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The influence of Group B streptococcal-carriership on pregnancy outcome

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1 Introduction

Group B streptococci (GBS) acquisition during the neonatal period may result in the devasting "early onset" or the "late onset" type of GBS disease. The major source of colonization and infection of the newborn infant is the mother, although some authors demonstrated the importance of the nursery environment too [1, 10].

The most important moment of transmission from the mother to the newborn seems to be the time of delivery, when the newborn passes through the birth canal. It has been shown that cervix, vagina, rectum and urethra are important reservoirs of GBS in pregnant women [3, 6, 11]. Maternal factors influencing the transmission of GBS to the newborn are persistent carriership [11], the heaviness and the number of sites of colonization [2, 11]. Other factors such as sex, race, length of gestation and birth weight of infants do not seem to influence the acquisition of GBS [1, 5, 6]. Prolonged rupture of membranes and low birth weight were found more frequently among neonates developing GBS disease than in those who did not [6, 10].

Reports on the risk of asymptomatic maternal carriership for the newborn and its influence on pregnancy outcome are lacking as far as we know. So it is also not clear if there is a relationship between specific obstetric factors of carriers, serotype distribution and transmission frequency to the newborn.

Therefore we investigated in a prospective study the influence of GBS carriership during pregnancy on the overall pregnancy outcome and tried to relate the risk of transmission to maternal/obstritrical factors. Neonatal colonization was followed during the first week of life. To establish the importance of the occurrence of certain GBS serotypes, specifically related to GBS disease (type III [7, 10]), we studied the serotype distribution among mothers and their infants.

Curriculum vitae

LEON JOSEPH GERARDS *was born in Maastricht in 1939. He studied medicine at the University of Utrecht and obtained his medical degree in 1970. He qualified in pediatrics at the Wilhelmina Children's Hospital, Utrecht from 1970 to 1974 and subsequently specialized as a neonatologist. Since 1976 he works as a staff-member of the Dept. of Neonatology, Wilhelmina Children's Hospital and has focused his main interests to perinatal infections with special attention to vertically transmitted disease-entities (hepatitis-B, GBS disease).*

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2 Material and methods

During the study period from February 12, untill July 23, 1980 762 pregnant women attending the obstetric service of the University Hospital (head Prof. Dr. A. A. HASPELS) were examined for GBS carriage before the 20th week of gestation by taking culture swabs from the vagina, cervix and rectum. Sixty four initially positive and seventy nine initially negative women were followed during pregnancy. Cultures were taken from the throat, nose, vagina, cervix, rectum and urine on the 28th, 34th week of gestation and during delivery.

Carriers of GBS were defined permanent positive when cultures of vagina, cervix or rectum were three or more times positive, intermittent positive when they were two times positive and transient positive when they were one time positive during pregnancy. Within six hours after birth and at time of discharge from the hospital (usually the seventh day of life) cultures were taken from the skin, throat, external ear canals and the umbilicus of the newborns. Meconium and/or feces was cultured if available. Specimens were inoculated on a 5% sheepsblood agar plate and placed into 5 ml selective broth medium of Pike. After incubation during 18 hours at 37 °C subcultures were made on the same blood agar plates. GBS were isolated, grouped and typed serologically by the capillary precipitin method; grouping sera were commercially obtained, typing sera were kindly provided by Dr. B. ENGEL from the National Institute of Health (RIV), The Netherlands.

Race, age, number of pregnancies and previous labors, obstetrical factors and carrierstate of positive and negative women were recorded. Additionally the serotype distribution of positive mothers and their children was determined. The overall pregnancy outcome was documented by the following items: Signs of fetal distress (a CTG showing signs of fetal distress [9] and/or fresh meconium staining of amniotic fluid in non breech presentations and/or abnormal values of microblood pH), APGAR-scores at 1 and 5 minutes, the number of prematures and Small for Gestational Age (S.G.A.) babies [12] and the number of vacuum, forcipal and Cesarian section deliveries.

3 Results

3.1 Maternal data and carrierstate

The overall carrier rate of the women screened before the 20th week of pregnancy was 13.9%. One hundred and sixty one women were involved in the follow-up; 64 of them were initially positive, 97 initially negative. During pregnancy 41 women appeared to be permanent carriers, 14 intermittent and 23 transient. A total of 83 women was permanent negative. Seventeen (22%) of the positive women and 33 (40%) of the negative women were of non-caucasian origin.

The age-distribution presented in Tab. I, showed no differences between the two groups. Carriership was found mainly among women between 20 and 30 year of age (73%). A small percentage was younger than 20 year or older than 35 years of age. The number of pregnancies and previous labors was equal in both groups.

Tab. I. Age distribution of positive and negative women.

Age in years	Positive women	Negative women
	n %	n %
< 20	2 (3)	12 (14)
20–24	28 (36)	33 (40)
25–29	29 (37)	24 (29)
30–34	13 (17)	9 (11)
⩾ 35	6 (7)	5 (9)
Total	78	83

3.2 Transmission of GBS to the newborn and neonatal colonization

The transmission frequency to the newborn was directly related to the maternal carrier state (Tab. II). It was the highest among permanent positive mothers (63.4%). Only three infants born to intermittent positive and another three infants born to transient positive mothers acquired GBS whereas one child was colonized which mother was negative.

After one week another six newborns previously negative carried GBS resulting in a total of 39 positive mother-infant pairs.

Tab. II. Newborn colonization rate in relation to their mothers carrier state.

Mothers			Positive infants	
Carrier state		Number	At birth	At discharge
Permanent	+	41	26 (63,4)	17 (41,5)
Intermittent	+	14	3 (21,4)	5 (35,7)
Transient	+	23	3 (13,0)	3 (13,0)
Permanent	–	83	1 (1,2)	3 (3,6)

The transmission frequency was not related to the time of rupture of membranes. Among the positive women 46 had ruptured membranes $\leqslant$ 6 hours with 18 positive infants (39%) and 22 had ruptured membranes $>$ 6 hours with 8 positive infants (36%). No information was obtained from ten women.

The numbers of neonatal sites colonized are presented in Fig. 1. The skin and ear canals were most frequently positive at birth, whereas after one week GBS were mainly isolated from the umbilicus. A number of children had more than one site positive. At birth 13 infants had one site positive, 9 had two sites and 11 had three or more sites positive. After one week 13 infants had one site positive, 9 had two sites and only 1 had three sites positive.

The heaviness of colonization varied. At birth 12% of the newborns were heavily colonized and 88% lightly; after one week 39% of the positive infants had high colony counts, 7% were moderately colonized and 53% lightly.

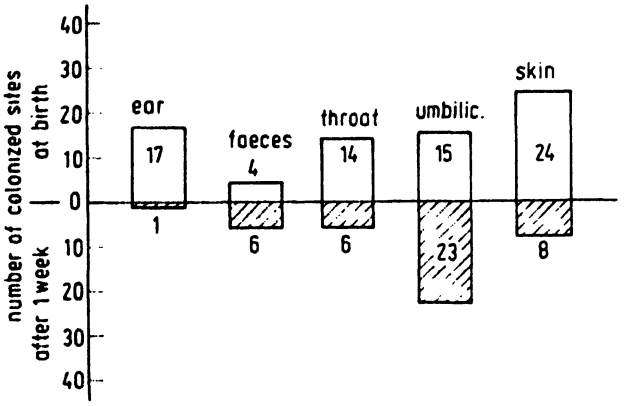

Fig. 1. Newborn GBS colonization sites at birth and after one week.

3.3 Pregnancy outcome

Several parameters to document the neonatal outcome were related to the maternal carrier state (Tab. III). The mean birth weight, mean gestational age, mean APGAR-scores were found to be the same in both groups. Also the numbers of vacuum, forcipal and Cesarian section deliveries

Tab. III. Perinatal characteristics of children born to GBS positive and negative mothers. S.G.A. = small for gestational age, V.E. = vacuum-extraction, F.E. = forcipal-extraction, S.C. = sectio cesarea.

	Children born to GBS + mothers	Children born to GBS – mothers	
Number	78	83	
♂:♀	33:45	46:37	
Mean birth weight (and range) in grams	3300 (1820–4740)	3215 (2100–4270)	
Fetal distress	24	7	$p < 0.003$
Mean APGAR-score 1′	8.1 (2–10)	8.6 (4–10)	n.s.
5′	9.6 (6–10)	9.7 (7–10)	n.s.
Premature	7	12	n.s.
S.G.A.	11	8	n.s.
VE/FE/SC	13	7	* n.s. ($p = 0.15$)

* square

did not differ in both groups. The number of children small for gestational age born to positive mothers [11] was not significantly higher than the number of S.G.A.-children born to negative mothers. However, most of these children were born to permanent positive mothers [7] and comparing this number with that of the permanent negative mothers, the difference was significant ($p \leqslant 0.003$).

The number of infants with fetal distress was significantly higher among those born to positive mothers than those born to negative mothers. It was noted however that mean birth weight, mean gestational age, APGAR-scores, number of SGA children and prematures, number of children with fetal distress were not influenced by GBS acquisition.

None of the newborns colonized developed any form of neonatal GBS disease.

3.4 Serotype distribution

The distribution of serotypes among the positive women (caucasian and non-caucasian) is shown in Tab. IV. Serotype III was significantly more isolated from non-caucasian than from caucasian women ($0.01 \leqslant p \leqslant 0.02$). The mean transmission frequency of all serotypes was 46% (range 40 –52%), except for type IIc, which was 22%.

Tab. IV. GBS serotype distribution of positive women (%).

		Types						
Women (No)		Ia	Ib	Ic	IIc	II	III	NT
Caucasian	(55)	2	38	27	11	14	20	7
Non-caucasian	(23)	0	30	13	4	13	48	4

The distribution of serotypes among the mother-infant pairs is shown in Fig. 2. As in the whole group studied, types Ib, III and Ic were most frequently encountered both in mother and children.

The serotypes isolated from the children were identical with those isolated from their own mothers, except in two cases, where once type IIc and once type Ib was isolated from the infants and not from the mothers. None of the serotypes was specifically related to fetal distress or smallness for gestational age.

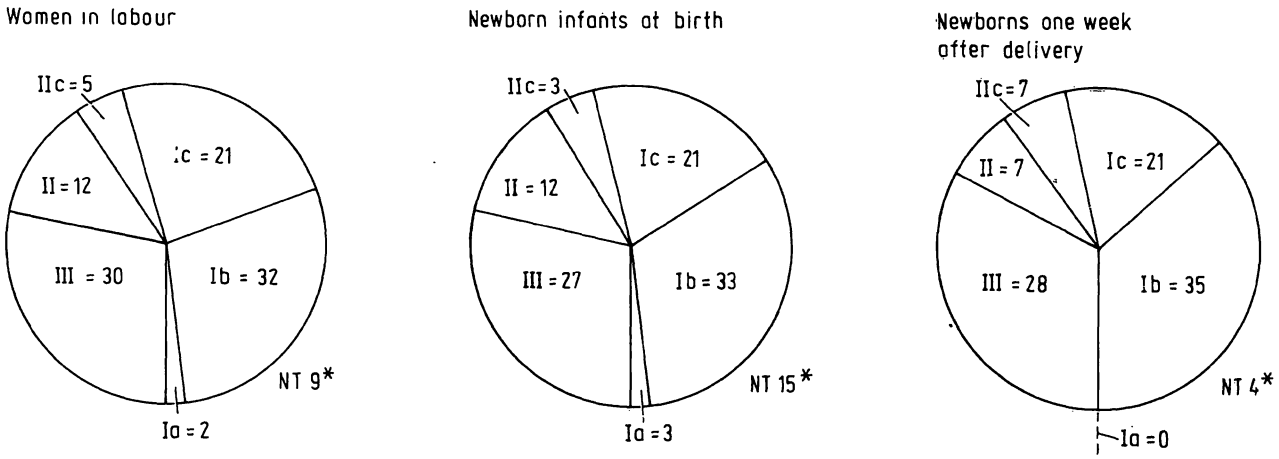

Fig. 2. GBS serotype distribution (%) from woman in labor, newborn infants at birth and after one week; * not typable GBS.

4 Discussion

The overall carrier rate of 13.9% of GBS in a population of pregnant women is rather high. Most workers have recorded carrier rates ranging from 5.6% [8] to 8% [2] and 12% [13]. These differences may be explained by geographic variations, different culture techniques and the number of sites cultured.

Our longitudinal study showed that 75% of all women positive before the 20th week of preg-

nancy appeared to be permanent (59%) and intermittent carriers (16%). This percentage is much higher than that of ANTHONY et al. [4] who found 36% permanent and 15% intermittent carriers. This implies that carriership is a rather constant phenomenon and this may account for the difficulty to eradicate carriage in women and their infants.

We did not observe any relationship between carriership and race in contrast to ABER et al. [1], who found non-caucasian women more frequently positive. The only difference between caucasian and non-caucasian women was the predominance of serotype III found among the non-caucasian women.

The age-distribution of culture positive and negative women was similar. The mean age of the positive and negative women was similar. The mean age of the positive women was 27.2 years (for the permanent positive 26.4 years of age); this is older than the mean ages given by ABER et al. (21.7 years) [1] and BAKER (21 years) [5]. The last mentioned an enhanced colonization rate below the age of < 21 years in contrast to our finding of a very low carrier rate in the youngest age group. A low carrier rate below the age of 21 years might be based on a different sexual behaviour, because sexual intercourse is an important factor related to acquisition and transmission of GBS [5].

Also the carrier rate over an age of > 35 years is low, suggesting an age-related development of immunological responses.

Persistent carriage was a very important determinant for transmission, not only resulting in the highest transmission frequency during delivery, but also influencing the colonization rate of the newborns in the first week. This remained high (41.5%) among permanent carriers in comparison with the other carriers. Prolonged rupture of membranes and prematurity could not be related to a higher colonization rate of the newborns born to positive mothers. Although these newborns are supposed to be at higher risk for infection and their colonization rate was high in our study, none of them developed GBS related disease.

Other determinants of pregnancy outcome such as gestational age, birth weight and the APGAR-scores were equal in both children-groups and therefor do not seem to be influenced by maternal carriership which is in accordance with other authors findings [1, 6].

The number of artificial deliveries tended to be higher among the positive mothers, but this was not significant. The same was observed for SGA-children born to positive mothers. The number of children with fetal distress born to positive mothers was significantly higher than those born to negative mothers, which may be related to the earlier mentioned number of SGA-children born to permanently positive women. It is not easily understandable that asymptomatic maternal carriership of GBS can be responsible for a worse pregnancy outcome in this way, unless it must be assumed that GBS carriership must be interpreted as an asymptomatic infection which can be harmfull to the infant in utero. Support for this hypothesis may be the immunological response among asymptomatic carriers resulting in an elimination from the genital tract at increasing age, a phenomenon not observed in purely commensal bacteria.

Immediately after birth the skin and the ear canals were mostly positive, conform the observations of others [8]. After one week the umbilicus was the most important culture site. Apparently GBS were eliminated from the normal intact skin and mucous membranes and maintenance on the umbilicus may be considered a wound-contamination or infection. The colonized umbilicus may be an important portal of entry and a primary focus of infection, easily resulting in bacteriemia and dissemination to other organs.

All serotypes were transmitted in the same frequency, except type IIc. Serotypes Ib and III were the most prevalent among both mothers and children. There was a complete concordance for identical serotypes from mothers and their infants in 37 pairs (86%). Therefore vertical transmission is the most important mode for GBS colonization of the infant.

Two children had serotypes not isolated from their mothers and another four children were born to negative mothers. These children may be colonized by nosocomial transmission (14%). The types involved were Ib (2 X), Ib (1 X), II (1 X), III (1 X) and a non-typable strain. So we have no support

for the view that nosocomial transmission is an important factor for infant colonization [1], neither could we confirm the finding that especially type III should be involved in that way of transmission [10].

Based on the findings described above we speculate that screening for GBS-carriership may be valuable in view of the fact that GBS-carriership seems to constitute a risk-factor for perinatal outcome.

Summary

762 women were screened for GBS-carriership in the first trimester of pregnancy. The mean age of carriers was 27.2 years. Follow-up was performed in 64 initially positive and 97 negative cases. Persistent carriership was the most important determinant for neonatal GBS-acquisition. Race, birth-weight, gestational-age, interval between rupture of the membranes and birth could not be associated with GBS-carriership or neonatal acquisition.
The number of neonates with fetal distress was significantly higher amongst those born to all GBS-carriers; the number of S.G.A.-infants was significantly elevated amongst those born to permanently positive women.
Vertical transmission was found in 86% of the mother-infant pairs. GBS serotype III and Ib were predominant. Serotype III was significantly more isolated from non-caucasian women.
The transmission frequency of all types was equal (46%), except for type IIc (22%). None of the serotypes was especially associated with fetal distress or smallness for gestational age.

Keywords: GBS-carriership, neonatal outcome, pregnancy, risk-factor.

Zusammenfassung

Der Einfluß einer latenten Streptokokkeninfektion auf die Schwangerschaft
762 Frauen wurden im ersten Drittel der Schwangerschaft untersucht, ob sie Träger von Streptokokken der Gruppe B sind. Ihr durchschnittliches Alter lag bei 27,2 Jahren. In die Langzeitbeobachtungen einbezogen wurden 64 von Beginn an positive Fälle und 97 negative Fälle. Ständiges Vorhandensein von Streptokokken der Gruppe B war der Hauptgrund für eine neonatale Infektion.
Rasse, Geburtsgewicht, Gestationsalter sowie Intervall zwischen Blasensprung und Entbindung konnten nicht mit einer erhöhten Streptokokkengefährdung oder einer neonatalen Infektion in Zusammenhang gebracht werden.
Bezogen auf das Kollektiv, in dem überhaupt je Streptokokken nachgewiesen wurden, fand sich unter den Neugeborenen eine signifikant erhöhte Inzidenz an fetalem Distress. Lag jedoch bei den Müttern eine permanente Infektion mit Streptokokken vor, war auch die Rate der Small-for-dates signifikant höher. Eine direkte Übertragung von der Mutter auf das Kind lag in 86% der Fälle vor. Vorherrschend waren Streptokokken der Serogruppe III und Ib, wobei der Serotyp III signifikant häufiger bei nichtkaukasischen Frauen gefunden wurde.
Im übrigen war die Übertragungshäufigkeit von allen Typen gleich (46%), mit Ausnahme des Typs IIc (22%). Keiner der Serotypen war im besonderen Maße mit fetalem Distress oder dem Auftreten von Small-for-dates assoziiert.

Schlüsselwörter: Neonataler Zustand, Risikofaktor, Schwangerschaft, Streptokokken-B-Träger.

Résumé

L'influence du portage de streptocoques du groupe B sur l'issue de la grossesse
762 femmes ont subi un dépistage systématique du portage de SGB au cours du premier trimestre de la grossesse. L'âge moyen des porteuses est de 27,2 ans. Un suivi a été établi pour 64 cas initialement positifs et 97 négatifs. La persistance du portage est le facteur le plus important pour l'acquisition néonatale de SGB.
La race, le poids de naissance, l'âge gestationnel, l'intervalle entre la rupture des membranes et la naissance ne peuvent pas être associés avec le portage de SGB ou l'acquisition néonatale.
Le nombre de nouveaux-nés ayant présenté une souffrance foetale est significativement plus élevé parmi ceux nés de l'ensemble des porteuses de SGB; le nombre d'enfants infectés par SGB est élevé de façon significative parmi ceux nés d'une mère porteuse en permanence.
La transmission verticale est retrouvée chez 86% de paires mère-enfant. Les SGB de sérotype III et Ib sont prédominants. Le sérotype III est plus isolè de façon significative chez les femmes non caucasiennes.
La fréquence de transmission de tous les types est équivalente (46%) à l'exception du type IIc (22%). Aucun des sérotypes n'est lié particulièrement à la souffrance foetale ou au retard de croissance in utero.

Mots-clés: Devenir néonatal, facteur de risque, grossesse, portage de SGB.

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