BACTERIAL MENINGITIS IN BABIES 0-90 DAYS OF AGE: A UK AND REPUBLIC OF IRELAND PROSPECTIVE STUDY. (neoMen)

Abstract E16

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Background and aims

Neonatal bacterial meningitis is associated with significant mortality and morbidity. The last surveillance in England and Wales 1996-1997 compared with 10 years earlier showed similar incidence of 0.2/1000 live births, causative organism *Group B streptococcus* (42% vs 38%) and *E coli* (16% vs 25%) and a decrease in mortality (10% vs 29%)[1,2].
A 5 year follow up of the survivors of both cohorts also showed that about 50% of survivors from both cohorts had a neurological sequelae with 25.5% (1980s) and 23.5% (1990s) of them severe[3]. There have been no UK studies since that time. In addition, none of the previous studies specifically looked at the timing and progression of presenting signs or assessed how these infants were managed.
It is important to define the current burden of disease (BPSU study) and how they are being managed (Healthcare delivery study: HCD) and identify any opportunities for improvements in diagnosis and management in order to prioritise treatment and prevention strategies and establish an evidence based management guideline.
With parental consent, babies recruited into the HCD study will also be contacted at two years of age for a neurodevelopmental assessment.

Methods

Data were collected prospectively using the BPSU "orange card" system (Fig.1) over a 13 month period from 1 July 2010 to 31 July 2011. During this time monthly cards are sent by the BPSU to over 3200 Clinicians (mainly Paediatricians) in the UK and ROI with a 92% return rate.
Using the orange card respondents were asked to report all cases of bacterial meningitis that they had managed in the previous month and to return the card even when there was nothing to report. Following notification of a potential case a standardised clinical questionnaire was sent to the Clinician. Cases were also reported via other sources: the Health Protection Agency laboratory reporting system in England and Wales, Health Protection Scotland, parents and meningitis support charities).
For the HCD study, a pack containing an information sheet, consent form and parental questionnaire is sent to a named local Paediatrician for onward forwarding to the parents of babies identified through the above sources.
Ethics approval was given by Cambridgeshire 2 REC (Ref 10/H0308/45 and 10/H0308/64 and NIGB section 251 support (ref: PIAG 6-06 (FT1)/2008).
Analysis was performed using SPSS Statistics 18 (IBM SPSS, Chicago, Illinois).

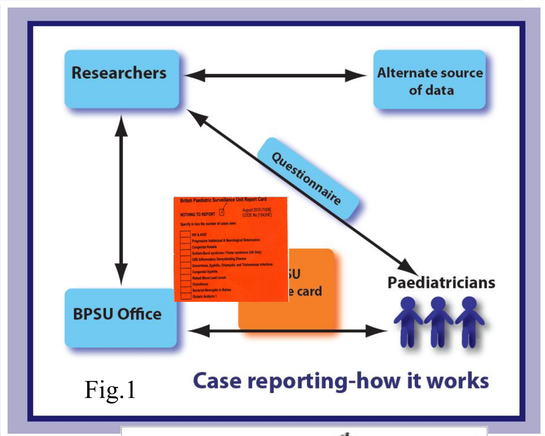


Fig.1 Case reporting-how it works

Results

During the study period 484 cases were notified via the BPSU. Cases notified via sources other than the BPSU are currently being verified and de-duplicated. We present results of the first 200 BPSU cases that met our analytical case definition (appendix 1).
Cases were reported from 125 different hospitals (Fig. 2) in England 173 (86.5%), Wales 10 (5%), Scotland 5 (2.5%), Northern Ireland 6 (3%) and Republic of Ireland 6 (3%). 115 (57%) were males, 160 (80%) were classified as any white background. The median age (range) was 13 days (0-88), median gestational age at birth 39 weeks (24.3-42); median birth weight (range) 3100grams (456-4600).
Most babies were admitted from home (134/200, 64%), and presented in the neonatal period (134 (67%): 0-6 days = 65, 7-28 days = 69) while 66 (33%) presented between days 29-90 (Fig.3).
The most common presenting signs were poor feeding (69%), irritability (65%), lethargy (61%) and fever ≥ 38 0C (54%) (Table 1).
Lumbar puncture was performed in 189/200 (94.5%) of the cases and was obtained after antibiotics in 115/189 (61%). 150/200 (75%) of the cases had an organism isolated from the CSF or blood cultures. Of the 154 organisms isolated 77/154 (50%) were Group B Streptococcus (GBS) and 16/154 (10%) *Streptococcus pneumoniae* (SPn) (Fig. 4). Empirical 3rd generation cephalosporins was used in 148 (75%) and gentamicin in 85 (43%) of cases.
Case fatality at the time of reporting was 15/200 (7.5%), 8 (53%) male, 12 (80%) 0-28 days of age; 7 (47%) were <37 weeks gestation at birth. Four of 77 (5%) with GBS and 4/16 (25%) with SPn died (p=0.03 (Fisher's Exact Test).
Research and Development approval has been granted in 37 NHS Trusts and ten babies have been recruited into the on going HCD study and the target is 100.

Condition	Frequency
Poor feeding	69%
Irritability	65%
Lethargy	61%
Fever ≥ 38.0°C	54%
Poor perfusion	45%
Respiratory distress	36%
Apnoea	25%
Convulsions	**25%**
Temp instability / hypothermia	21%
Vomiting	20%
Bulging fontanele	**19%**
Comatose	**5%**
Jaundice	3%
Neck stiffness	**3%**

Table 1 showing presenting features

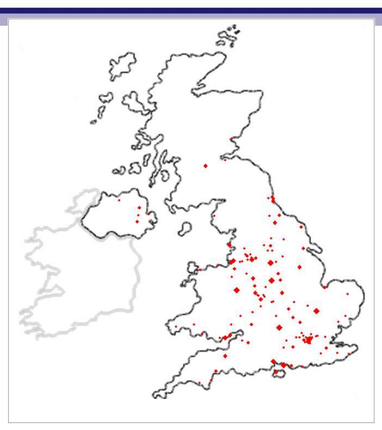


Fig 3. Map showing postcodes of UK hospitals where cases were from

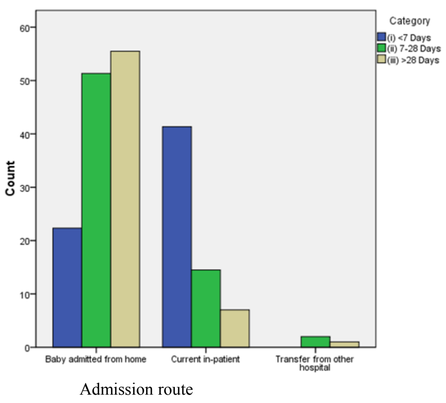
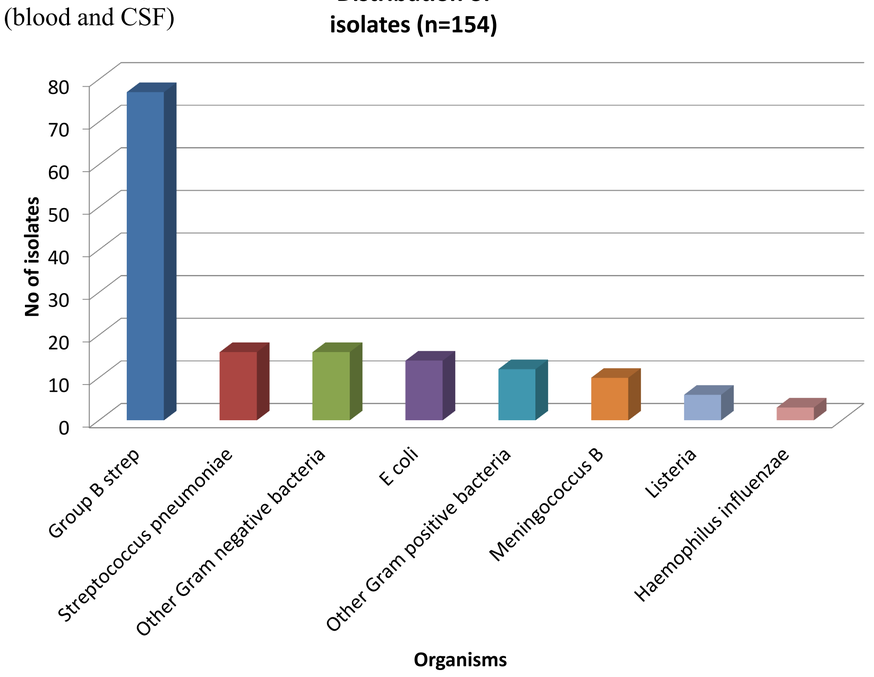


Fig3. showing admission route and age group

Fig4 Bar chart showing distribution of isolated organisms (blood and CSF)



Discussion

This is the first study in the UK & ROI specifically looking at bacterial meningitis in babies 0-90 days of age. Cases presented with nonspecific signs and the classical signs of meningitis are infrequently seen. Consistent with previous UK[1] and French studies[4] GBS is by far the most frequent isolate (50% vs 42% vs 59%); *E coli* appears to be less frequent in this study (9% vs 16% vs 28%). Blood cultures were negative in 43 (29%) of confirmed cases which reinforces the findings of other studies including Garges et al[5] that report that a substantial proportion (38%) of neonates with culture-proven meningitis have negative blood cultures. In 45/150 (30%) of cases blood culture was positive and CSF culture negative which highlights the role of blood culture in directing antibiotic therapy when CSF culture is negative. Although overall fatality is 7.5%, this is higher in the neonatal period 8.9% and compares with 10% in Holt study[1] and 13% (French National study)[4]. There is a significantly higher case fatality associated with SPn meningitis (25%) compared with GBS meningitis {5%, p=0.03 (Fisher's Exact Test)}.

Conclusion

Our study shows that there remains a significant burden from bacterial meningitis in babies 0- 90 days old in the UK and the ROI.
Group B Streptococcus and Gram negative bacteria collectively remain the leading causative organisms.
Presentation is nonspecific and efforts should be directed to prevention, through appropriate vaccines, and new strategies for recognition and management.

Limitations

There is no wide use of molecular diagnosis and therefore likely that some cases will be missed where conventional cultures were negative.
We are reliant on the clinical information provided by Paediatricians from medical notes.

References:

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Appendix 1

*Confirmed cases: isolation of a significant bacteria from CSF or CSF pleocytosis with significant bacteria from blood.
Probable cases: Clinical signs and CSF pleocytosis and no organism from CSF or blood.
Possible cases: Clinical signs and significant bacteria from blood but no CSF obtained.
CSF pleocytosis: 0-28 days (≥20 white blood cells/mm^3) and 29-90 days (≥10 cells/mm^3).
Clinical signs of meningitis are: fever or hypothermia or temperature instability PLUS 1 or more neurological findings e.g. coma, seizures, neck stiffness, apnoea, bulging fontanel.
Exclusion criteria: Any baby with an intraventricular shunt device or any spectrum of spina bifida.

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