Rates, timing and causes of neonatal deaths in rural India: implications for neonatal health programmes

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Objective To assess the rates, timing and causes of neonatal deaths and the burden of stillbirths in rural Uttar Pradesh, India. We discuss the implications of our findings for neonatal interventions.

Methods We used verbal autopsy interviews to investigate 1048 neonatal deaths and stillbirths.

Findings There were 430 stillbirths reported, comprising 41% of all deaths in the sample. Of the 618 live births, 32% deaths were on the day of birth, 50% occurred during the first 3 days of life and 71% were during the first week. The primary causes of death on the first day of life (i.e. day 0) were birth asphyxia or injury (31%) and preterm birth (26%). During days 1–6, the most frequent causes of death were preterm birth (30%) and sepsis or pneumonia (25%). Half of all deaths caused by sepsis or pneumonia occurred during the first week of life. The proportion of deaths attributed to sepsis or pneumonia increased to 45% and 36% during days 7–13 and 14–27, respectively.

Conclusion Stillbirths and deaths on the day of birth represent a large proportion of perinatal and neonatal deaths, highlighting an urgent need to improve coverage with skilled birth attendants and to ensure access to emergency obstetric care. Health interventions to improve essential neonatal care and care-seeking behavior are also needed, particularly for preterm neonates in the early postnatal period.

Introduction

Every year, there are an estimated 4 million neonatal deaths, accounting for almost 40% of deaths in children younger than 5 years. 1, 2 About a quarter of global neonatal deaths occur in India, which has a neonatal mortality of 43 per 1000 live births. 1, 3 Therefore, interventions to address neonatal mortality are crucial if child mortality is to be reduced globally and in India. 2, 4, 6

Globally, the main causes of neonatal deaths are thought to be preterm birth (28%), sepsis or pneumonia (26%), and birth asphyxia (23%). 4, 12 In the South-East Asia Region, WHO has attributed 30% of neonatal deaths to preterm birth, 27% to sepsis or pneumonia, 23% to birth asphyxia, 6% to congenital abnormalities, 4% to tetanus, 3% to diarrhoea and 7% to other causes. 7 However, most stillbirths or neonatal deaths occur at home and vital registration systems are incomplete, 3, 4, 8 and as such current estimates have been generated from a limited set of data. 9, 10

Verbal autopsies, which are interviews with caregivers, 11, 13 have been used to establish causes of neonatal deaths. 10, 14–21 Data on timing and causes of neonatal deaths are very important for the design of interventions to reduce mortality, yet only one study with a small sample size (n = 40) has previously described causes of neonatal deaths by day. 13

Here, we describe the rates, causes and timing of 1048 neonatal deaths and stillbirths in a rural population in Uttar Pradesh, India, where the neonatal mortality rate has been estimated at 57 deaths per 1000 live births. 3 The findings of this study have important implications for community-based research and programmes to improve maternal and neonatal health and survival not only in rural north India, but also in other similar developing world settings.

Methods

Sample group

Data were collected to establish baseline rates and causes of neonatal mortality. Then, we randomly selected 17 rural sectors in two districts of Uttar Pradesh, Barabanki and Unnao.

We obtained informed consent from all participants. Institutional review boards of the Johns Hopkins Bloomberg School of Public Health, Baltimore MD, USA, and King George Medical University, India, reviewed the study protocol and study conduct for ethical considerations.

Verbal autopsy

The verbal autopsy questionnaire was adapted by an expert panel (see Acknowledgements) from the instrument used in a WHO three-country verbal autopsy validation study, 22 with added questions about pregnancy, childbirth, common causes of death in newborn babies, and

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a new module to distinguish between stillbirths and early neonatal deaths. The instrument was further adapted to the local context and culture. The verbal autopsy started with open-ended questions to elicit a narrative about the neonate’s death, followed by close-ended questions. The instrument was translated from English into Hindi, and local terms for specific illnesses were used when appropriate.

**Data collection**

All data collectors received 2 weeks of training that included classroom lectures, field practice sessions, and observations at a children’s hospital. Whenever possible, efforts were made to interview the mother. If the mother was absent, an adult relative who had the closest contact with the child during the terminal illness was the primary respondent. Data collectors conducted the interviews in Hindi using local vocabulary and the surveys lasted for about an hour.

All questionnaires and data forms were reviewed by the research team for accuracy, consistency and completeness, and if necessary, data collectors made additional field visits to clarify data entries. One week after data collection, quality control teams randomly selected and re-interviewed 5% of the sample. These data were compared with the original interview data to check for consistency. After editing, the data were entered in databases designed with use of Visual FoxPro (Microsoft, Redmond, Washington, USA).

**Data analysis**

Stillbirths were defined as births after 28 weeks’ gestation that resulted in a baby that failed to cry, move, or breathe. To identify fresh stillbirths, respondents were asked to describe whether the baby’s flesh appeared normal. All live births that resulted in deaths on days 0–6 per 1000 live births; and late neonatal mortality rate (deaths on days 7–27 per 1000 live births).

We defined skilled birth attendants as any attendant at delivery who was reported to be a qualified doctor, nurse, lady health visitor or auxiliary nurse midwife.

For each cause of death, we used definitions selected from the WHO verbal autopsy validation study. A single cause of death was assigned by application of definitions in a hierarchical manner as shown in Fig. 1. This cause-of-death ascertainment was done with use of a computer algorithm created with Stata software (version 8). A variable was created for each factor and symptom used in the causal definitions, and the algorithm applied the cause-of-death definitions uniformly for each death. Birth asphyxia and birth injury were initially reported separately, but later they were grouped because of their common underlying causes and because this had been done in previous studies.

We used a life-table approach for survival analysis. To explore overlapping causes of death, the definitions for tetanus, preterm birth, birth asphyxia or birth injury, and sepsis/pneumonia were each applied to all neonatal deaths in a nonhierarchical manner, then cross-tabulated with the other causes of death. This assignment of cause was also made with use of a computer algorithm.

**Results**

A survey of 61,591 households identified 57,007 ever-married women aged 13–49 years. From the pregnancy histories of 49,365 women (86%), 1,248 stillbirths and neonatal deaths were reported during the 2 years before the survey, of which 10,488 (84%) were later investigated through verbal autopsy. The mean and median recall periods were 62.4 weeks and 57.6 weeks after death, respectively. Maternal and delivery characteristics are shown in Table 1.

We calculated that the stillbirth rate was 31.8 deaths per 1000 births; the early neonatal mortality rate was 35.1 per 1000 live births and the late neonatal mortality rate was 13.9 per 1000 live births. There were 430 stillbirths, representing 41% of deaths in this sample; 87% were reported as fresh stillbirths (Table 1). Of the 618 live births that resulted in neonatal death, 32% took place on the same day as birth and 71% occurred during the first week of life (Fig. 2).

Analysis with the algorithm to assign a single cause of death showed that the most common causes of death overall were preterm birth (27%), sepsis or pneumonia (24%) and birth asphyxia or injury (14%) (Table 2). Birth asphyxia and birth injury were originally distinct causal definitions, but only 2 cases of birth injury were identified with use of the algorithm. Birth asphyxia or injury (31%) and preterm birth (26%) were the most common causes of death on day 0 (Table 2). On day 1 and during the first week of life, the proportion of deaths caused by birth asphyxia or injury was lower than on day 0 (14%). On days 1–6, the most frequent causes of death were preterm birth (30%) and sepsis or pneumonia (25%). The proportion of deaths caused by sepsis or pneumonia increased to 45% during days 7–13 and 36% during days 14–27. Congenital abnormalities and diarrhoea were relatively infrequent causes of death (<10%) at all times during the neonatal period, although they were both more important during and after the first week of life, respectively. For 141 deaths (23%) a cause of death could not be established. A comparison of the survival curves for the main causes of death shows that the probability of death due to preterm birth was higher in the early neonatal period than the probability of death due to infection (Fig. 3).

When multiple causes of death were considered, 47% of neonatal deaths showed signs of sepsis or pneumonia, of which 32% also met the criteria for preterm birth (Table 3). The proportion of deaths related to birth asphyxia or birth injury was 23%, and a substantial proportion of these also met the definition for sepsis or pneumonia (35%) or preterm birth (29%).

**Discussion**

In settings where most deaths occur outside of the health system, verbal autopsy is considered the only practicable method for assignment cause of death; however the method has its limitations. For example, problems are inherent in certain case definitions. Symptoms of respiratory illness are thought to be difficult to elicit from verbal autopsy interviews and the definition of sepsis or pneumonia used here could include both viral and bacterial infections of various etiologies. Likewise, the definition used for preterm birth (“baby very small or smaller than...
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Fig. 1. Algorithms and hierarchy used to assign primary cause of death

- **Tetanus**: Age at death 3–27 days AND EITHER local word for tetanus OR convulsions/spasms and able to suckle or cry normally after birth and stopped suckling or crying
  - 25 deaths

- **Congenital abnormality**: Physical malformation or gross malformation present at birth
  - 40 deaths

- **Preterm birth**: Baby very small or smaller than usual at birth
  - 164 deaths

- **Birth asphyxia**: Age at death ≤7 days AND not able to cry after birth or not able to breathe after birth or not able to suckle normally after birth
  - 85 deaths

- **Birth injury**: Age at death ≤7 days AND signs of injury at birth
  - 2 deaths

- **Sepsis or pneumonia**: At least two of the following signs: stopped suckling; fever OR cold to touch; unresponsive or unconscious OR lethargic; bulging fontanelle; convulsions; vomiting (redness OR drainage from the umbilical cord stump); OR skin bumps containing pus or blisters or single large area of pus with swelling; chest in-drawing, fast breathing OR local term for pneumonia
  - 154 deaths

- **Diarrhoea**: Local term for diarrhoea or frequent/watery/loose stools
  - 10 deaths

- **Cause not identified**: 138 deaths

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usual”) is subjective, but is the only validated, feasible definition currently available in this setting, given that neonates are seldom weighed after birth and most women do not access antenatal care. This definition may also include low-birth-weight (LBW) neonates, but preterm birth is generally attributed as a direct cause of death, while LBW is considered a risk factor or underlying condition. No standard definition for birth asphyxia exists, particularly at community level, and remedying of this situation has been identified as a research priority.\(^6,23,27\) The definition used in this study was found to have more than 70% sensitivity and specificity in Bangladesh.\(^22,25\) The proportion of deaths assigned to some causes, particularly sepsis/pneumonia or prematurity, are highly dependent upon their placement within the hierarchy. When multiple causes of death are examined, substantial overlap is observed. Since birth asphyxia usually occurs in term infants weighing >2000 g,\(^28\) the overlap between birth asphyxia and preterm birth is probably the result of misclassification.

Another limitation of our study is that only neonatal symptoms have been...
considered. Information about maternal health status, including complications during pregnancy and delivery, could corroborate or increase the validity of the cause-of-death assignment. A verbal autopsy validation study currently being conducted by our research group plans to assess the usefulness of information on maternal health and complications during pregnancy in assessing cause of death in neonates.

Two strengths of this study are the large sample size and the use of previously validated methods. Only one previous study has reported the cause structure of deaths by day for neonates, but the sample was much smaller \( (n = 40) \).21

Global estimates and results from a previous study in Uttar Pradesh suggest that stillbirths occur at about the same rate as neonatal deaths, but that available data probably lead to underestimates of the burden of stillbirths.21,23 In our study, seven stillbirths were recorded for every ten neonatal deaths, suggesting that stillbirths were undercounted as a result of the retrospective nature of the survey design. Globally, 26% of stillbirths are thought to be related to acute intrapartum events.21 In our study population, 87% of stillbirths were reported to be fresh, although the questions used to distinguish between types of stillbirth have not been validated. A prospective, population-based study of pregnant women could improve the accuracy of stillbirth recording, particularly in a context of community engagement that would facilitate dialogue about stillbirths. Improved accuracy of data could have important programmatic implications, since prevention strategies differ for intrapartum and antepartum stillbirths.21

Stillbirths are currently low on public policy and public health research agendas, in part because of a lack of data.

Our findings on the categorization of neonatal deaths are within the range of WHO estimates, with the exception of birth asphyxia at 14%.1 When multiple causes of death were assigned, however, 23% showed signs of birth asphyxia, a proportion equal to regional estimates. The difficulty of distinguishing birth asphyxia from other causes with use of the verbal autopsy has been noted in validation studies.21,25

Results from community-based studies in South Asia since 1995 have reported neonatal causes of death within the following ranges: preterm birth, 8–38%; sepsis or pneumonia, 7–52%; birth asphyxia 10–28% (sometimes including birth injury); tetanus 2–36%; and diarrhea 9%.8,13,14,18,21,24,30,31 However, methodological differences between studies make direct comparisons very difficult, if not impossible. For example, some studies included different definitions and categorizations of cause, or included other causes that might overlap those used in this study, or excluded some causes that have been included here. The establishment of common methods for researchers to categorize

## Table 1. Sociodemographic and delivery characteristics by birth outcome

<table>
<thead>
<tr>
<th></th>
<th>Stillbirths*</th>
<th>Neonatal deaths*</th>
<th>Total*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>73 (17.0)</td>
<td>114 (18.4)</td>
<td>187 (17.8)</td>
</tr>
<tr>
<td>20–35</td>
<td>304 (70.7)</td>
<td>439 (71.0)</td>
<td>743 (70.9)</td>
</tr>
<tr>
<td>&gt;35</td>
<td>53 (12.3)</td>
<td>65 (10.5)</td>
<td>118 (11.3)</td>
</tr>
<tr>
<td><strong>Maternal education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal schooling</td>
<td>307 (71.4)</td>
<td>450 (72.8)</td>
<td>757 (72.2)</td>
</tr>
<tr>
<td>Primary school</td>
<td>52 (12.1)</td>
<td>75 (12.1)</td>
<td>127 (12.1)</td>
</tr>
<tr>
<td>Secondary school or higher</td>
<td>71 (16.5)</td>
<td>93 (15.0)</td>
<td>164 (15.6)</td>
</tr>
<tr>
<td><strong>Household standard of living index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>194 (45.1)</td>
<td>303 (49.0)</td>
<td>497 (47.4)</td>
</tr>
<tr>
<td>Middle</td>
<td>173 (40.2)</td>
<td>245 (39.6)</td>
<td>418 (39.9)</td>
</tr>
<tr>
<td>High</td>
<td>63 (14.6)</td>
<td>70 (11.3)</td>
<td>133 (12.7)</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>183 (42.6)</td>
<td>116 (18.8)</td>
<td>299 (28.5)</td>
</tr>
<tr>
<td>2–5</td>
<td>190 (44.2)</td>
<td>356 (57.6)</td>
<td>546 (52.1)</td>
</tr>
<tr>
<td>6</td>
<td>57 (13.3)</td>
<td>146 (23.6)</td>
<td>203 (19.4)</td>
</tr>
<tr>
<td><strong>Mutiple birth</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Institutional delivery</td>
<td>143 (33.3)</td>
<td>111 (18.0)</td>
<td>254 (24.2)</td>
</tr>
<tr>
<td>Skilled attendant, home or institution</td>
<td>171 (39.8)</td>
<td>132 (21.4)</td>
<td>303 (28.9)</td>
</tr>
<tr>
<td><strong>Stillbirth classification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh</td>
<td>374 (87.0)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Macerated</td>
<td>56 (13.0)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Timing of neonatal deaths</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (0–6 days)</td>
<td>–</td>
<td>437 (70.7)</td>
<td>–</td>
</tr>
<tr>
<td>Late (7–27 days)</td>
<td>–</td>
<td>181 (29.3)</td>
<td>–</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>430</td>
<td>618</td>
<td>1048</td>
</tr>
</tbody>
</table>

* Figures in parentheses are percentages.
and assign neonatal cause of death is an important priority.\textsuperscript{5,6} The algorithm used in this study failed to assign a cause for 23\% of deaths. Others have reported similar proportions of deaths for which no specific cause could be identified by verbal autopsy.\textsuperscript{8,10} This finding may reflect limitations in verbal autopsy studies, which could be addressed through improved and validated methods.

The process of examining causes of death by number of days since birth yielded useful insights for health programme planning and illustrates the need for a continuum of care.\textsuperscript{32} Some evidence-based behaviours during and immediately after the birth, such as clean delivery practices, immediate breastfeeding and care-seeking for complications would require antenatal education for families. Previous estimates of the proportion of deaths that occur on the first day have ranged from 25–45\%.\textsuperscript{1} Most deaths on the first day of life were the result of birth asphyxia, birth injury, or complications of preterm delivery. In combination with the high rates of fresh stillbirths, these data highlight the vital need to increase coverage of skilled birth attendants, to ensure prompt referral and access to quality emergency obstetric care as well as neonatal care, and to equip birth attendants with the capabilities to identify and manage birth asphyxia.\textsuperscript{33}

Recent evidence suggests that improved care of preterm or LBW infants can substantially improve survival.\textsuperscript{3,4} Early postnatal vitamin A dosing;\textsuperscript{34} promotion of early and exclusive breastfeeding;\textsuperscript{6,53} hypothermia prevention and management, including skin-to-skin care;\textsuperscript{36,37} topical skin cleansing with chlorhexidine;\textsuperscript{38,39} and topical emollient treatment for hospitalized infants\textsuperscript{40,41} may also reduce mortality and morbidity in LBW or preterm neonates.\textsuperscript{3,42,43} Furthermore, the substantial proportion of early deaths that occurred in the absence of distinct symptoms suggests that programmes to reduce neonatal mortality should also focus on routine, preventive care for all newborn babies in addition to responding to care-seeking for perceived presence of danger signs.

On days 1 and 2, sepsis or pneumonia deaths made up 23–25\% of deaths and the proportion of deaths attributed to this cause increased thereafter. Most of the early infection deaths were probably due to pathogens acquired from the mother.\textsuperscript{39} Treatment of maternal asymptomatic bacteriuria, urinary tract infections and reproductive tract infections are effective in reducing the incidence of neonatal infections.\textsuperscript{5} Intrapartum use of chlorhexidine, coupled with community-based interventions to improve hygiene (such as hand-washing and clean delivery) and neonatal care practices (clean cord cutting and care, skin care) may reduce the incidence of neonatal infections.\textsuperscript{6,36,44,45} Later deaths from infections including tetanus can be strongly linked to environmental exposures and practices during home delivery and care.\textsuperscript{6} Neonatal tetanus can be prevented through maternal tetanus immunization, as well as clean cord care. Recent evidence shows that cord antisepsis with chlorhexidine can significantly reduce neonatal mortality.\textsuperscript{36} Although

![Fig. 3. Cumulative mortality by cause](image-url)
facility-based treatment of neonatal sepsis is the current WHO standard of care, home-based management of sepsis by community health workers has been shown to be efficacious.47 Our findings suggest, however, that surveillance and treatment must begin very early in the postnatal period.

This study has important insights for both research and health programme planning. A key finding of this study is that the burden of stillbirths is high, but better data collection methods are essential to more precisely define the burden of stillbirths, to track changes in stillbirths and cause-specific neonatal deaths over time, and to evaluate the effect of health programmes. Improved methods are also needed to ascertain the cause of the unexplained deaths. Finally, half of all deaths occur by day 3, which suggests that greater coverage of antepartum, intrapartum and early postnatal health interventions, in combination with promotion of care-seeking behaviour and links between communities and health facilities to ensure prompt treatment, would be expected to have the greatest effect in this setting and other areas with high neonatal mortality and low use of health-care services. A combination of community outreach and family–community care to promote essential neonatal care practices and health system strengthening would be necessary to achieve these goals.45,46 A small number of community-based intervention studies have tested models for improving neonatal care through these strategies, and other trials are in progress.43,49–51 Further community-based trials and effectiveness studies are needed to replicate previous findings, scale up the interventions and assess their cost-effectiveness.52

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Résumé

Taux, répartition dans le temps et causes des décès néonataux dans l’Inde rurale : implications pour les programmes de santé néonatale

Objectif Évaluer les taux, la répartition dans le temps et les causes des décès néonataux et de la charge de mortalité dans une population rurale de l’Uttar Pradesh, en Inde. Les implications des résultats de l’étude pour les interventions en santé néonatale sont ensuite examinées.

Méthodes On a analysé 1048 cas d’enfants mort-nés ou décédés pendant la période néonatale à partir des interrogatoires réalisés dans le cadre des autopsies verbales.

Résultats Le nombre de cas d’enfants mort-nés notifiés s’élevait à 430, soit 41 % de l’ensemble des décès dans l’échantillon. Sur les 618 enfants nés vivants, 32 % sont morts le jour de la naissance, 50 % au cours des 3 premiers jours de vie et 71 % pendant la première semaine. Les principales causes de décès au premier jour de vie (appelé jour 0) étaient l’asphyxie ou les traumatismes à la naissance (31 %) et la naissance avant terme (26 %). Pendant les jours 1 à 6, les causes de décès les plus fréquentes étaient la naissance avant terme (30 %) et la présence d’une infection grave ou d’une pneumonie (25 %). La moitié des décès par infection grave ou par pneumonie se produisaient pendant les périodes allant du 7e au 13e jours et du 14e au 27e jours respectivement.

Conclusion La mortalité néonatale et les décès intervenant le jour de la naissance représentent une fraction importante des décès périmaternels et néonataux, ce qui met en lumière la nécessité urgente d’améliorer la couverture des naissances par des accoucheurs compétents et de garantir l’accès à des soins obstétricaux d’urgence. Des interventions sanitaires visant à améliorer les soins néonataux essentiels et les comportements en matière de recours aux soins, en particulier pour les nouveau-nés prématurés au début de la période postnatale, s’imposent également.
Resumen

Tasas, momento y causas de la mortalidad neonatal en la India rural: implicaciones para los programas de salud neonatal

Objetivo Evaluar las tasas, el momento y las causas de la mortalidad neonatal en zonas rurales de Uttar Pradesh (India). Consideramos aquí las implicaciones de nuestros resultados para las intervenciones neonatales.

Métodos Utilizamos entrevistas de autopsias verbales para investigar 1048 defunciones neonatales y prenatales.

Resultados Se notificaron 430 casos de muerte prenatal, que suponían el 41% de todas las defunciones de la muestra. Entre los 618 nacidos vivos, el 32% de las defunciones se produjeron en el mismo día de nacimiento, el 50% se produjeron durante los 3 primeros días de vida, y el 71% se registraron durante la primera semana. Las causas principales de defunción en el primer día de vida (día 0) fueron la asfixia y los traumatismos (31%) y la prematuridad (26%). Durante los días 1 a 6, las causas más frecuentes de muerte fueron la prematuridad (30%) y una septicemia o neumonía (25%). La mitad de todas las defunciones por septicemia o neumonía se produjeron durante la primera semana de vida. La proporción de defunciones atribuidas a septicemia o neumonía aumentó al 45% y el 36% durante los días 7 - 13 y 14 - 27, respectivamente.

Conclusión Las muertes prenatales o en el primer día de vida representan una gran proporción de las defunciones perinatales y neonatales, lo que pone de manifiesto la necesidad urgente de mejorar la cobertura con parturientas calificadas y de garantizar el acceso a la atención obstétrica de urgencia. También es necesario implementar intervenciones de salud que mejoren la atención neonatal básica y el comportamiento de búsqueda de atención, en particular para los recién nacidos prematuros en el periodo posnatal temprano.

References

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