Age- and Cause-specific Childhood Mortality in Lombok, Indonesia, as a Factor for Determining the Appropriateness of Introducing *Haemophilus influenzae* Type b and Pneumococcal Vaccines

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ABSTRACT

Using age and cause-specific childhood mortality in Lombok, Indonesia, as a factor for determining the appropriateness of introducing *Haemophilus influenzae* type b (Hib) and pneumococcal vaccines, the study describes a cross-sectional, hamlet-level mortality survey in 40 of 305 villages in Lombok Island, Indonesia. Causes of death were assessed with a standardized verbal-autopsy questionnaire. One thousand four hundred ninety-nine births and 141 deaths occurring among children aged less than 2 years were identified, with 43% of deaths occurring during the first 2 months of life. The infant mortality rate was 89 (95% CI: 75, 104) per 1,000 live-births. All mortality rates are reported per 1,000 live-births. To examine children whose deaths could potentially have been prevented through vaccination with Hib or pneumococcal vaccine, deaths due to acute respiratory infection (ARI) and central nervous system (CNS) infections among children, aged 2-23 months, were analyzed. ARI and CNS infections caused 58% (mortality rate: 31 per 1,000 live-births; 95% CI: 23, 41) and 17% (mortality rate: 9 per 1,000 live-births; 95% CI: 5, 16), respectively, of all deaths within this age group. Between the ages of 2 and 23 months, 5% of all babies born alive died of ARI, and another 1% died of CNS infections. Our results indicate that current efforts to reduce childhood mortality should focus on reducing ARI and meningitis. These efforts should include evaluating the impact of Hib and pneumococcal vaccines within the routine Expanded Programme on Immunization system.

Key words: Infant mortality; Child mortality; Acute respiratory infections; *Haemophilus influenzae*; Pneumococcal vaccines; Cross-sectional studies

INTRODUCTION

Lombok has about three-quarters of the population of the eastern Indonesian province of Nusa Tenggara Barat (NTB). NTB has consistently had the highest infant mortality rate in Indonesia. The infant mortality rate figures from various sources for 1995-1997 ranged between 83 and 111 per 1,000 live-births (1,2).
To gather current mortality data in Lombok, we developed and implemented a rapid assessment system based on a review of the existing health records supplemented by targeted household interviews. The purpose for conducting the survey was to collect data on age- and cause-specific mortality rates to evaluate the potential impact on mortality of adding *Haemophilus influenzae* type b (Hib) and pneumococcal conjugate vaccines to the routine Expanded Programme on Immunization (EPI) in Indonesia. Since Hib and pneumococcus may be significant causes of acute respiratory infection (ARI) and meningitis, these were of particular interest. The mortality survey was conducted as a baseline for a study in Lombok examining the proportion of radiologically-confirmed pneumonia and other pneumonias due to Hib, using Hib conjugate vaccine as a probe. The Hib-pneumonia study runs from 1998 to 2002.

**METHODS AND MATERIALS**

**Study site**

Lombok Island is located near the centre of the Indonesian archipelago, 30 km east of Bali. The population (2.6 million) is predominantly Muslim and of the Sasaek ethnic group. A rural agrarian economy predominates. Mataram—the provincial capital—is the largest city, with an urban population of approximately 325,000. In 1997, 40 of Lombok’s 305 villages were selected to participate in the Hib-pneumonia study. Ten villages were selected from each of Lombok’s 4 districts, based on their previous participation in health projects, their ability to refer pneumonia cases to hospitals, and their socioeconomic and geographic diversity. Each village was divided into a number of smaller units called hamlets, varying in size from 500 to 2,000 inhabitants.

Rather than randomly selecting villages from the entire island, we used the 40 villages selected for participation in the Hib-pneumonia study as the population base for the current mortality survey. This decision was made for several reasons. In the 40 study villages, previous work had been performed to improve birth and death recording and to implement the verbal autopsy; information from other villages would have been of varying and unknown quality. Working relationships had already been developed between the study team and many of the healthcare providers in these villages. Finally, mortality data from these 40 villages would be of more direct relevance to the Hib-pneumonia study.

**Data-collection method**

Mortality data were collected by 12 provincial-level staff of the Indonesian Ministry of Health and field staff of a Lombok-based non-government health organization. These 12 interviewers spent 2 weeks conducting field visits. Village nurses and midwives provided health centre records for each study hamlet. Hamlet leaders and volunteers of the monthly integrated health posts provided input and assisted in the interviews. The study year (365 to 380 days, depending on interview date) ran from 11 February 1997—the Muslim holiday of Eid-ul-Fitr—to the study interview date, between 11 February and 26 February 1998. Marking the end of the Ramadan fasting month, Eid-ul-Fitr was selected as the beginning date of the study year, since it provided a distinct reference date for most Lombok residents. It was assumed that people would more easily recall whether a death occurred before or after Eid-ul-Fitr than in any other month. We ascertained all births and deaths among children aged less than 2 years that occurred during the study year.

As the first step in determining the number of births and deaths within the study year, health centre records were checked. These records have been the focus of a long-term child-survival project, but had not been validated by an independent survey. From these records, we made a list of all births in each hamlet that occurred since 11 February 1995 to assist with locating all deaths among children aged less than 2 years that occurred since 11 February 1997. This list was then reviewed with the nurse and midwife from that village. Any other births or deaths known to the staff were added to the list. The revised list was then taken to the hamlet and reviewed by several community members: the hamlet leader, members of the Indonesian Family Welfare Movement (a nationwide volunteer organization for family planning and community health), and when available, traditional birth attendants. Each name was discussed and noted as living, dead, moved, or unknown. Names not found in the list were identified and recorded. Exact dates of deaths were recorded, if known.

The accuracy of the health centre records was evaluated during data collection. Birth records contained 90-100% of the actual births, and death records contained 70-80% of the actual deaths confirmed through interviews. Approximately, 10% of infants moved in or out of their places of birth prior to their second birthday.

The homes of all children listed as dead or of unknown status were visited. The mothers or closest relatives of dead children were interviewed to determine the cause of death using a verbal-autopsy form (described below). Dates of death were determined as accurately as possible, using memorable events, such as the previous Eid-ul-Fitr celebrations. All mothers and community leaders interviewed were asked if they knew of other infant deaths since the last Eid-ul-Fitr holiday, or of any recent births. Any additional birth and death reports were followed up for interview.

Deaths which occurred between 11 February 1997 and the time of the study were used as numerators for...
all mortality calculations. A “2-23-month mortality” rate was determined to examine children whose deaths potentially could have been prevented through immunization with Hib or pneumococcal conjugate vaccines (if implemented, immunization with these vaccines in Lombok would begin at 6 weeks of age). Deaths among children aged over 60 days but less than 731 days were used for the numerator of 2-23-month mortality rates. Infants were defined as children aged less than one year.

Verbal autopsy
A verbal autopsy was used for determining the cause of death. The verbal-autopsy questionnaire was adapted for local use from a questionnaire developed by the Society for Education, Action, and Research in Community Health (SEARCH) project in India (4, 5). The SEARCH group developed a set of standardized criteria for determining the cause of death among children by verbal autopsy. The criteria were based on validation and field studies in an area of India with mortality patterns similar to Lombok. Since 1994, this system had been used and refined in Lombok for a child-survival project, although the questionnaire was not validated locally. The system used a structured questionnaire that a midwife administered to the person who was closest physically to the deceased before death—usually the mother. If affirmative responses were obtained about physical presence of a relative during death, he or she was interviewed for cause of death. Questionnaire and cause-of-death assignment were reviewed by a physician for consistency. The system allowed for multiple causes of death and classified causes of death as possible or probable. However, only probable causes of death were used for calculating cause-specific mortality reported in this study. If difficult or fast breathing for more than 2 hours before death was reported, along with fever or cough for more than 3 days, blue lips or inability to eat or drink, the verbal autopsy assigned ARI as the probable cause of death. A probable CNS infection-related death was assigned if fever and convulsions occurred in association with unconsciousness or decreased level of consciousness.

Sample size and selection of study hamlets
Sample size was calculated with the Statcalc function in Epi Info version 6.04 statistical software. Using the calculator for a population survey, we estimated that the population of the 40 study villages was 10,000; that the mortality rate among children aged less than 2 years was 100 per 1,000 live-births (10%); and that if this was the actual mortality rate, the lowest result we would accept would be 80 per 1,000 live-births (8%). With these data, and using a 95% confidence interval (CI), we estimated a required sample size of 796 births. Based on previous estimates of birth rates per hamlet, we estimated that 60 hamlets would provide this number of births. Hamlets were randomly selected using a random number generator.

Statistical analysis
All mortality rates are presented as deaths per 1,000 live-births. Exact 95% CIs were calculated with Epi Info version 6.04 software.

RESULTS
From a population of approximately 67,100, the study identified 1,499 births and 141 deaths. This included 34 deaths among infants aged less than 29 days, 26 deaths among infants aged 29-60 days, 73 deaths among infants aged 2-11 months, and 8 deaths among children aged 12-23 months. The age-specific mortality rates were 40 (95% CI: 31, 51) per 1,000 live-births for infants aged less than 2 months; 54 (95% CI: 43, 67) for children aged 2-23 months; and an infant mortality rate of 89 (95% CI: 75, 104). Stated proportionally, neonatal mortality represented 26% of infant mortality, mortality among infants aged less than 2 months represented 45% of infant mortality, and mortality among children aged 2-23 months represented 57% of mortality among all children aged less than 2 years.

Verbal autopsy provided cause-of-death information for all deaths. ARI, CNS infections, diarrhoea, complications of delivery, and prematurity/low birthweight were the most commonly-assigned causes of death (Table 1). Diseases preventable through vaccinations included in the current Indonesian EPI (diphtheria, pertussis, tetanus, polio, tuberculosis, measles, and hepatitis B) accounted for 3% of infant deaths; specifically, 2 deaths from neonatal tetanus and 2 from pertussis.

The median age of death was 2 months, while the mean age of death was 3.9 months. Age distribution of deaths varied among the main causes, i.e. ARI, CNS infections, and diarrhoea (Fig. 1). ARI-related deaths occurred at a median age of 3 months compared to 7 months for CNS infections and 9.5 months for diarrhoea.

Births per month ranged from 103 to 153. Seasonal variability was seen for all deaths (range: 6-6 per month), and particularly for ARI deaths (range: 3-14 per month). The peak months of ARI deaths were February through April, and corresponded to the seasonal transition from wet season to dry season (Fig. 2).

The Mataram urban district showed significantly lower mortality than in the rural areas of Lombok. Mataram and the rural districts of West, Central, and East Lombok showed infant mortality rates of 46 (95% CI: 30, 69), 108 (95% CI: 79, 145), 109 (95% CI: 75, 152), and 112 (95% CI: 81, 150) respectively.
There were significant differences between the urban and rural districts in cause-specific mortality rates (Table 2). Fifty-two percent of deaths (in children aged less than 2 years) in urban areas were related to prematurity, low birth-weight, or complications of delivery, while only 7% of deaths in rural areas were due to conditions relating to these causes. CNS infections showed a higher prevalence in rural areas, accounting for 14% of rural and 4% of urban deaths. ARI-related deaths were similar between the urban and rural areas, accounting for 43% of urban and 50% of rural deaths. The median age of death from all cases was 1 month in urban Mataram and 3 months in the rural districts. The median age of CNS infection-related death was 4 months in urban Mataram and 7.5 months in the rural districts.

**DISCUSSION**

Almost 10% of the children in our study area died before 2 years of age—a finding consistent with official government figures (1). Fifty-seven percent of these deaths occurred in children aged over 2 months, and among the 2-23-month age group, our verbal autopsy assigned ARI and CNS infections as the causes of death for 58% and 17% respectively. A portion of these deaths should be preventable using currently-available Hib and pneumococcal conjugate vaccines. Using radiologically-
defined pneumonia among children aged 2-23 months as the outcome, a study in Gambia found that Hib conjugate vaccine prevented 20% of pneumonias (6), while in California, the newly-licensed 7-valent pneumococcal conjugate vaccine prevented 70% of radiologically-confirmed pneumonias (7). The proportion of pneumonias due to these two organisms in Lombok remains unknown. The authors of the current study are part of a team conducting a randomized placebo-controlled trial of Hib conjugate vaccine to determine the proportion of pneumonia due to Hib in Lombok. Future studies will examine the contribution of pneumococcus to morbidity and mortality due to pneumonia and meningitis.

Over 1% of the children born in rural areas died before 2 years of age, with CNS infections assigned as the cause of death, indicating that the caretakers reported
seizure as a common preterminal event. Seizures may occur from a variety of causes, including causes not related to CNS infections. Additionally, the local translation of the word seizure may connote stiffness rather than shaking. Despite these limitations, it is likely that a substantial proportion of these deaths resulted from CNS infections, including viral encephalitis and viral and bacterial meningitis. The case-fatality rates of CNS infections may be exacerbated in Lombok, because traditional beliefs in rural areas encourage treatment for convulsions and consciousness-altering symptoms by traditional healers rather than the recommended health systems. While altering these long-established cultural patterns may be difficult, vaccines are currently available to prevent the 3 most common causes of childhood bacterial meningitis: Hib, pneumococcus, and meningococcus.

Previous intervention projects in Lombok have focused on decreasing deaths due to diarrhoea and deaths preventable with current EPI vaccines. The success of these projects is evidenced by the high immunization rates (Table 3) and low number of deaths that were identified in our study due to these causes. For example, this study found a neonatal, tetanus-specific infant mortality rate of 1 per 1,000 live-births. In 1988, neonatal tetanus was responsible for up to 40% of neonatal deaths in Indonesia (8). Our results indicate that current efforts to reduce the infant mortality rate in Lombok should focus on reducing ARI.

Vaccines are not the only intervention to decrease morbidity and mortality due to ARI and CNS infections. Other areas of Indonesia and neighbouring countries do not include Hib conjugate vaccine in their routine EPI. Yet, the 1996 infant mortality rate in Indonesia was 47, while the 1996 infant mortality rates among close neighbours–Malaysia and the Philippines–were 11 and 32 respectively (9). Improving the clinical care of infants with pneumonia has been shown through other studies to be an effective method of reducing ARI-related mortality (10). In Lombok, improved clinical care will require improvements in identification, referral, and treatment through improving maternal education and removing barriers to care. This recommendation is reinforced by our finding that urban childhood mortality rates were lower than rural childhood mortality rates, a finding that has been true throughout Indonesia (2). Compared to the urban centre, rural areas of Lombok have lower female literacy and educational attainment, lower income, fewer births attended by a health worker, and a lower life expectancy (Table 3). Although preventative health services, such as antenatal care and immunization, are high in both urban and rural areas, access to obstetric and paediatric services may differ by rural status. For example, several obstetrical care and

### Table 3. Education, economic, and health factors among different districts in Lombok Island, Indonesia

<table>
<thead>
<tr>
<th>Possible factor</th>
<th>Urban areas</th>
<th>Rural areas</th>
<th>Urban areas</th>
<th>Rural areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women’s literacy (women’s age &gt;10 years) (13)</td>
<td>82%</td>
<td>62%</td>
<td>63%</td>
<td>70%</td>
</tr>
<tr>
<td>Education level (persons &gt;10 years old who attended or graduated from elementary school) (13)</td>
<td>80%</td>
<td>65%</td>
<td>65%</td>
<td>69%</td>
</tr>
<tr>
<td>Income % of working population earning over Rp 130,000 (approx. US$ 20) per month†</td>
<td>70%</td>
<td>43%</td>
<td>38%</td>
<td>40%</td>
</tr>
<tr>
<td>Life expectancy (13)</td>
<td>62.9 years</td>
<td>57.7 years</td>
<td>55.1 years</td>
<td>52.5 years</td>
</tr>
<tr>
<td>Antenatal care (women receiving at least 4 check-ups during pregnancy)‡,§</td>
<td>78%</td>
<td>77%</td>
<td></td>
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</tr>
<tr>
<td>Safe birth (birth attended by health personnel)‡,§</td>
<td>54%</td>
<td>21%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete immunization (by age 1 year)‡,§</td>
<td>76%</td>
<td>84%</td>
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</tbody>
</table>

birth-related private practices exist in the urban district, while none exist in the rural areas; distances to hospitals are greater in rural areas; and discussions with local healthcare providers indicate a much higher level of traditional practices in birth and infant care in the rural districts.

At the time of the current study, the verbal autopsy had not been validated. We have collected surveillance data on children admitted to the hospital for physician-diagnosed severe pneumonia during 1998. Overall, 69 children admitted for severe pneumonia died, and 58 of these had a verbal autopsy performed. Of the 58 children, the verbal autopsy assigned ARI as the cause of death for 52 (90%). All children included in the hospital database were admitted with physician-diagnosed severe pneumonia. This means that the sensitivity of the verbal autopsy for ARI deaths, using physician-diagnosed pneumonia as the gold standard, was 90%. This sensitivity is equal to or better than that reported from the WHO survey instrument in 3 countries, using radiologically-proven pneumonia as the gold standard (11). Since only pneumonia cases were collected, specificity could not be calculated. Although malaria has been shown to have a confounding effect on verbal-autopsy results, particularly for the diagnosis of ARI (12), the ongoing Hib-pneumonia study found among its study sites that less than 1% of the children admitted for pneumonia had malaria.

Other than a lack of specificity data for the verbal autopsy, the major limitation of the current study was that our sample was taken from 40 villages selected for the Hib-pneumonia study, and not selected randomly. It is likely that these 40 villages have better health status than the remainder of the island, since they were chosen partly because of their proximity to one of the 3 major hospitals in the island, as well as to a well-functioning primary health clinic. Consequently, we may have underestimated overall mortality as well as vaccine-preventable disease mortality.

Our finding that over 5% of all children born in Lombok died of ARI, while less than 1% died of diarrhoea and diseases preventable with current EPI vaccines, suggests a clear priority for future health efforts in Lombok. Improvements in community education, diagnosis capability, treatment availability, and hospital referral are needed, while vaccine-feasibility studies may lead to introduction of effective new measures in the control of ARI and CNS infections. Improvements in both clinical care and vaccine introduction will require that considerable local, national and international resources be mobilized. Moreover, the relative priority to be placed on these 2 interventions will require careful assessment of cost and benefits of each.

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