ESTABLISHMENT OF POPULATION-BASED SURVEILLANCE FOR INVASIVE PNEUMOCOCCAL DISEASE IN BANGALORE, INDIA

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ABSTRACT

BACKGROUND: Invasive pneumococcal disease (IPD) is vaccine-preventable but few data on the incidence of PD exist for Indian children. AIMS: To assess the feasibility of implementing prospective, population-based surveillance for PD among children less than five years of age. SETTINGS AND DESIGN: Hospitals and health agencies, Bangalore, India. Retrospective review and analysis of hospitalization records as well as public health and demographic data. MATERIAL AND METHODS: Records for 2006 hospitalizations for pneumococcal disease-associated syndromes (meningitis, pneumonia and sepsis) were identified at three pediatric referral hospitals (Indira Gandhi Institute of Child Health, Kempegowda Institute of Child Health and Vani Vilas Hospital) in Bangalore using International Classification of Diseases, 9th revision codes. Hospital microbiology laboratory records were assessed to ensure capacity for identifying S. pneumoniae. Population data were identified from national census and polio surveillance data. RESULTS: The Bangalore city southern zone includes 33 wards occupying 51 Km² with 150,945 children between 0-5 years of age served by three referral pediatric hospitals. From January--December 2006, records of these three hospitals showed 2,219 hospitalizations of children less than five years of age with PD-associated diagnoses (southern zone area incidence: 0.15/100,000 PD-associated hospitalizations, less than five years of age). There were 178 deaths in children less than five years of age, of which 87 were attributable to sepsis, 56 to pneumonia and 35 to meningitis. CONCLUSION: Our analysis suggests that the PD-associated disease burden in Bangalore is high and local institutions have capacity for population-based surveillance. In a prospective study, systematic attention to potential barriers in identifying children with pneumococcal infections will improve estimation of IPD incidence in India.

Key words: Bacteria, epidemiology, India, S. pneumoniae, surveillance

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INTRODUCTION

Each year, an estimated 875,000 pneumococcal-associated deaths occur worldwide with a disproportionate share of these deaths reported among infants in developing countries.[1-3] In India, previous studies of childhood invasive bacterial diseases showed high case-fatality rates (CFR) associated with pneumonia (19%), meningitis (34%) and sepsis (21%).[4] These clinical syndromes are leading manifestations of invasive bacterial diseases such as that due to Streptococcus pneumoniae. Reduction in the pneumococcal disease (PD) burden following introduction of pneumococcal conjugate vaccine (PCV) into national immunization programs has led to a global effort to obtain local data to guide pneumococcal vaccination strategies.[5] Over the past decade, it has been recognized that incidence data are difficult to obtain in India due to its large population and geographic size, the absence of a national surveillance system for invasive PD (IPD), a limited number of medical centers with appropriate lab facilities and the widespread use of pre-hospitalization antibiotics.[6] Despite well-done studies in India, there remain large gaps in our knowledge of the IPD burden among Indian children. To address these gaps, we initiated a field site assessment to study the feasibility of prospective surveillance for childhood IPD.

MATERIALS AND METHODS

Overview
We identified three major pediatric hospitals located in Bangalore, India to assess the feasibility of a population-based study of IPD and to describe PD-associated hospitalizations (using the International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9 CM]) by age and geographic area. This study was conducted in collaboration with Kempegowda Institute of Medical Science (KIMS), Indira Gandhi Institute of Child Health (IGICH), Vani Vilas Hospital (VVH). Geographically, to understand the field site, based on available information Bangalore city is divided into three zones (eastern, western and southern). The southern and eastern zones are composed of 33 wards each while the western zone has 34 wards. Information collected during field site visits to these areas as well as population data and analysis of hospital utilization/discharge data indicate that the southern zone (with 33 wards) contained an adequate target population to support a population-based estimate of PD incidence.

Population data
To describe the catchment population, we collected information on the total population, numbers of children less than one year of age, and numbers of children less than five years of age residing in the proposed study area. We obtained 2001 population data for the three geographic zones of Bangalore city (Kendriya Sadan-census office Bangalore). We also collected population data from the Bangalore polio surveillance office for January—December 2006 for children less than five years of age. In addition, we identified the 2006 infant population data from the Karnataka state Expanded Program on Immunization (EPI) for the year 2006.

Catchment area analysis
Using population data, we estimated the total
population, number of children less than five years of age and infants <12 months of age in the three Bangalore city zones (eastern, western, and southern). We analyzed available discharge data from the three hospitals to determine the total number of hospitalizations, the hospitalization distribution for syndromes of invasive bacterial diseases (IBD) (using ICD-9 CM diagnoses), and deaths associated with IBD-related syndromes in children less than five years of age and the residential distribution of children hospitalized in the three proposed study hospitals. ICD-9 CM discharge data were also analyzed to determine the percentage of children under five years of age that were admitted with a diagnosis of IBD-associated syndromes of meningitis, pneumonia, and septicemia (ICD-9 CM) and deaths caused by IBD-associated syndromes among children less than five years of age.

Study site hospital data
We accessed hospital discharge records for the period January--December 2006 at KIMS, VVH and IGICH to calculate the percentage of patients living in Bangalore city zones and to identify the catchment area for this study. Hospital laboratory records were inspected to assess the capacity of microbiology laboratories to isolate S. pneumoniae. Review of microbiology records (January--December 2006) of the three hospitals showed more than 60 isolates of S. pneumoniae from blood and CSF specimens. Study site hospitals were assessed to facilitate the design of a referral system for patients with suspected IPD and determine their ability to implement a web-based data capture system.

Statistical data analysis
Statistical analysis was performed using “STATA 10 (STATA Corp. College Station, TX) Analysis of categorical data was conducted using the standard Chi Square test and Mantel-Haenzel test.

RESULTS

Study population
The western zone of Bangalore has 123,145 children less than five years old and 25,134 infants <12 months old. The southern zone has 150,945 children less than five years of age and 30,805 infants while the eastern zone has 134,770 children less than five years old (polio surveillance data 2006) and 27,503 infants (EPI 2006 data). The southern geographic zone contains 33 wards in a 51 km² area (population density: 19,435 per km²). In Bangalore city, there are 41 secondary and ten tertiary hospitals. The western zone has 13 secondary and two tertiary hospitals. The southern zone has 17 secondary and five tertiary, and the eastern zone has 11 secondary and three tertiary hospitals [Table 1].

Study hospitals
The Bangalore city southern zone population is served by three major pediatric hospitals (KIMS, VVH, and IGICH) [Figure 1].

KIMS: There are a total of 90 pediatric beds at KIMS plus five PICU (pediatric intensive care unit), and 20 NICU (neonatal intensive care unit) beds. From January--December 2006 (among children age 0-16 years) there were annual 19,388 OPD visits and 3,635 inpatient visits at KIMS [Table 2].

IGICH: There are a total of 180 pediatric beds at IGICH plus 20 PICU, and 20 NICU beds. For January--December 2006 (among children age 0-16 years), there were annual 36,500 OPD
visits and 7,300 inpatient visits at IGICH.

VVH: There are a total of 120 general pediatric beds plus an additional six beds in the PICU, and 20 beds in the NICU. During January--December 2006 (among children age 0-16 years), VVH records showed there were annual 54,750 OPD visits and 7,300 inpatient visits. According to discharge records, 582/838 (69%) of total hospitalized children less than five years of age from KIMS, 1,733/3,123 (56%) children less than five years of age from IGICH and 1,546/3,711 (42%) children less than five years of age from VVH lived in the southern zone of Bangalore city, so 45% of children living in the southern zone attended IGICH, 40% attended VVH and 15% attended KIMS hospital [Table 3].

**IBD-associated clinical syndromes**

There were 2,219 total hospitalizations for IBD-associated syndromes from January--December 2006 in the three study site hospitals yielding an incidence of 15/1000 children less

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**Table 1: Childhood population and distribution of hospitals in Bangalore city, 2006**

<table>
<thead>
<tr>
<th>Bangalore City Zones</th>
<th>Population</th>
<th>Total Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age Group (years) n (%)</td>
<td>Secondary n (%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 1</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>West</td>
<td>25,134 (30)</td>
<td>123,145 (30)</td>
</tr>
<tr>
<td>South</td>
<td>30,805 (37)</td>
<td>150,945 (37)</td>
</tr>
<tr>
<td>East</td>
<td>27,503 (33)</td>
<td>134,770 (33)</td>
</tr>
<tr>
<td>Total</td>
<td>83,442 (100)</td>
<td>408,860 (100)</td>
</tr>
</tbody>
</table>

Bangalore city is divided into East, West, and South zones. Column percents are shown. Infant population data 2006 are courtesy of the Bangalore city EPI surveillance office. Childhood population data 2006 are courtesy of the Bangalore city polio surveillance office.

**Table 2: Bed capacity, outpatient clinic visits and inpatient admissions to three study pediatric hospitals, Bangalore city, January through December, 2006**

<table>
<thead>
<tr>
<th>Department</th>
<th>KIMS n (%)</th>
<th>IGICH n (%)</th>
<th>VVH n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td># Pediatric department beds</td>
<td>90 (23)</td>
<td>180 (46)</td>
<td>120 (31)</td>
<td>390 (100)</td>
</tr>
<tr>
<td># PICU beds</td>
<td>5 (16)</td>
<td>20 (65)</td>
<td>6 (19)</td>
<td>31 (100)</td>
</tr>
<tr>
<td># NICU beds</td>
<td>20 (33)</td>
<td>20 (33)</td>
<td>20 (33)</td>
<td>60 (100)</td>
</tr>
<tr>
<td># Annual OPD clinic visits</td>
<td>19,388 (18)</td>
<td>36,500 (33)</td>
<td>54,750 (49)</td>
<td>110,638 (100)</td>
</tr>
<tr>
<td># Annual Inpatient</td>
<td>3,635 (20)</td>
<td>7,300 (40)</td>
<td>7,300 (40)</td>
<td>18,235 (100)</td>
</tr>
</tbody>
</table>

*KIMS, Kempegowda Institute of Medical Science; IGICH, Indira Gandhi Institute of Child Health; VVH, Vani Vilas Hospital. PICU denotes pediatric intensive care unit; NICU denotes neonatal intensive care unit; OPD denotes outpatient. Row percents are shown, Admissions and OPD visits of patients: age group ≤16 years.
than five years of age. There were 967 (43.6%) pneumonia, 768 (34.6%) sepsis, and 484 (21.8%) meningitis hospitalizations. Among KIMS IBD-associated syndrome patients (104; 5% of total), 69 (66%) had pneumonia, 25 (24%) meningitis, and 10 (10%) sepsis. IGICH IPD syndrome patients (992; 45% of total) included 348 (35%) with pneumonia, 212 (21%) with meningitis, and 432 (44%) with sepsis. Of VVH BD-associated syndrome patients (1,123; 50% of total), 550 (49%) had pneumonia, 247 (22%) meningitis, and 326 (29%) sepsis [Table 4]. There were total 178 deaths in-hospital associated with sepsis, pneumonia or meningitis. Mortality was highest among infants (1 to 11 months) and deaths in this age group constituted 49% of total mortality due to IBD-associated syndromes. Twenty-three per cent of total mortality occurred in the age group 12--23 months, 13% of total mortality occurred in the age group 24--35 months, 11% of mortality occurred in the age group of 36--47 months and 3% of mortality was seen among children of 48--60 months. There were 87 (48.9% of all IBD-associated deaths) deaths associated with sepsis, 56 (31.5%) pneumonia-associated deaths, and 35 (19.7%) meningitis-associated deaths respectively [Table 5].

**Microbiology laboratory reports**

Microbiology laboratory records in the three study site hospitals showed a total of 4,509 blood specimens and 843 CSF specimens that were obtained from children less than five years of age from January--December 2006 [Table 6]. The total *S. pneumoniae* yield from children less than five years old was 1.14%. *S. pneumoniae* was isolated in 41 (0.9%) blood cultures and 19 (2.3%) CSF cultures. No pneumococcal isolates were identified from blood and CSF in infants aged one to 11 months [Table 7]. Among all pneumococcal isolates from blood, 24% were found in ages 12--23 months, 15% in children aged 24--35
months, 25% in those 36--47 months old and 36% in children aged 48--60 months. Among isolates of *S. pneumoniae* from CSF, 10% were from children 12--23 months of age, 30% from those 24--35 months old, 25% from children 36--47 months old, and 35% from children 48--60 months old. Although the latex agglutination test (LAT) for CSF was not done routinely in VVH, KIMS, and IGICH, 24 meningitis patients tested positive for *S. pneumoniae* by the LAT from January through December 2006.

**DISCUSSION**

The Bangalore southern zone has a total population of 150,945 children less than five years of age and this population is served by three large pediatric referral hospitals. From January--December 2006, there were total of 2,219 children hospitalized with IBD-associated
disease yielding an incidence of 15/1000 in the southern zone. Of these 2,219 hospitalizations, 967 (44%) were associated with pneumonia, 768 (35%) with sepsis and 484 (21%) with meningitis. Of these 2,219 IBD patients, 178 (8%) children died, including 87 (49%), with pneumonia, 56 (32%) with sepsis and 35 (20%) with meningitis, respectively. Mortality among infants (<12 months of age) was highest and constituted 49% of the total mortality associated with IBD syndromes. In our review of records in Bangalore hospitals, the total pneumococcal yield from microbiology cultures in children less than five years old who were admitted to study site hospitals was 1.14% during January-December 2006.

A number of studies from India have identified children and adults with PD-associated syndromes. These studies were done in a number of important geographic areas but the study methods varied substantially. The IBIS study was a four-year prospective hospital-based surveillance study in six large academic referral hospitals (New Delhi, Lucknow, Chennai, Thiruvanathapuram, and Vellore). The IBIS study found that 37% of enrolled children had meningitis, 30% pneumonia, 8% sepsis and 25% had other IPD-associated syndromes. In the IBIS study that enrolled patients of all age groups (33% of patients were less than five years of age), the laboratory yield for pneumococcus was 2.1%. *S. pneumoniae* was the most common etiological agent of community-acquired meningitis in all age groups accounting for 62% cases in a study done in the National Institute of Mental Health and Neuroscience (NIMHANS), Bangalore, India in the department of neuro-microbiology.

In Bangladesh, a study of PD among children less than five years of age showed that 24% of IPD cases presented with pneumonia, 62% with upper respiratory tract infections and 14% with other febrile disease. Overall, investigators reported an IPD incidence of 447/100,000 child-years. A retrospective study from Thailand reported culture-confirmed IPD among children aged two days to five years in which 44% presented with meningitis, 29% with pneumonia, 12% with sepsis, and 15% with peritonitis. In a population-based study from the United States, Robinson *et al.*, reported an IPD incidence among children less than two years of 167/100,000 and a disease syndrome distribution of 53% pneumonia, 40% bacteremia, and 5% meningitis. In Bamako, Mali, a prospective surveillance for IPD showed an IPD disease incidence of 84/100,000 in children less than three years, including 44% meningitis, 42% pneumonia and 13% with the diagnosis of other IPD-associated syndromes.

### Table 8: CSF isolates (*S. pneumoniae*) from children less than five years old admitted to KIMS, VVH, and IGICH January through December, 2006

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>Total</th>
<th>Age (months) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1-11</td>
</tr>
<tr>
<td>KIMS</td>
<td>9 (45)</td>
<td>-</td>
</tr>
<tr>
<td>IGICH</td>
<td>9 (45)</td>
<td>-</td>
</tr>
<tr>
<td>VVH</td>
<td>2 (10)</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>20 (100)</td>
<td>-</td>
</tr>
</tbody>
</table>

*KIMS, Kempegowda Institute of Medical Science; IGICH, Indira Gandhi Institute of Child Health; VVH, Vani Vilas Hospital; Data source: KIMS, VVH and IGICH Microbiology lab data; January through December 2006*
syndromes.[11] In Costa Rica, Arguedas et al., conducted a seven-year survey among children from 0 to 11 years of age and found that meningitis (41.5%) was the most common IPD-associated syndrome, followed by pneumonia (26.7%), bacteremia (22.2%), peritonitis (7.4%), septic arthritis (1.5%), and osteomyelitis (0.7%). In Costa Rica, the IPD CFR was 14.4% and children less than two years of age had the highest rates of complications, sequelae and death.

In the course of establishing and sustaining prospective, population-based surveillance for IPD, a number of barriers may be encountered including huge geographic area, absence of national surveillance system for IBD and the widespread use of pre-hospitalization antibiotics. Laboratory services are one of the most neglected areas of healthcare in developing countries including India. Unreliable and inaccurate laboratory diagnostic testing leads to unnecessary expenditures in a region already plagued by resource shortages and these practices promote the perception that laboratory testing is both unhelpful and risks compromising patient care. The use of pre-hospitalization antibiotics further reduces the bacterial isolation rates. In our review, prior treatment with antibiotics may, in part, explain the lack of pneumococcal isolates found in blood and CSF cultures of infants (0-11 months). In addition, the reluctance of parents to give up their infant’s blood or CSF for testing, de-emphasis of laboratory testing even when available as clinicians often perceive them as unreliable and unhelpful, scarcity of skilled healthcare personnel, and the lack of consumable supplies (e.g., butterfly needles for specimen collection) may also explain low isolation rates of \( S. \ pneumoniae \) among the 0-11 months age group.[12-15]

In the development of prospective, population-based studies, the identification of an appropriate field site is a critical activity. Bangalore is a city with a population of diverse origin which represents different parts of India. Among our three study site hospitals (serving patients from the southern zone of Bangalore), two are public (consultation and treatment are provided free of charge) and one is privately owned and operated. Because of this patient mix, we expect to have a more accurate representation of all patient classes from the southern zone in this study by including these three major pediatric hospitals. Our review of this field site in Bangalore suggests that it is possible to develop a patient referral system that encourages care of children with signs and symptoms of IBD and living in the southern zone of Bangalore.

For this study site development, the polio surveillance office, EPI office and state census office provided data on the population distribution in the area selected for study. Other study activities have included the recruitment of clinical study personnel who will identify, define, and measure PD-associated syndromes starting with activities from recruitment of patients to collection and entry of study data. Before initiating surveillance, study personnel will be trained in clinical, epidemiologic, and microbiology methods that are required for this study. Periodic monitoring is planned to evaluate the usefulness and quality of surveillance.

In Bangalore, the definition of a catchment
area for this study is challenging because many patients participating in the study may not be able to report their address due to low literacy. In some hospitals, systematic or computerized patient records containing clinical and microbiology data are not maintained. In some hospitals, paper medical records are available but there is incomplete recording of clinical data. In Bangalore, patterns of patient hospital utilization are incompletely understood because there is no requirement or guideline for patients to seek care at specific hospitals. All of these issues pose challenges in evaluating available data during a retrospective site evaluation.

There are certain limitations to this study. First, while analyzing residence information for patients, we found some address information was incomplete. These missing data made it impossible to determine the zone of residence for some patients. Also, the diagnoses of IBD-associated syndromes were identified in records with ICD-9 CM codes but they were not all confirmed with blood or other sterile body fluid bacterial cultures. Patients presenting to our study site hospitals may not reflect the spectrum of S. pneumoniae disease in the community, however, two of three study hospitals are public hospitals and there is no charge for patient treatment. Therefore, we believe that patients who may be enrolled in a southern zone field site are likely to originate from a broad range of economic strata. Pneumonia accounts for 19% of the 10 million childhood deaths worldwide.\[5\]

Up to half of all cases of severe childhood pneumonia are caused by pneumococcus in developing countries.\[16\] Pneumococcal conjugate vaccines are shown to be safe, immunogenic, effective and induce immunological memory in infants.\[17\] Based on our review of available hospitalization data, the burden of disease associated with IBD in Bangalore appears to be high. To achieve success in a prospective study of childhood IPD conducted in Bangalore, there will need to be a high level of cooperation among healthcare institutions, clinicians, epidemiologists and microbiologists. Such collaborations must be sustained over time and involve public-private partnerships. Our data suggest that local institutions have the capacity to successfully complete population-based surveillance. Thus, a prospective surveillance study of IBD is expected to provide critical data on the disease burden in a representative Indian population that will support public health policy development in India.

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REFERENCES

4. Invasive Bacterial Infection Surveillance Group,
INCLEN. Prospective multicentre hospital surveillance of *Streptococcus pneumoniae* disease in India. The lancet 1999;353:1216-21.


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