Low levels of antibody directed to the N-terminal domains of Rib and Alp1 surface protein and invasive Group B Streptococcal disease

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Introduction

- Group B Streptococcal (GBS) disease is a common cause of sepsis and meningitis in young infants, and stillbirths[1,2].
- Widely expressed surface protein vaccine candidates have been identified[3].
- Alp family proteins (Rib, Alpha C, and Alp 1-4) are present in most GBS isolates, irrespective of serotype[4-7].
- Natural IgG antibodies are directed against these Alp protein epitopes.

Objectives

- To determine the association between maternal and infant N-terminal domain GBS surface-protein Rib (Rib-N) and Alp1 (Alp1-N) IgG antibodies and invasive GBS disease in young infants.

Method

- We retrospectively analysed serum samples from a case-control study to determine a correlate of protection against invasive GBS disease in Johannesburg, South Africa
- Maternal and infant serum from cases and controls were tested for N-terminal domains of Rib (Rib-N) and Alp1 (Alp1-N) IgG using validated assay at Lund University, Sweden.
- Alp protein typing on the GBS isolates from cases and colonized controls was performed by PCR for Alp 1(Epsilon), Rib, Alp C, Alp 2/3 with primers that target the genomic regions for Epsilon, Rib, Alp C, Alp 2/3 at Staten serum institute.
- GMCs and 95% CI were reported as well as reverse cumulative distributions. We used a Bayesian approach to estimate absolute disease risk at various IgG concentrations.

Results

Table 1: GMC's (µg/mL) between cases and control for maternal IgG and Infant IgG

Protein	Variable	Case	Control	p-value [a]
Rib-N	Maternal IgG	0.03 (0.02,0.05) n=41	0.05 (0.04,0.07) n=45	0.041
Rib-N	Infant IgG	0.01 (0.01,0.02) n=46	0.04 (0.03,0.06) n=44	<0.001
Alp1-N	Maternal IgG	0.08 (0.05,0.13) n=24	0.11 (0.08,0.16) n=36	0.212
Alp1-N	Infant IgG	0.02 (0.01,0.03) n=24	0.05 (0.04,0.07) n=36	<0.001

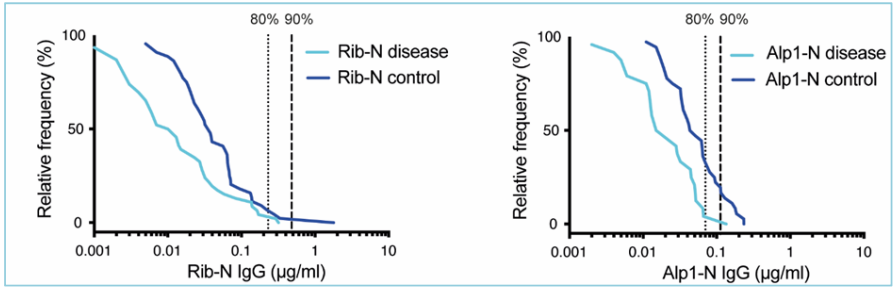
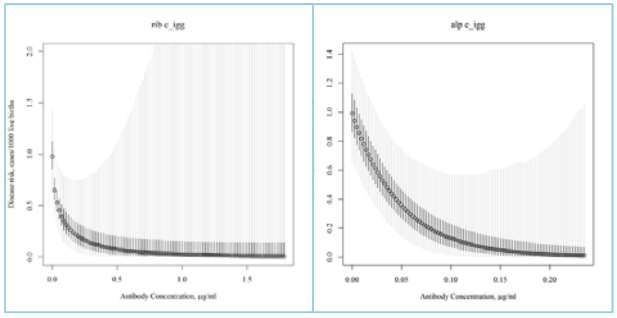


Figure 1: Infant RibN and Alp1N IgG levels in GBS cases and controls born to mothers colonized with Rib and Alp1 expressing isolates



Protein	90% Reduction
Alp1-N	0.1128
Rib-N	0.4284

Figure 2 (left): Posterior distributions of the probability of invasive group B streptococcal disease risk to Alp and Rib type disease at varying infant serum IgG antibody concentrations using a Bayesian model.
Table 2 (top): Infant threshold estimates for Rib-N and Alp1-N IgG

Discussion

- Lower Rib-N and Alp1-N IgG GMC's were detected in sera of infants with invasive GBS disease compared with controls born to women colonized with GBS expressing those proteins.
- A Rib-N and Alp1-N IgG antibody threshold of 0,4µg/mL and 0,1µg/mL was associated with 90% risk reduction of disease in infants, respectively.
- A maternal vaccine targeting the Alp family may prevent invasive GBS disease in young infants.

References

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