Transmission of Group B Streptococcus in Malawi: A Prospective Cohort Study

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MALAWI-LIVERPOOL-WELLCOME TRUST CLINICAL RESEARCH PROGRAMME
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GBS Neonatal Sepsis

Leading infectious cause of morbidity and mortality among infants.

Common GI/GU commensal bacteria: Maternal carriage rate 10-36%

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<th>USA (1990)</th>
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<td>Early</td>
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Study Objectives

1) Describe GBS carriage rates amongst pregnant women in third trimester of pregnancy.

2) Chronicle the pregnancy/early life outcomes in these women & babies.
   a) Compare maternal carriage GBS & neonatal invasive GBS to determine mother-infant linkage
   b) Investigate for markers of virulence through GBS DNA whole genome sequencing from study and archived samples (2004-2014)

3) Assess the colonisation with GBS of well babies with GBS in the first month of life.
Study Overview

Prospective Cohort Study

Antenatal Clinic at Zingwangwa Health Centre

GBS carriage:
• Vaginal and rectal swab for GBS analysis

Livebirth

Week 1
Week 2
Week 3
Week 4
Week 5
Week 6

Neonate followed-up until 6 weeks of age.

Sick babies:
• Blood/CSF cultures taken – admitted and treated.

Healthy babies:
• Invited to participate in the GBS colonisation sub-study.

GBS DNA whole sequence analysis of study & historic archived samples (2004-2014) sent to University of Oxford
GBS Colonization Sub-Study

Healthy babies born to recruited mothers were invited to participate.

- Aim to establish the relationship between maternal GBS colonisation, and the subsequent surface colonisation of well infants in the first month of life.

1. Maternal GBS vaginal/rectal swabs repeated on post natal visit
2. Baby had umbilical, ear and throat swabs taken on each subsequent visit till week 4.
Interim Results: Study Population

- 3247 women screened
- 1712 women eligible
- 713 women enrolled (42%)
- 509 deliveries
  - 508 livebirths
  - 1 still birth
- 128 women colonised with GBS (19%)

Non-participation:
- 654 not interested
- 104 fear of participation
- 210 need to ask husband
- 31 no reason given

Events:
- 27 neonates investigated for sepsis
- 3 neonatal deaths
- 102 mother/baby pairs enrolled in colonisation sub-study

Mean parity: 2.3
HIV prevalence: 13.6%
GBS Maternal Carriage Data

2014-2015 COHORT (N=128)
- Ia: 18%
- Ib: 6%
- II: 2%
- III: 47%
- V: 27%

2008-2010 COHORT (N=390)
- Ia: 19%
- Ib: 6%
- II: 11%
- III: 40%
- V: 24%

Interim Results: Neonatal Outcomes

Of the 27 babies (N=508 livebirths) investigated for suspected sepsis (5.3%):

• **Zero** GBS positive blood/CSF
  • All specimens culture negative.
  • No deaths in the suspected sepsis group.
Interim Results: Colonization Sub-Study

MOTHERS WHO WERE GBS COLONIZED

14 mothers with GBS carriage (Total N=102):

- Serotype 1A: 2 (14%)
- Serotype 3: 9 (64%)
- Serotype 5: 3 (21%)

7 infants (50%) showed surface colonization with GBS:

- 6 infants had identical GBS to maternal serotype
- 1 infant had acquired different GBS serotype to mother

MOTHERS NEGATIVE FOR GBS COLONIZATION

Of 88 mothers with negative GBS colonisation...

9 (10%) of infants showed evidence of GBS surface colonization

- Serotype 1a: 5 (55%)
- Serotype III: 3 (33%)
- Serotype VIII: 1 (11%)
Limitations

- Small sample size – neonatal GBS disease is high impact, but relatively rare

- Difficulties in carrying out a study in resource-limited settings
  - Unreliable electricity and water supply can affect equipment/sample storage
  - Lack of existing health infrastructure, difficulty in following up mother/infant pairs

- Lack of structured antenatal care – accurate determination of gestation difficult

- Possible microbiological sampling errors or contamination
  - However, robust quality control in place, and whole genome sequencing has identified GBS from samples collected
What does the study add?

Demonstrates that maternal GBS colonization and serotype distribution is comparable to similar settings in the region.

Indication of intrapartum transfer of maternal GBS to infant leading to surface colonization, but also infant acquisition of GBS from non-colonized mothers.

Whole genome sequencing of invasive neonatal GBS disease in a Malawi population to compare with known GBS virulence factors, ultimately to aid GBS vaccine development.

Potential to explore maternal microbiome characteristics in relation to GBS colonization and neonatal outcomes.
Acknowledgements

Malawi-Liverpool Wellcome Trust
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- Mac Mallewa
- NET-GBS Study Team
- Doctors & Nurses at QECH

Liverpool University:
- Prof Neil French

Oxford University:
- Prof Martin Maiden
- Odile Harrison
- Andrea Gori
Thank you
### Colonisation Sub-Study

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<th>Infant Serotype (weekly)</th>
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