14.2%, whereas rectovaginal cultures done in several other studies(3;8;16;21;24;26) revealed higher rates between 19.4% and 31%, similar to the 21% found in our study.

Since vaginal and in particular rectal flora contains numerous micro-organisms, the use of selective enrichment broth is recommended to maximise the isolation of GBS and to avoid the overgrowth of other organisms. When direct agar plating is used instead of selective enrichment broth, as many as 50% of woman who are GBS carriers have false-negative culture results(32). Ferrieri(13) and Kubota(23) did not use selective culture medium and only found prevalence rates of 5.6% and 11.4% respectively, whereas studies that used selective medium reported rates of 19.8%(16) and 18.6%(2).

Discordant results are reported regarding the effects of age and parity on GBS prevalence(5;14;27;28;33;34). In various studies(27;29;35;36) no significant differences in colonization rates were noted on the basis of age or parity, but increasing age(5) and parity(5;14) have also sometimes been associated with lower rates of carriage. However, Regan(2) described GBS carriage as being more common among older women and women of lower parity. In our study we found no association between colonization and age or parity.

Although the importance of infection as a cause of preterm delivery is gaining recognition, little is known about the role of GBS infection in miscarriages. McDonald et al.(37) stated that GBS was a key pathogen in unsuspected intrauterine infections underlying spontaneous midgestation abortions. The study of Daugaard(38) demonstrated an association between the occurrence of group B streptococci in the urine and cervix and late spontaneous abortions, but El Kersh et al.(24) found no correlation with a history of repeated spontaneous miscarriages. We did not find any relation between women who had a history of miscarriages and GBS carriage, but at this point our population is selected since we only screened almost term pregnant women.

Collection of cultures between 35 and 37 weeks' gestation is recommended to improve the sensitivity and specificity of the identification of women who are colonized at the time of delivery(4;31).

Serial cultures done in antenatal patients suggest that women may be intermittent carriers of Group B streptococci and demonstrate that concordance with intrapartum culture status improves as the interval between antenatal cultures and delivery is shortened(4). Yancey et al(4) found in a population with 26,5% carriage a positive predictive value of 87% and a negative predictive value of 96%, when cultures were done within six weeks before delivery. To improve the accuracy of antenatal cultures, the Centres for Disease Control and Prevention has suggested that the collection of these cultures should occur at 35-37 weeks' gestation instead of earlier in pregnancy(39). In our study we cultured 761 women again on admission for delivery and then calculated the positive and negative predictive values of the first culture for carriage during labour. The intention to reculture all GBS positive women and 400 of GBS negative women during labour was not fulfilled, probably because of hectic in the labourrooms and lack of attention to the studyprotocol.

The PPV of 79% and the NPV of 93% in our study is low compared to other studies and probably would have been higher if we recultured all initially GBS positive women during labour. Both our results and the somewhat higher but still low predictive values of others underline the need for rapid tests to detect GBS colonization status. These bedside-tests might obviate the need for antenatal culture based screening if their sensitivity and specificity are comparable to culture in selective broth media and they yield results rapidly enough to permit the administration of adequate intrapartum antibiotic prophylaxis to women detected as carriers(9). Thus far, these tests have not been reliable enough to be used as an alternative to rectovaginal cultures.

In the USA, the screening based strategy is recommended since 2002(9). This recommendation is based on data found in a recent study of comparison of screening based and risk factor based strategies. The conclusion of this study was that the screening based strategy was over 50% more effective than the risk-factor based strategy(40). Management strategy depends on local factors like the percentage of GBS carriers and the percentage of pregnant women with perinatal risk-factors within the population, the organisation of perinatal care and the local availability of laboratory facilities.

The choice for a preventive strategy should be based on rationality, cost-effectiveness and the current knowledge and possibilities(11). Since the GBS prevalence found in our Dutch study population is more or less similar to prevalences in the USA, the present Dutch recommended risk factor based strategy for GBS disease prevention should be reconsidered.

We show that it is not possible to identify a group of pregnant women at high risk for GBS colonization with regard to age, parity or socio-economic factors. There are ethnic differences between colonized and noncolonized women. We demonstrated that positive and negative predictive values of antenatal genital group B streptococci cultures at 35-37 weeks' gestation for intrapartum GBS carriage are lower than previously reported.

Results of this study can be useful in the process of finding the best preventive strategy for neonatal GBS-disease in the Netherlands.

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