AETIOLOGY OF NEONATAL INFECTION IN SOUTH ASIA
The ANISA project has now reached one year of surveillance. The mission was challenging but the team has navigated it successfully with magnificent support from all our affiliates, including the site teams, TAG members, CDC group and BMGF. This publication will briefly sketch out how the ANISA team established and is currently maintaining the population-based surveillance system to detect the aetiology of neonatal sepsis in South Asia.
**COX’S BAZAR, BANGLADESH**
6-7 Dec 2010
Finalisation of project structure, methodology and implementation plan.

**PHUKET, THAILAND**
Mid-project retrospective, first look at data from sites, defining strategies for further improvement and planning for the final year.
Tools and steps for implementation of surveillance

1. Mapping and listing of households
2. Development of SOP and translated data forms
3. Establishment of real time data upload
   i. Programming and refinement of data system, establishment of network
   ii. Real time registration of enrolled newborns, identification of sepsis cases & simultaneous algorithm based selection of healthy controls
4. Recruitment and training of study staff to facilitate standardized application of project protocol across sites.
5. Establishment of appropriate specimen collection, transportation preservation and tracking procedure.
6. Establishment of standardized microbiological and molecular test procedures.
ANISA innovatively planned for an open ended pilot phase. The sites were allowed to plan and implement study components at field sites, laboratories and data systems based on the protocol and centralized training. The site and coordination teams closely monitored the progress, identifying and addressing the challenges. The site PI and coordination team members, based on preset criteria, reviewed the progress and stabilization of all study components. The date when the main study started was then set retrospectively based on a consensus between the site and coordination teams.
Criteria of Graduation

Other Criteria

1. Successful blood cultures accomplished and results reported to treating physicians at real-time.
2. Data collections on ANISA data forms and subsequent management is working well.
3. The lists of detected bacteria are shared with the coordination centre periodically.
4. Healthy controls are assigned using the automated selection algorithm.
Graduation of sites into main study
Monitoring

Being a multi-country and multi-site project, ANISA has inherent complexities that deserve constant monitoring. ANISA, in addition to conventional monitoring visits, has built a robust system for real time monitoring by the PIs at the sites and the distant coordination team. The monitoring tools are built in the data management, and mobile texting system. All these help to detect any deviation from the protocol at real time.

A matrix has been developed based on multiple critical indexes to weigh the performance of each site against the target and the threshold required to achieve the study objectives.
Critical study steps being monitored

1. Eligible women enrolled & pregnancy detected.
2. Early detection and enrollment of live births
3. Suspected sepsis cases detected and referred by CHW
4. Compliance with referral
5. Physician confirmation of possible sepsis
6. Successful collection of specimens
7. Successful implementation of lab method
62% CHW referred cases were confirmed as PSBI by physician 1678

Physician confirmed PSBI among self referred babies N=354

PSBI (Total) confirmed by Physician N=2,032
AETIOLOGIES

86% (1,753/2,032)
Of PSBI Babies gave CONSENT for SPECIMEN COLLECTION

89% (1,567/1,753)
BLOOD and
97% (1,739/1,753)
Respiratory specimen (NP/OP) collected from CONSENTED babies

94% (1,479/1,567)
BACTEC bottles placed in the machine within 6 hours

46% (3%, 46/1,567)
PATHOGEN/PROBABLE PATHOGEN isolated from blood culture

6% (100/1,567)
of Blood culture got contaminated*
*As defined by the site

ALL collected BLOOD successfully inoculated into BACTEC bottle
91% (1,437/1,567) of collected blood preserved in EDTA tube

Total 616 Respiratory specimen (NP/OP) collected from 1739 cases were tested by TLDA

Pathogen / Probable pathogen isolated from Blood Culture (N=46)

- S. aureus
- E. Coli
- S. pyogenes
- Campylobacter sp.
- N. meningitidis
- Actinobacter Sp.
- K. pneumoniae
- Streptococcus sp.
- Group B streptococcus
- Pseudomonas sp.
- P. vulgaris
- P. luteola
- B. cepacia
- Salmonella sp.

Organisms detected by TAC from Respiratory specimen (N=616)

- K. pneumoniae
- Rhinovirus
- E. coli & Shigella sp.
- Group B streptococcus
- Ureaplasma
- B. pertussis & B. holmesii
- Enterovirus
- Respiratory Syncytial Virus
- Adenovirus
- Parainfluenza Virus 3
- Parainfluenza Virus 1
- Influenza Virus B
- Influenza Virus A
- Herpes Simplex Virus type-1
- Human Metapneumovirus
- Rubella Virus
- C. trachomatis
- M. pneumoniae
- C. pneumoniae
All Excellent ANISA achievements of ANISA will be ruined if blood cultures get contaminated.
Communication

To maintain the study quality during the planning and implementation phases, the ANISA management team ensures regular communication between the ANISA team members across the world. An attempt is continually made to keep everyone abreast of new progress, challenges and/or achievements and to bolster relations with the teams at the sites. Establishment of this communications from this developing country was a real challenge. However, ANISA managed to establish global conference calls from Dhaka via Cisco’s WebEx system. Due to the global distribution of partners, call timing is also a challenge. Often, ANISA-CDC members are taking the calls at 5.00 am and in the say way the Dhaka team is taking it at 9.00 pm. Small group calls are happening even at midnight. Nevertheless, consideration and dedication of the entire ANISA team is making it possible to arrange the calls with challenging times at either end.

The management team in Dhaka is convening around 16 conference calls per month with different collaborators which includes the site teams, ANISA coordination team, the CDC, ANISA TAG and BMGF.
New Sites
Welcome to ANISA Family

Due to unforeseen logistical challenges, the original proposed site in India at Shivgarh in Uttar Pradesh was discontinued and this created a challenge for the ANISA project. Without an Indian site, it would lack data from the largest and most populous country in the sub-continent, which may lessen the impact of the study findings on both Indian and global policy makers. In order to redress this issue, the ANISA team embarked on a search for suitable Indian sites. Two sites with desirable characteristics have been identified, Vellore and Odisha.

VELLORE
SITE DESCRIPTION

Site PI
Dr. Pinaki Panigrahi

Population at ANISA site
237,600

Birth Rate/1000 year
21.4

Neonatal Mortality Rate/1000 year
43

Facility-based deliveries
80%

Available ANISA Newborns per year
4500

Expected infants with PBSI (10%)
450

Number of specimens per year (80% of PBSI cases)
360

Per year Bacterial Isolation estimate (5%)
21

Per year viral Isolation estimate (30%)
110
ODISHA
SITE DESCRIPTION

Site PI
Dr. Anuradha Bose

Population at ANISA site
250,000

Birth Rate/1000 year
16.5

Neonatal Mortality
Rate/1000 year
26

Facility-based deliveries
90%

Available ANISA
Newborns per year
4000

Expected infants with
PBSI (10%)
400

Number of specimens per
year (90% of PSBI cases)
360

Per year Bacterial
Isolation estimate (5%)
18

Per year viral Isolation
estimate (30%)
108
Aetiology of Puerperal Sepsis
A supplement to ANISA

Population based studies are pertinent to understanding the true burden of any disease. However, established sites with the capacity to identify numerator along with known denominators are few, specially in South Asia. Further, maintenance of these sites and implementation of disease surveillance is expensive and time consuming. Therefore, exploration of possibilities to introduce additional studies on any ongoing study is desirable to make the rational use of the team's effort and the invested resources. ANISA is no exception, it explored the possibility of introducing other relevant studies using the same infrastructures, study design and logistics, specially when all the MWRAs in the study sites are enrolled and followed up for ANISA main study.

ANISA, in collaboration with Prof. Linda Bartlett of Johns Hopkins University developed a proposal to find aetiology of post partum infection of enrolled mothers. This supplement aims to capture the PP sepsis cases using the customized clinical algorithm derived from the formative research done in the same community. Endometrial swabs will be collected and processed for aetiologies using the ANISA facilities.