Establishment of the MAL-ED Birth Cohort Study Site in Vellore, Southern India

Sushil M. John,1 Rahul J. Thomas,2 Shiny Kaki,2 Srujan L. Sharma,2 Karthikeyan Ramanujam,2 Mohan V. Raghava,3 Beena Koshy,4 Anuradha Bose,2 Anuradha Rose,2 Winsley Rose,5 Anup Ramachandran,2 A. J. Joseph,2 Sudhir Babji,2 and Gagandeep Kang2

1Low Cost Effective Care Unit, 2Department of Gastrointestinal Sciences, 3Department of Community Health, 4Department of Developmental Pediatrics, and 5Department of Child Health, Christian Medical College, Vellore, India

The Indian Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) site is in Vellore, Tamil Nadu, in south India and is coordinated by the Christian Medical College, Vellore, which has many years of experience in establishing and following cohorts. India is a diverse country, and no single area can be representative with regard to many health and socioeconomic indicators. The site in Vellore is an urban semiorganized settlement or slum. In the study site, the average family size is 5.7, adults who are gainfully employed are mostly unskilled laborers, and 51% of the population uses the field as their toilet facility. Previous studies from Vellore slums have reported stunting in well over a third of children, comparable to national estimates. The infant mortality rate is 38 per 1000 live births, with deaths due mainly to perinatal and infectious causes. Rigorous staff training, monitoring, supervision and refinement of tools have been essential to maintaining the quality of the significantly large quantity of data collected. Establishing a field clinic within the site has minimized inconvenience to participants and researchers and enabled better rapport with the community and better follow-up. These factors contribute to the wealth of information that will be generated from the MAL-ED multisite cohort, which will improve our understanding of enteric infections and its interactions with malnutrition and development of young children.

Keywords. birth cohort; India; malnutrition; MAL-ED.

The strengths of longitudinal studies lie in their ability to document the natural history of outcomes over time and to elucidate temporal and possibly causal relationships among variables. Although expensive, long, and difficult, cohort studies largely overcome the problems of recall and can be used to investigate multiple exposures and determinants with a low possibility of selection bias, recall bias, and confounding [1, 2].

MATERIALS AND METHODS

The 2005–2006 Indian National Family Health Survey 3 (NFHS 3), a nationally representative survey, showed that 48% of Indian children <5 years old were stunted, 43% underweight, and 20% wasted [3]. It was estimated that in India about 54% of deaths in children <5 years old were related to malnutrition, and approximately 70% of children aged 6–59 months have some level of anemia [3]. Given these alarming statistics and a large population that contributes to nearly one-fourth of all
deaths and malnutrition in children <5 years old worldwide, the 
Indian cohort represents an important part of the MAL-ED 
study.

The Christian Medical College, Vellore (CMC), is located in 
the southern Indian state of Tamil Nadu and has many years of 
experience and expertise in setting up and following cohorts for 
various studies, in particular the documentation of infections 
and morbidity and growth [4–6]. However, CMC has not par-
ticipated in a multisite cohort study with standardized methods. 
In this article, we describe the establishment of the MAL-ED 
study site and its relationship to the surrounding community 
and discuss the need for specific approaches.

MAL-ED India Cohort Study Site
The MAL-ED study site is located in Vellore, a city with a pop-
ulation of approximately 500 000 inhabitants about 130 km 
from Chennai, the capital of the southern state of Tamil 
Nadu and the nearest large city. The climate of Tamil Nadu 
ranges from dry subhumid to semiarid. The state has 3 distinct 
seasons: advancing monsoon with the southwest monsoon from 
June to September; the northeast monsoon period from Octo-
ber to December; and the dry season from January to May. The 
language predominantly spoken is Tamil, and the main religion 
is Hinduism (89%); Muslims and Christians comprise 11% of 
the state’s population.

The CMC is a private, not-for-profit medical school and 
2600-bed referral hospital. It has 1.6 million outpatient visits 
and 120 000 inpatient admissions annually and also provides 
primary and secondary care to local residents and approximately 
250 000 residents of periurban and rural service areas through 
a range of outreach facilities.

Old Town, Salavanpet, and neighboring areas in central Vellore 
have an approximate population of 13 000. The CMC Low Cost 
Effective Care Unit provides healthcare to the 13 000 residents of 
this low-income urban population through field visits, clinic, and 
outpatient and inpatient services at a small base hospital. Because 
CMC personnel were aware of the basic population demographics 
and anticipated an appropriate recruitment and retention rate for 
the MAL-ED study, Old Town, Salavanpet, and neighboring areas 
in central Vellore were selected as the cohort sites.
Data Sources
Several service areas of CMC in Vellore were previously mapped, and a geographic database was created. In 2007–2008, a population survey and geographic information system mapping were completed in the MAL-ED study area of Old Town, Salavanpet, and contiguous areas before the start of MAL-ED cohort recruitment. A demographic survey form was completed, and geographic coordinates of each household were obtained with a hand-held global positioning system (GPS) receiver (Garmin GPS V; Garmin International). The “way points” and “track points” provided by the GPS were downloaded using GPS Utility 4.10.4 software (GPS Utility). The points were then converted to “shape files” using ArcView GIS 9 and 10 software (Environmental Systems Research). Two data entry operators performed double data entry of the demographic data collection using Epi-Info software (version 3.5.1; Centers for Disease Control and Prevention), and the 2 data sets were compared and cross-verified with the questionnaires. All data collection and entry procedures followed MAL-ED study protocols [7].

MAL-ED India Study Recruitment
For study recruitment, a team of field workers identified pregnant women and new births in the area [8]. The size of the study catchment area was chosen based on the expected recruitment of approximately 10 children per month over a period of 2 years, such that every child born within the study area had the opportunity to participate in the study. Recruitment began in March 2010 and ended in February 2012.

Establishment of a Study Clinic
A study clinic was established in the catchment area to provide a space for the intensive examinations and procedures required for the study. The lack of privacy and small size of most study households were limiting factors in conducting examinations within the homes. The study clinic is used for anthropometry, sample collection, cognitive function testing, and first-line medical evaluation and treatment. The clinic serves as the central base for all MAL-ED study-related activities and procedures for participants and study staff; central data management is done elsewhere.

Study Staff Recruitment and Training
The complex and intensive assessments of the MAL-ED study required that the study staff be both appropriately trained and monitored during the study to ensure a high and consistent level of performance and adherence to study specific procedures. For the India Vellore study site, a faculty member or co-investigator was assigned to lead and supervise each aspect of the study: field workers and supervisors and clinic staff (S. M. J.), dietitians (A. B.), data entry operators and manager (M. V. R. and A. Ro.), psychologists (B. K.), and microbiologists and technicians (S. B., A. J. J., and A. Ra.). Study staff was hired and trained before the start of the study, and their performance was assessed and retraining provided whenever necessary before and during the study.

Ethics Review
Before subject recruitment permission was obtained from the CMC Institutional Review Board and the Indian government’s Health Ministry Screening Committee.

RESULTS
The MAL-ED study area and its relationship to Vellore are shown in Figure 1. The study area is crowded with a population density of nearly 42 000/km². The main occupation of the men is daily wage labor in the local market, with work in small shops, and a small proportion are skilled laborers. Women work at home or as daily wage laborers. In general, the state of Tamil Nadu has better health statistics than the rest of India, as shown in Table 1. The data collected from the study site before initiation of recruitment enabled comparison of the recruited children and their families with the population of the whole study area (Table 2).
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Vellore Area</th>
<th>MAL-ED Cohort Families</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational level for head of household, mean (range), y</td>
<td>4.06 (0–17)</td>
<td>6.81 (0–18)</td>
</tr>
<tr>
<td>Highest educational level in family, mean (range), y</td>
<td>8.52 (0–20)</td>
<td>NA</td>
</tr>
<tr>
<td>Family size, mean (range), No.</td>
<td>4.56 (1–19)</td>
<td>5.70 (3–13)</td>
</tr>
<tr>
<td>Age distribution, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–19</td>
<td>35</td>
<td>NA</td>
</tr>
<tr>
<td>20–34</td>
<td>32</td>
<td>NA</td>
</tr>
<tr>
<td>≥35</td>
<td>33</td>
<td>NA</td>
</tr>
<tr>
<td>Occupation, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agriculture-related occupation</td>
<td>0.1</td>
<td>NA</td>
</tr>
<tr>
<td>Skilled labor</td>
<td>5.9</td>
<td>NA</td>
</tr>
<tr>
<td>Small business owner</td>
<td>0.8</td>
<td>NA</td>
</tr>
<tr>
<td>Service-related occupation</td>
<td>1.4</td>
<td>NA</td>
</tr>
<tr>
<td>High-income group/professionals</td>
<td>0.2</td>
<td>NA</td>
</tr>
<tr>
<td>Unskilled labor</td>
<td>33.1</td>
<td>NA</td>
</tr>
<tr>
<td>Not gainfully employed (including students)</td>
<td>58.5</td>
<td>NA</td>
</tr>
<tr>
<td>Type of house, No. (%) of households</td>
<td>Pucca in 753 (37), mixed in 628 (31), and kutcha in 666 (32)*</td>
<td>Main floor material: earth, sand, clay, mud, or dung in 14 (6), ceramic tiles in 23 (10), and cement or concrete in 198 (84); main roof material: thatch in 45 (19), tiles in 30 (13), and other in 159 (68); main exterior wall material: mud in 36 (15), cement or concrete in 190 (81), and other in 9 (4)</td>
</tr>
<tr>
<td>Rooms in house, mean (range), No.</td>
<td>2 (1–6)</td>
<td>2 (1–6) (separate kitchen in 102 households [43%])</td>
</tr>
<tr>
<td>Main source of drinking water, No. (%) of households</td>
<td>Public tap in 1862 (91), public bore well (hand pump) in 42 (2), public bore well (tap) in 17 (1), tanker in 30 (2), private bore well in 15 (1), private well in 5 (&lt;1), water cans in 17 (1), and house tap in 59 (3)</td>
<td>Piped into dwelling in 2 (1), piped to yard or plot in 15 (6), public tap or stand pipe in 201 (86), and tube well or bore hole in 17 (7)</td>
</tr>
<tr>
<td>Cooking mode, No. (%) of households</td>
<td>Firewood in 1322 (65), kerosene stove in 538 (26), gas stove in 159 (8), and &gt;1 cooking mode in 28 (1)</td>
<td>Kerosene stove in 89 (38), gas stove in 61 (26), open fire in 80 (34), open fire or stove with chimney or hood in 3 (1), and electric heaters in 2 (1)</td>
</tr>
<tr>
<td>Place of cooking, No. (%) of households</td>
<td>Outside of house in 47 (2), inside of house in 1778 (87), and separate kitchen in 222 (11)</td>
<td>Outside of house in 53 (22), inside of house in 180 (77), and both in 2 (1)</td>
</tr>
<tr>
<td>Possessions, No. (%) of households</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fan</td>
<td>1676 (82)</td>
<td>223 (95)</td>
</tr>
<tr>
<td>Tape recorder</td>
<td>505 (25)</td>
<td>NA</td>
</tr>
<tr>
<td>Transistor radio</td>
<td>NA</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Television</td>
<td>None or government provided in 1203 (59), black and white in 220 (11), and color in 624 (30)</td>
<td>222 (94)</td>
</tr>
<tr>
<td>Vehicle</td>
<td>None in 1156 (57), nonmotorized in 532 (26), motorized in 315 (15), and both in 44 (2)</td>
<td>Bicycle in 96 (41)</td>
</tr>
<tr>
<td>Cupboards</td>
<td>Steel cupboard in 4995 (53)</td>
<td>Cupboards in 49 (21)</td>
</tr>
<tr>
<td>Telephone</td>
<td>None in 1273 (62), landline in 324 (16), cell phone in 442 (22), and both in 8 (&lt;1)</td>
<td>Cell phone in 198 (84)</td>
</tr>
<tr>
<td>Electricity, No. (%) of households</td>
<td>NA</td>
<td>230 (98)</td>
</tr>
<tr>
<td>Toilet facility, No. (%) of households</td>
<td>NA</td>
<td>No facility, bush, or field in 119 (51), pit latrine in 3 (1), flush to piped sewer system in 2 (1), flush to septic tank in 21 (9), flush to somewhere else in 83 (35), and other in 7 (3)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not available (or data not collected).

*Pucca means brick and cement walls with a concrete or tile roof; mixed, brick and cement walls with a roof of asbestos, thatched leaves, or tin; and kutcha, walls and roof of mud, tin, asbestos, or thatched leaves.
DISCUSSION

Longitudinal birth cohort studies provide a rich source of information about antecedents of diseases that originate in pregnancy or childhood [1]. Although Tamil Nadu is not representative of all parts of India, it is not always possible to conduct a complex study in all settings. Given that previous cohort studies in Vellore [9] have shown stunting of well over a third of children in similar slum settings, the MAL-ED Vellore study site is expected to yield valuable data on enteric infections and malnutrition.

Although most indicators from the data collected are broadly similar between the Vellore population and the study children and families, it is interesting to note that between the prerecruitment survey and the end of the 2-year recruitment period, the proportion of families with cell phones increased very rapidly; by 2012, most families had ≥1 cell phone.

As anticipated by the study investigators, subject recruitment and the collection of specimens in young children was a challenge owing to the cultural practice of going to the mother’s natal home for delivery and the first few weeks of the newborn’s life. However, overall the proportion of eligible families who refused participation in the study was <10%. After recruitment, retention rates were also high, with only a few families discontinuing participation, mainly because of migration out of the study area. Recognizing that participation in a longitudinal study is demanding for families, it is best to try to minimize inconvenience to participants.

Regarding the quality control of data, the most important emphasis is on proper staff training and monitoring. It is essential to select study staff with adequate skills in communication and the ability to build rapport with the community. Pilot testing of forms and surveys and staff training were extremely important though it involved cost, effort, and time. In populations with limited education and low literacy, regular communication with study participants at all levels was important. Given the level of data collection and monitoring within the MAL-ED cohort, the supervision of study staff was essential to maintaining data quality. Having a base at the study clinic that both study families and staff could reach rapidly was important for quick responses and follow-up when necessary. A system of weekly staff meetings and monthly reviews by all study site investigators ensured that updated information was available and lags in data generation was minimized.

CONCLUSION

The MAL-ED multisite cohort study will provide critical information for understanding which geographic, social, cultural, biological, and nutritional factors play major roles in physical growth, cognitive development, and immune response. The close integration of the study sites and central teams has been necessary to ensure high-quality data. Longitudinal studies are expensive undertakings, and to fully make use of them requires careful coordination and planning. In the MAL-ED Network, the development of harmonized protocols and tools and the refinement of their use to ensure high-quality data have been at the core of network activities.

Notes

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