Microbiology laboratory capacity building at a resource-poor setting in Bangladesh: Impact on child health policy

Samir K Saha, Ph.D.
Department of Microbiology
Dhaka Shishu Hospital
Bangladesh
Bangladesh

- 144 million people
  - 7th most populous country in the world
- Population density 1,002 persons/square kilometer (global mean 42)
  - Per capita income - US$ 362 ()
- ICDDR,B – the ‘state of the art’ International Centre
  -Focused on diarrhoeal diseases
  - Until recent past, other diseases were overshadowed, and .............
Leading Killer of Children in Bangladesh

- ARI 21%
- Possible serious infection 31%
- Birth asphyxia 12%
- Prematurity / LBW 7%
- Others? 7%
- Malnutrition 4%
- Injury 4%
- Diarrhea 5%
- ARI+diarrhea 2%
- Other neonatal 7%
- Others? 7%
Etiology of these deaths

• How much do we know about it?

• What do we need to explore this?

• Techniques and technologies

• Availability of technology Vs prevalence of diseases
Childhood mortality
Countries with technologies
Why are the microbiology laboratories “resource poor”?

• “Resource poor” labs may not be financially poor
  – Annual budget Vs expenditure of public institutes

• How much do we know about these labs and what is the basis of our knowledge?
  – ICDDR,B, AKU, MRC, etc.
    • Do these ‘state of the art’ institutes represent the laboratories of resource poor countries?
Budget and priority identification

- New system comes with lot of fanfare
- Policy makers get convinced
  - Reference labs Vs Service labs
- Few examples
  - Platelet separator
    - Where blood bank can not ensure to provide safe blood
    - Lying idle
  - Automated blood culture machine
    - Where labs still use human blood
    - No budget to buy the culture bottles
    - Laboratories bought automated machines never used.
Microbiology laboratories in Bangladesh

• Non existent at district level hospitals

• Leading Medical colleges
  – While working for capacity building of microbiology laboratories in 6 large hospitals
    • Staffs are highly qualified
    • Teaching *S. pneumoniae* and *H. influenzae* for decades
    • Log books showed almost no isolation of Hib or Pneumo
    • Minimum or no resources and thus less or no specimen; or *vice versa*
    • Least communication between clinicians and microbiologists
Poor microbiology lab: impact on policy decisions

• This if the 15th year of Hib and 5th year of Pneumo vaccine introduction in USA
  – These vaccines are not available in the countries where 90% of the diseases occur
    • GAVI fund could not be utilized by most of the eligible countries

• What is the main obstacle?
  – Disease burden data
  – We have medical colleges, hospitals, great academicians but no data!
  – Non functional laboratories

Why?
Hospital dynamics and laboratory capacity building

• Hospital management is the most complicated dynamics due to multi-disciplinary groups
  – Administration, finance, clinicians, nurses, laboratory personal, other staffs
  – Shishu is no exception from this

• How can we work within these complexities?
  – Involved leading clinician with the lab related work
  – Related that with their work
We need to change the "Vicious Cycle" of Developing Countries.

Limited Resources

Improper or inadequate use

Lack of evidence

Generation of evidence

Optimum and rational use

Adequate resources
Capacity building occurs when all 3 work collaboratively.
Dhaka Shishu Hospital

• Largest Pediatric Hospital
  – 470 beds in different disciplines
  – 53% of the beds are free for poor
  – Large out patient department -
    ~150,000 patients/year
Shishu Microbiology in 1989

- Photo frame size space in the veranda of clinical pathology
  - Arranged a bench, pressure cooker, incubator and few glass plates
- My teachers on those days
Why to present this at IUB?

• We want to see
  – more functional microbiology laboratory
    • Good laboratory practice
    • Increased capacity
  – Impact on child health policy
How things started rolling?

• Proactive laboratory
  – Communicating results
  – Volunteering to do additional diagnostic work

• Work was based on the need of the clinicians
  – Indigenous Lysis direct-plating/centrifugation method
    • Rapid and quantitative blood culture
  – Rapid antimicrobial susceptibility test (RAST)

• Influence on clinical colleagues and administration
Lysis-direct plating/centrifugation method

Mix

Growth of Bacteria at 12-18 hours

Saha et al. 1991; Trans Royal Soc Trop Med Hyg
Saha et al. 2001; J Clin Microbiol
Advantage of working in a pediatric hospital

- Magnitude of bacteremia is indirectly proportional to age.
- Implications in deciding blood volume

Base line work – impact on policy

- Pneumonia, septicaemia and meningitis
  - Always focused on public health issues
  - Drug resistance
  - Implications on treatment
  - Serotype distribution of S. pneumoniae and H. influenzae
  - Implications on vaccine formulation
  - Age group distribution
  - Implication on vaccination policy
Surveillance on drug resistance – Typhoid perspective

- Progressive increase in relative resistance to Ciprofloxacin
  - Delay in clinical response
  - Higher dose
  - Treatment failure
  - Recurrence

- Decrease in drug resistance
- Remarkable difference between hospital and community isolates.
  - Ideal practice in Bangladesh and...
  - Hospital Vs community

VNTR Pattern of Ciprofloxacin Resistant S. Typhi Compared to Sensitive Strains

- Identical clone
- Encountering many other strains
- Possible reason:
  - Misleading definition of Ciprofloxacin resistance
    - >2.0 µg/ml

Lane 1: 100 bp marker; Lane 2-4: Ciprofloxacin resistant strains (MIC 512 µg/ml), Lane 5-7, Ciprofloxacin sensitive strains, MIC 0.032, 0.064, 0.25 µg/ml respectively.

Saha et al. J Clin Microbiol 2006
Age group distribution of Typhoid cases impact on typhoid vaccination policy

New recommendation for vaccination.

Existing vaccine will not be effective in 23% of cases.

97% coverage with effective conjugate vaccine.

Saha et al. Pediatric Infectious Diseases Journal, 2000
Progressive increase in MDR of Hib: impact on outcome of meningitis

Saha et al. Journal of Pediatrics 2005
Outcome of Hib meningitis cases in relation to drug resistance (n=425)

- Progressive increase of MDR
- MDR is directly related to disability and death
  - Most deaths occur before antibiotic can do anything

Saha et al. J Pediatrics, 2005
Application of molecular techniques: definitive therapy in culture negative cases

- MDR Plasmid genome of *H. influenzae*
  - Used as a tool to see phylogenetic evolution of MDR strains
- How are we using that?
  - Detecting the genome in culture negative CSF specimens
  - Contributing in treatment policy
Application of molecular techniques: definitive therapy in culture negative cases

- Culture, 19
- Latex, 33
- ICT, 10

H. influenzae (52) S. pneumoniae (62)

LP +ve, 43%
LP -ve, 57%
Culture, 19

Bex

LP
Serotype and drug resistance of *S. pneumoniae*: implications in treatment of vaccination policy

- Low penicillin resistance
- High resistance to Cotromoxazole

**Serotypes**
- Diverse and different from developed part of the world
- Low coverage by existing vaccine type
- 25-30%
- Our serotypes are considered for inclusion in upcoming vaccine formulation

Validation of BinaxNow® to diagnose pneumococcal meningitis

- BinaxNow - developed to detect Pneumococcal antigen in urine
  - Not useful
- We used the largest series of meningitis cases
  - Gold standard – PCR
  - 100% sensitive and specific
  - Implications in measuring disease burden
- Treatment policy

Saha et al 2005 Pediatric Infectious Diseases
Limitation of Pneumococcal antigen detection

- Importance to public health and donors
  - New serotypes
  - More output within short time
  - Cost effective
Most significant impact of our work in country policy decision

- BBC film on Hib
- World Bank, WHO, UNICEF and our Government prepared MYP
  - Applying to GAVI and introduce Hib vaccine in EPI by 2008
  - It all based on the data generated from Shishu microbiology
The "Vicious Cycle" of Developing Countries

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Adequate resources
The team is getting bigger
Our mentors

Prof. T. Nagatake, Nagasaki University, Japan

Prof. Robert Black, Johns Hopkins University

Prof. Mathuram Santosham, Johns Hopkins University
Dhaka Shishu Hospital

- Largest Pediatric Hospital
  - 387 beds in different disciplines
  - 53% of the beds are free for poor
  - Large out patient department - ~150,000 patients/year
- Adequate Laboratory Facilities
- Research (Public Health)
  - Clinical trial
  - Vaccine trial
  - Surveillance for invasive diseases
- Collaborating with
  - JHU
  - Nagasaki University
  - Oxford University
  - WHO
  - ICDDR, B
  - Save the Children, USA
  - GAVI’s PneumoADIP
  - GlaxoSmithKline