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# Developing Neonatal Health Research Networks: Challenges, Lessons and Wider Implications

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## Introduction

It is widely recognized that India's future lies in emerging as a knowledge society. This would require that we build an all-round capacity to explore new frontiers in sciences, to innovate at the cutting edge of technology, and to use the knowledge gains to uplift the society. For the overall progress of the nation, we have to excel in all spheres of science and technology including the biomedical disciplines.

Biomedical research today has a wide landscape. It encompasses basic, translational, clinical, community and health systems research. Major, decisive research in any of these domains today would often require large and complementary technological resources, patients and populations - beyond the capacity of a single individual or institution. Although individual-based research would always be relevant, exciting, and at times, game-changing, it is often not possible to answer the big questions in health without mounting a multi-centre research effort. Can one visualize any breakthrough in biological basis of prematurity or vaccine development or new treatment of diabetes or new ways to avert Iodine deficiency in the community or quality assurance program for hospitals by a single site research?

A look at any issue of the Lancet or the New England Journal of Medicine would convince that we live in an era of multi-centre research – research accomplished by research teams and networks.

## National Neonatal Perinatal Database (NNPD)

Neonatal health emerged as a key child health priority in the 1980s.

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Neonatal mortality by this time was accounting for over 60% of the infant mortality. The founding fathers of neonatology in the country had forged the National Neonatology Forum (NNF). In an expert group meeting on Neonatal Nomenclature and Data Collection in New Delhi in 1988 mooted the creation of a 'national database network involving neonatal units across the country' (1).

Initial attempts to start the network did not materialize due to lack of resources. It was in 1994 that in a workshop sponsored by the Ministry of Health and Family Welfare that the instruments and the methodology was finalized. This led to the creation of the NNPD network with nodal centre at the division of neonatology, All India Institute of Medical Sciences. There have been three phases of activities of the network.

**NNPD Phase I (1995)**

The objectives of this phase of NNPD were:

1. To generate generic neonatal-perinatal data on intramural deliveries from neonatal units across the country using a uniform protocol; and
2. Document the bacterial etiology of systemic neonatal sepsis and the antibiotic sensitivity of the organisms isolated from blood/CSF.

A total of 16 centres volunteered to participate in the activity by providing data on intramurally born infants. Data on each intramural birth was collected using definitions recommended by NNF. The period of observation was 27 days or till discharge. Each centre analysed their data and sent the report according to a standard schema to the nodal centre. The nodal centre checked the reports for inconsistencies and analysed the cleaned data using EpiInfo 6.

Except for a total of Rs 15000 provided by the Forum out of the Dr Vidyasagar Endowment Fund, the activity was supported by the individual sites and the nodal centre through their own resources.

NNPD 1995 covered a cohort of 38592 births (Tables 1-3) (2).

**NNPD Phase II (2000)**

The objectives of this phase of NNPD were the same as for phase I plus generation of neonatal-perinatal data on extramural neonatal admissions as well.

Thus, this time data on not only the intramural births (n=51905) from 16 centres was obtained (Tables 1-3), but also information on outborn newborn admissions at 10 centres (n=3831) was documented and analysed (3).

The methodology was similar to phase I. There was no funding for the activity this time and the respective centres and the nodal centre met the cost through local resources.

**NNPD Phase III (2002-03)**

This was the most advanced phase of the network, essentially because of a generous grant from the Indian Council of Medical Research. Electronic data systems were established at the participating sites. Data were collected for a period of two years from 18 centres for intramural births (n=151436) and 18 centres (some common) for outborn neonatal admissions (n=11026) (4).

The objectives of this phase were:

1. To generate and disseminate prospective data on neonatal – perinatal morbidity and mortality and mortality among intramural deliveries at the network institution, with focus on:

- Causes of maternal, perinatal and neonatal deaths;
- Incidence of LBW and prematurity;
- Incidence and outcome of birth asphyxia;
- Organisms causing infections in neonates;
- Antibiotic resistance pattern of neonatal infections;
- Incidence of other morbidity: hypothermia, respiratory distress, hyperbilirubinemia, intraventricular hemorrhage, etc.
- Incidence and profile of birth defects.

2. To describe the profile of morbidity and mortality of extramural neonatal admissions at the Networks institutions.

In this phase, all the study instruments were revised and electronic data collection was carried out on all babies at all sites. All centers started data collection form 1st January 2002 and sent monthly data to the nodal centre. This was either sent on floppy diskettes or by e-mail to the nodal center. At the nodal center, quality checks were conducted on the data received and feedback was sent to the individual centers. After due corrections, data from all the centers was amalgamated. The data thus collated was analysed using the Stat 7 statistical software and Microsoft Excel 97. The database has taken into consideration over about 300 variables while still retaining ease of data collection. The results obtained were scrutinized by the Coordinators of the participating centers and any discrepancy noted was submitted to re-analyses. Representative data are shown in Tables 1-3.

This phase also included another arm encompassing district hospitals

**Table 1: Key information of the NNPD cohorts**

| | Phase I 1995 | Phase II 2000 | Phase III 2002-03 |
|---|---|---|---|
| Intramural centres | 16 | 16 | 18 |
| Extramural centres | - | 10 | 18 |
| Total births | 38592 | 51905 | 151436 |
| Live births | 37082 | 49964 | 145623 |
| Stillbirths | 1510 | 1941 | 5813 |
| Total neonatal deaths | 1400 | 1513 | 3680 |
| Neonatal mortality rate (NMR) per 1000 live births | 37.7 | 30.7 | 25.3 |
| Early NMR per 1000 live births | 33.8 | 25.6 | 22.2 |
| Late NMR per 1000 live births | 3.9 | 4.7 | 2.9 |
| Perinatal mortality rate per 1000 live births | 71.6 | 66.5 | 59.7 |
| Still birth rate per 1000 births | 39.1 | 41.7 | 38.4 |

**Table 2: Mortality by birth weight groups in the three phases (NNPD)**

| Birth weight (g) | Year 1995 (16 centre) | | Year 2000 (16 centres) | | Year 2002-03 (18 centre) | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| <1000g | 265 | 77.7 | 399 | 72.4 | 973 | 55.0 |
| 1000-1249 | 371 | 55.5 | 619 | 41.7 | 1662 | 31.0 |
| 1250-1499 | 589 | 30.8 | 814 | 24.6 | 2383 | 18.3 |
| 1500-1749 | 1054 | 14.0 | 1385 | 11.3 | 4174 | 10.4 |
| 1750-1999 | 1515 | 7.7 | 2277 | 5.2 | 5691 | 5.2 |
| 2000-2249 | 3280 | 4.0 | 4363 | 2.7 | 12319 | 2.4 |
| 2250-2499 | 4804 | 2.0 | 6563 | 1.3 | 18321 | 1.4 |
| 2500-2999 | 16090 | 1.1 | 20195 | 1.0 | 59558 | 1.0 |
| 3000-3499 | 7504 | 0.9 | 10819 | 0.6 | 32615 | 0.8 |
| 3500 and + | 1610 | 0.8 | 2557 | 0.8 | 7927 | 0.8 |

**Table 3: Causative organisms of neonates sepsis (NNPD)**

| | 1995 | 2000 | 2002-03 |
|---|---|---|---|
| Incidence of systemic sepsis | 3.9% | 3.8% | 3% |
| | | Isolates | |
| Number of isolates | 996 | 909 | 1158 |
| *K. pneumoniae* | 30.0 % | 31.2% | 32.5% |
| *S. aureus* | 13.0% | 17.5% | 13.6% |
| *E. coli* | 12.2% | 10.5% | 10.6% |
| *Pseudomonas* | 6.7% | 6.8% | 5.6% |
| *S. albus* | 6.7% | 6.3% | 5.9% |
| Others | 31.4% | 27.7% | 31.2% |

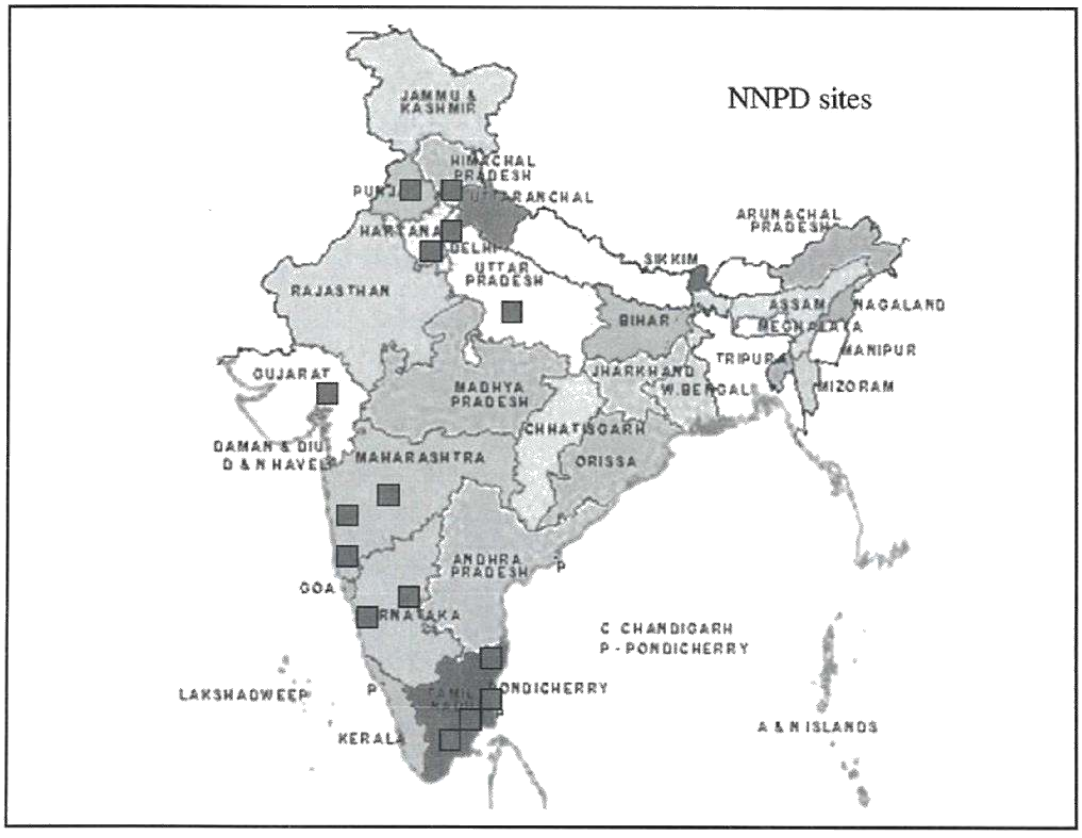


Fig. Showing representative sites of the National Neonatal Perinatal Database Network

belonging to the Human Reproductive Research Centres (HRRCs). Thus, for the first time, information on neonatal-perinatal care from district level facilities became available.

**Lessons and achievements**

The NNPD network has been a unique experiment. There a few other neonatal networks in the world. These include: the NIH Neonatal Research Network, the Vermont Oxford Network, Neonatal Research Network of NIH and the California Neonatal Network.

Key achievements of NNPD network are:

- This is the only neonatal network in the developing world;
- It brought together the leading institutions and teams in neonatal academia together for research and yielded several publications (2-14);
- It demonstrated the ability of the centres and investigators to:
  - Plan a multi-site research program;
  - Develop common protocols of data collection;
  - Collect high quality scientific data systematically on common protocols;
  - Sustain the activity over extended periods and on multiple cycles;
  - Analyse, synthesise, disseminate, publish and use information.
- Most significantly, the experience has paved way for multi-site research. For this, in order to take the initiative to the next level, a meeting of the investigators was held in 2007 to decide on priority research protocols. It was decided to develop multi-centre studies on the following areas:
  - Impact of zinc supplementation on morbidity and mortality of preterm neonates;
  - Developing fetal growth standards of Indian babies;
  - Developing short course protocols for the treatment of neonatal sepsis.

These protocols have been developed and are with the ICMR for funding.

- WHO requested the replication of the model in South East Asia Region as a SEAR Neonatal Perinatal Database network was created in 2007.

In future, the network may be used as a quality assurance system. It also could be expanded to have community sites for field and health systems research.

## Challenges

The most difficult challenge has been to find resources to undertake the activity. It was only in the third phase, after 7 years of work that formal funding became available. Even that has not been sustained thereafter. Ideally, it should be a seen as a virtual ICMR institution on newborn health research with continuous funding with inbuilt governance and accountability mechanisms.

A major constraint resulting from lack of resources has been the paucity of opportunities for the investigators to meet face to face to discuss scientific issues and share ideas. The worst effect of this has been that a number of potential analyses and publications (especially from the Phase III data) could not materialize. It also hampered collective endeavour to enlarge the scope of the network, thus hampering the growth and further development of the network. Face to face meetings on a periodic basis are a must to build trust and ownership of the partners as well as for creative thinking and progress.

## Wider implications

NNPD network is not only poised for serving as a platform for facility-based multi-centre research studies, but also has several other potential roles:

- It provides a role model to other disciplines (and respective professional bodies and institutions) to develop similar research networks and databases.
- It provides a resource for enhancing capacity in research and epidemiology. The centres can be readily engaged in holding workshops and courses in research methods in order to have critical mass of trained researchers in child health and other disciplines.

## Acknowledgements

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