

# Comparative Study of Outcome of Neonatal Septicaemia among Inborn and Outborn In a Tertiary Care Hospital in Rural West Bengal

Paul S<sup>1</sup>, RahamanSk M<sup>2</sup>, Das K Kanti<sup>3</sup>, Corresponding Author- Dey S<sup>4</sup>

1. Dr Sudipto Paul, Senior Resident, Dept of Pediatrics, Burdwan Medical College & Hospital. 2. Dr SkMoshihurRahaman, Resident Medical officer cum Clinical Tutor, Dept of Pediatrics, Burdwan Medical College & Hospital. 3. Dr KuntalKanti Das, Resident Medical officer cum Clinical Tutor, Dept of Pediatrics, Burdwan Medical College & Hospital. 4. Dr Subhendu Dey, Associate Professor, Dept of Pediatrics, Burdwan Medical College & Hospital, Burdwan

## Abstract

**Objectives:** We sought to compare the prevalence, pattern of causative organism and outcome of newborn with culture proven sepsis admitted in SNCU inborn and outborn for the last 12 months in a tertiary care hospital in rural Bengal.

**Methods:** A prospective observational study was conducted over a total of 2880 inborn and 2545 outborn babies over 1 year period. Data were collected in a predesigned proforma and analysed in Microsoft excel 2010 using standard statistical techniques.

**Results:** Inborn babies with sepsis with proven culture positive, the main organism found is Klebsiella (25.5%) in EOS, followed by MSSA (23.3%), MRSA (21.1%) then Pseudomonas (13.3%). Whereas in LOS in inborn babies majority of sepsis is caused by MSSA (48.8%) followed by MRSA (31.7%). Majority of the organisms are sensitive to piperacillin-tazobactam, amoxicillin, 3<sup>rd</sup> generation cephalosporins, vancomycin and fluroquinolones but candida is responsive to amphotericin B and Acinetobacter is responsive to Colistin.

**Conclusions:** 89% of babies with culture positive sepsis are successfully discharged of inborn whereas 84% of babies of outborn found culture positive are discharged successfully with a 16% death rate with sepsis.

**Keywords:** culture proven sepsis. SNCU inborn and outborn, recovery, antibiogram

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## I. Introduction:

Neonatal sepsis is a significant cause of morbidity and mortality among newborns throughout the world. World health organisation has estimated that 1.6 million deaths occur globally every year due to neonatal infections and 42% of neonatal deaths occur in developing countries. In India, the blood culture proven sepsis was reported as 9 per 1000 live births for the year 2007 -2008 by National Neonatal Perinatal Database. Most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics.

Neonatal sepsis is classified as two big chapters like early and late onset sepsis depending upon the postnatal day of presentation. Early onset sepsis (EONS) occurs within first 72hrs of life whereas the late neonatal sepsis (LONS) occurs between 72hrs to 90 days of life. The bacterial agents implicated in early-onset sepsis include group B Streptococcus (GBS), Escherichia coli, coagulase-negative Staphylococcus, Haemophilus influenzae and Listeria monocytogenes. The organisms commonly associated with late-onset sepsis include coagulase-negative staphylococci (CONS), Staphylococcus aureus, Klebsiellapneumoniae, Escherichia coli, Enterobacter spp., Pseudomonas aeruginosa and Acinetobacter species.

The bacteriological profile for causative organisms of neonatal sepsis differs significantly between developed and developing countries. Klebsiella pneumoniae is the most common bacterial agent causing neonatal sepsis in developing countries, while group B Streptococcus and coagulase-negative staphylococci (CONS) are the common agents in developed countries. Even among developing countries, regional variation in prevalence of the bacterial agents causing neonatal sepsis exists. The overall improvement in the neonatal survival due to newer drugs, better neonatal care and advanced life support facilities has led to a change in the spectrum of agents causing neonatal sepsis in developed countries. However, there is a paucity of data on the recent trends of organisms causing neonatal sepsis in developing countries.

As delay in the treatment of neonatal sepsis is associated with increased mortality, empirical therapy is the cornerstone in the management of neonatal sepsis. A combination of ampicillin or third generation

cephalosporins with an aminoglycoside (gentamicin) is the commonly used empirical regimen. However, the appropriateness of this empirical therapy is being challenged in the present era of changing bacteriological profile and increasing antimicrobial resistance. Knowledge of common organisms causing neonatal sepsis in a particular area and their antibiotic sensitivity pattern should be borne in mind before setting guidelines for empirical therapy.

Hence, there is a need for surveillance to understand the trends in pathogens causing neonatal sepsis and the antibiotic susceptibility profile of those pathogens in a particular area. This study was therefore undertaken to determine the common bacterial agents associated with neonatal sepsis and their antibiotic susceptibility pattern in a tertiary care hospital in India.

## **II. Materials and Methods:**

This prospective observational cohort study was conducted in the division of neonatology, of our tertiary care hospital over a period of 1 year from May 2020 to April 2021. This study was approved by the Research and Ethical committees of our institute and informed consent was obtained from each patient's next of kin.

During the study period, all the inborn and outborn suspected babies were screened for sepsis. Sepsis was clinically suspected if the neonate had symptoms and signs suggestive of sepsis such as poor feeding, poor activity, respiratory distress, apnea, seizure, lethargy, bulging anterior fontanel, fever, hypothermia, jaundice, vomiting, loose stools, abdominal distension, cyanosis, bleeding, mottling, tachycardia, weak pulse, grunting, retractions, nasal flaring etc. Septic screening tests like band cell count, C- reactive protein, and micro erythrocyte sedimentation rate were done in all these cases. All neonates in whom sepsis was suspected and had at least two positive screening tests been included in the study. A detailed antenatal, natal and postnatal history was taken. The birth weight, sex and day of onset of sepsis were noted. Details regarding risk factors such as ventilator support, CPAP, central line and exchange transfusion prior to the onset of sepsis were also noted. Blood culture was done for all the neonates. Blood was collected with aseptic precautions before starting antibiotics and 2 ml of blood was added to each of two bottles containing 25 ml of Brain heart infusion broth (Hi Media, Mumbai, India). Both the bottles were incubated aerobically at 37°C for 7 days. Subculture was done on sheep blood agar and MacConkey agar (Hi Media, Mumbai, India) routinely after 48 h and 7 days. Subculture was also done in between if visible turbidity appeared. The isolates were identified based on standard bacteriological techniques. The growth of an organism was considered pathogenic if the same organism was isolated from both broths and contaminated if either the growth was obtained in only one bottle or a mixed growth was obtained. If coagulase negative staphylococci (CONS) were isolated from neonates with sepsis, a repeat blood culture was performed to confirm the infection.

The susceptibility of the clinical isolates to some routinely used antibiotics was determined by the Kirby-Bauer disk diffusion method according to Clinical Laboratory Standards Institute guidelines. All the antibiotic disks were obtained from Hi Media, Mumbai, India. Ampicillin, gentamicin, ceftriaxone, ciprofloxacin, ceftazidime, amikacin, chloramphenicol and meropenem were tested for gram-negative bacteria. Penicillin, oxacillin, gentamicin, ciprofloxacin, erythromycin and vancomycin were tested for *Staphylococcus* spp. Oxacillin, erythromycin and vancomycin were tested for *Streptococci pneumoniae*. Double-disk test using both cefotaxime and ceftazidime, alone and in combination with clavulanic acid, was performed for detection of extended spectrum  $\beta$ -lactamase (ESBL) in *Klebsiella pneumoniae*, according to CLSI guidelines. In this test, an overnight culture suspension of the test isolate adjusted to 0.5 McFarland standard was inoculated using a sterile cotton swab on the surface of a Mueller Hinton Agar. The Cefotaxime (30  $\mu$ g) and cefotaxime-clavulanic acid (30  $\mu$ g/10  $\mu$ g) disks were placed 20 mm apart on the agar. Similarly, the ceftazidime (30  $\mu$ g) and ceftazidime-clavulanic acid (30  $\mu$ g/10  $\mu$ g) disks were placed 20 mm apart. After incubating overnight at 37°C, a  $\geq 5$  mm increase in the zone diameter for either antimicrobial agent tested in combination with clavulanic acid vs. its zone when tested alone was interpreted as positive for ESBL production. *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus pneumoniae*, obtained from Christian Medical College, Vellore, were the QC strains used for quality control of Kirby-Bauer disk diffusion method. *Klebsiella pneumoniae* and *Escherichia coli* were used for quality control of ESBL testing.

Proven sepsis was defined as the presence of clinical features of sepsis along with the isolation of an organism in blood culture. Early-onset neonatal sepsis was defined as sepsis occurring within the first 3 days of life, while late-onset sepsis was defined as sepsis occurring after 3 days of life.

Data entry and analysis were done using SPSS for Windows Version SPSS 16.0 (SPSS Inc, Chicago, IL, USA). Means and standard deviations (SD) were calculated as required for numerical variables. The Chi-square test or Fisher's exact test was used to compare two groups. *P* value < 0.05 was considered statistically significant.

### III. Results:

A total 2880 inborn and 2545 outborn babies were admitted during this period. In the admitted babies who are found sick sepsis screen and blood culture were sent for treatment beneficiary purpose. Amongst the inborn graduates 520 (18%) found culture proven sepsis and among the outborn graduates 560(22%) babies found culture proven sepsis. In the inborn babies 740 babies were preterm and 860 (33.7%) babies found preterm in outborns.

Girls found among the culture positive babies is 44% in outborn and 38%in inborn. Male percentage is found predominant in inborn babies as such 62% and 56% in outborn babies.

Maternal factors play a very important role is newborn sepsis, such as premature rupture of membranes (PROM) and history of meconium-stained liquor (MSL). In culture positive sepsis cases h/o PROM found in inborn cases 2.3% and in outborn cases this is 4.6%. H/o MSL is found in 9% in outborn culture positive cases and 5% in inborn cases.

76% of inborn babies with sepsis are delivered spontaneously and 20.6% are delivered by LUCS and delivered by instrument help is 2.8%. whereas 81.2% of outborn babies with sepsis are delivered spontaneously and 17% by LUCS and 1.7% by instrumentation help.

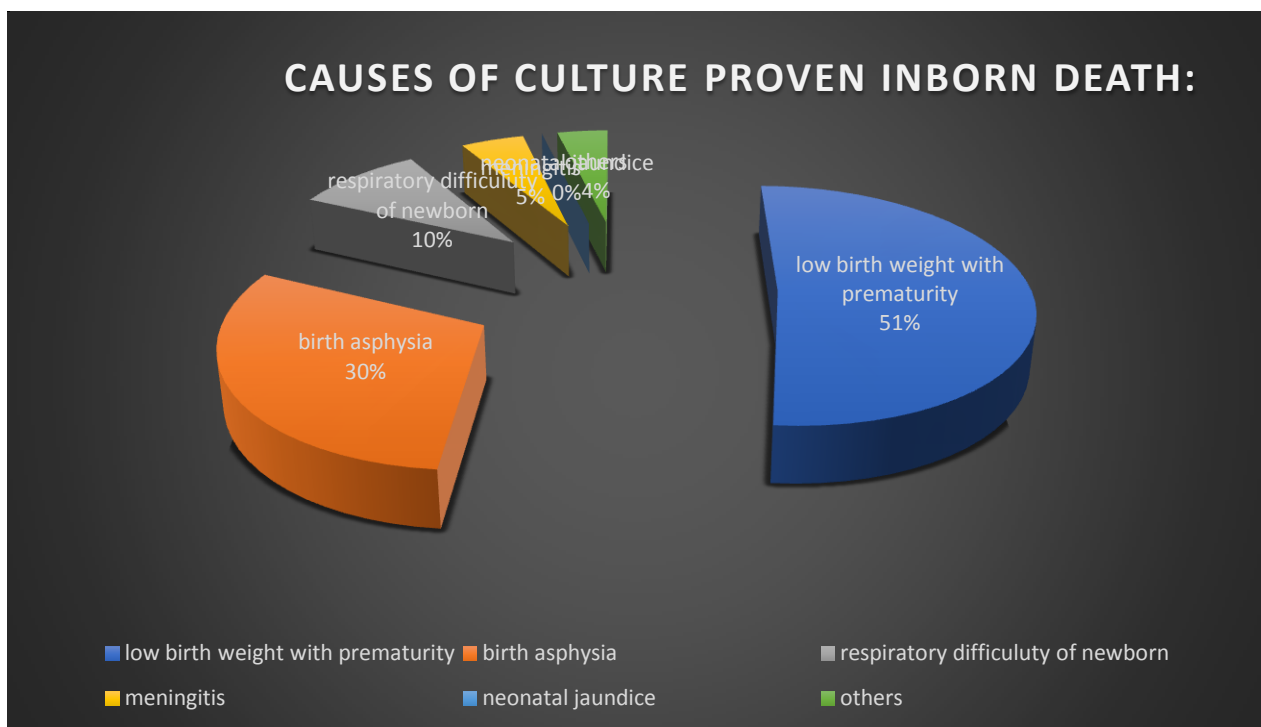


Diagram 1: Causes of culture proven death of sepsis of inborn.

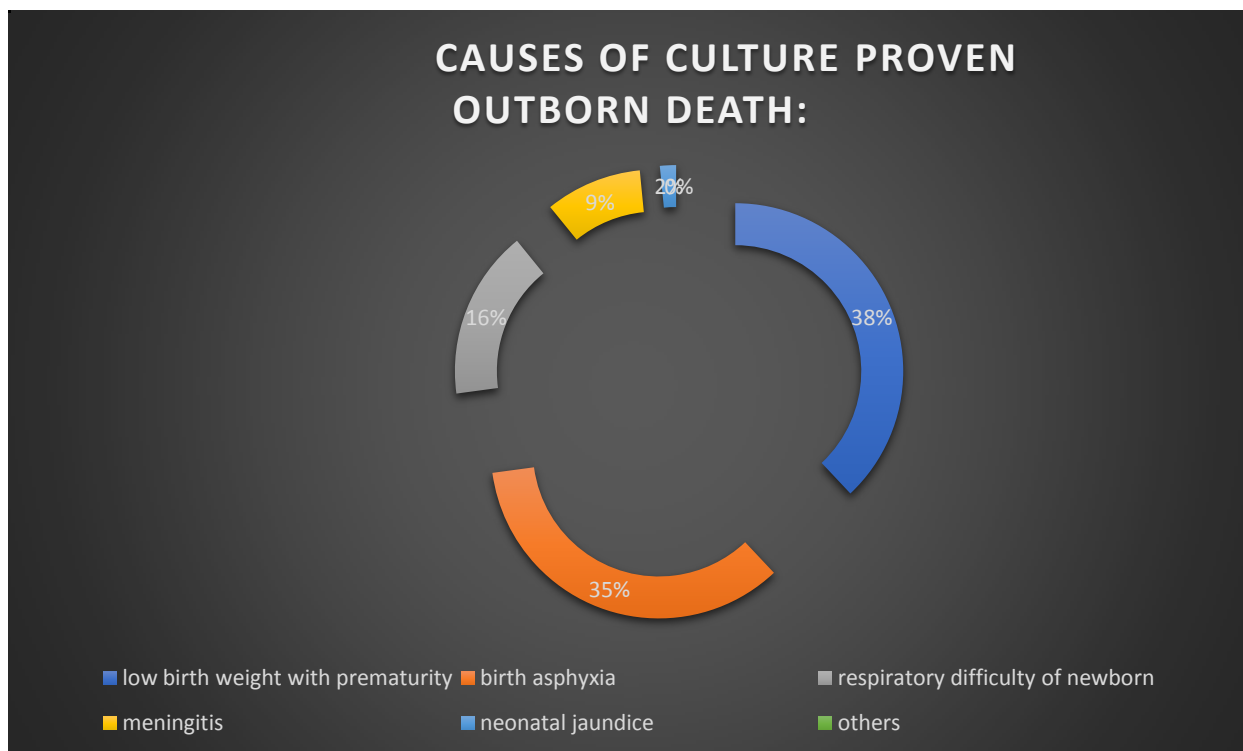


Diagram 2: Causes of culture proven death of sepsis of outborn.

Table 1: Basic characteristics:

A	Neonate regarding:	Inborn (%)	Outborn (%)
1.	No of preterm neonates	740(25.6%)	860(33.7%)
2.	Birth weight; mean +/- SD(Range)	2.1 +/- 0.9	2.3+/-0.6
3.	Age; mean +/- SD(Range)	0.9+/- 0.6	2.3+/-0.6
4.	Sex		
4a.	No of male percentage (%)	62(%)	56(%)
4b.	No of female percentage (%)	38(%)	44(%)
B	Maternal Factors:		
1.	No. of cases with PROM(>24 hrs)	2.3(%)	4.9(%)
2.	No. with h/o MSL	5(%)	9(%)
C.	Type of delivery: (%)		
1.	Spontaneous delivery	76(%)	81.2(%)
2.	LUCS	20.6(%)	17(%)
3.	Instrumental	2.8(%)	1.7(%)
4.	Assisted breech	0.6(%)	0.1(%)

**Table 2 : Type of organisms:**

	Types of organism	EOS INBORN	in LOS INBORN	in EOS OUTBORN	in LOS OUTBORN
1.	Methicillin sensitive staph. aureus	32(23.3%)	187(48.8%)	34(16.1%)	211(60.5%)
2.	Methicillin resistant staph. aureus	29(21.1%)	121(31.7%)	7(3.3%)	67(19.2%)
3.	Klebsiella	35(25.5%)	34(8.9%)	59(27.9%)	35(10.1%)
4.	E.coli	9(6.7%)	12(3.1%)	25(11.8%)	12(3.4%)
5.	Pseudomonussps.	18(13.3%)	4(1.0%)	35(16.7%)	18(5.0%)
6.	Acinetobacter sps.	4(2.9%)	15(3.9%)	23(10.9%)	2(0.6%)
7.	Candida sps.	0	2(0.5%)	0	2(0.6%)
8.	Coagulase negative staph (CONS)	4(2.9%)	2(0.5%)	17(8.1%)	0
9.	Gr B streptococcus	6(4.3%)	6(1.6%)	11(5.2%)	2(0.6%)
	Total	137(100%)	383(100%)	211(100%)	349(100%)

**Table 3: Outcome of the babies who had culture proven sepsis according to aetiology:**

	Outcome as per aetiology	Inborn discharged (%)	Death Inborn (%)	Outborn discharged (%)	Death outborn(%)
1.	Birth asphyxia	87(16.7%)	17(3.2%)	189(33.7%)	25(4.5%)
2.	Respiratory difficulty of newborn	97(18.6%)	5(1.0%)	90(16%)	12(2.1%)
3.	Neonatal jaundice	54(10.5%)	0(0)	43(7.7%)	01(0.2%)
4.	Pneumonia	56(10.7%)	2(0.4%)	38(6.8%)	15(2.8%)
5.	Meningitis	17(3.4%)	3(0.5%)	12(2.1%)	07(1.2%)
6.	LBW having prematurity	147(28.2%)	28(5.4%)	84(15%)	27(4.9%)
7.	Others	5(1.0%)	2(0.4%)	15(2.7%)	02(0.3%)
	Total	463(89.1%)	57(10.9%)	471(84%)	89(16%)

#### **IV. Discussion:**

In our discussed study period a total of 2880 babies were admitted in inborn and 2545 babies were admitted in outborn during the study period

Inborn babies with sepsis with proven culture positive, the main organism found is Klebsiella (25.5%) in EOS, followed by MSSA (23.3%) , MRSA (21.1%) then Pseudomonas (13.3%). Few sepsis is caused by E.coli (6.7%), CONS(2.9%) , Gr B streptococcus (4.3%)s and Acinetobacter (2.9%). Majority of the organisms are sensitive to piperacillin-tazobactam , amoxicillin , 3<sup>rd</sup> generation cephalosporins , vancomycin and fluroquinolones .

Whereas in LOS in inborn babies majority of sepsis is caused by MSSA (48.8%) followed by MRSA (31.7%). Other sepsis is caused by klebsiella (8.9%), CONS (0.5%), candida (0.5%), Acinetobacter (3.9%) and E.coli (3.1%), Gr B streptococcus(1.6%). Majority of the organisms are sensitive to piperacillin-tazobactam, amoxicillin, 3<sup>rd</sup> generation cephalosporins, vancomycin and fluroquinolones but candida is responsive to amphotericin B and Acinetobacter is responsive to Colistin. In some cases linezolid proven very effective.

In case of early presentation of sepsis in outborn babies major organism found is klebsiella (27.9%) followed by pseudomonas (16.7%) and MSSA (16.1%). Few cases of sepsis is caused by other organisms like MRSA (3.3%), E.coli(11.8%) , Gr B streptococcus(5.2%) and Acinetobacter(10.9%). The majority are responsive to piperacillin-tazobactam, amoxicillin, 3<sup>rd</sup> generation cephalosporins, vancomycin and fluroquinolones but few strains are responsive to aztreonam and ticarcillin.

In LOS cases in outborn babies major organism is MSSA(60.5%) followed by MRSA(19.2%), klebsiella(10.1%)a and pseudomonas(5.0%). The majority are responsive to piperacillin-tazobactam, amoxicillin, 3<sup>rd</sup> generation cephalosporins, vancomycin and fluroquinolones but meropenem and metronidazole have a good outcome in few cases.

#### **V. Outcome:**

Regarding outcome inborn babies have got very rapid interventions than outborn babies thus the sepsis rate in our SNCU is low in inborn babies rather than outborn babies.

Majority of inborn babies found culture proven sepsis are admitted due to low birth weight with prematurity (33.6%) followed by birth asphyxia (19.9%) and respiratory difficulty of new born(19.6%). Other

admissions comprised of neonatal jaundice (10.5%), congenital pneumonia (10.7%), meningitis (3.4%) and congenital anomalies (1.0%) like omphalocele, imperforate anus, cleft lip and/or cleft palate. 10.9% of total inborn culture positive babies become dead. Majority of mortality are found due to low birth weight with prematurity (5.4%) followed by birth asphyxia (3.2%). There is no death in the inborn babies found culture positive sepsis admitted due to neonatal jaundice in the scheduled study time.

89% of babies with culture positive sepsis are successfully discharged of inborn whereas 84% of babies of outborn found culture positive are discharged successfully with a 16% death rate with sepsis. The majority of death are caused by low birth weight with prematurity (4.9%) followed by birth asphyxia (4.5%) and congenital and acquired pneumonia (2.8%) and respiratory difficulty of newborn (2.1%). 1.2% babies of outborn having culture proven sepsis found dead.

In the study period a total of 520 inborn babies and 560 outborn babies have found culture proven sepsis which is 18% of the total babies admitted in inborn and 22% of the total babies admitted in outborn for the scheduled 1 year.

#### **VI. Limitations:**

There are few limitations like sometimes bactec-bottle for culture are not available and as this is a retrospective data there is a chance of loss of some culture positive reports.

#### **Acknowledgments:**

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#### **References:**

- [1]. O. Campbell, R. Gipson, A. El Mohandes, *et al.* The Egypt National Perinatal/Neonatal Mortality Study 2000 *J Perinatol*, 24 (2004), pp. 284-289
- [2]. UNICEF/WHO/The World Bank/UN Pop Div. Levels and Trends in Child Mortality. Report 2014.
- [3]. Ministry of Health and Population and National Population Council. El-Zanaty F, Way A, editor, Egypt Demographic Health Survey 2000. Calverton, MD: Macro International; 2001. A.Z. Jan, S. Ahmad, S.B. Zahid
- [4]. Clinical audit of admission pattern and its outcome in a neonatal ICU Gomal *J Med Sci*, 11 (2013), pp. 31-36
- [5]. V. Prasad, N. Singh Causes of morbidity and mortality in neonates admitted in government medical college, Haldwani in Kumaun Region (Uttarakhand) India *J Pharm Biomed Sci*, 8 (2011), pp. 1-4
- [6]. F. Rahim, A. Jan, J. Mohammad, H. Iqbal Pattern and outcome of admissions to neonatal unit of Khyber teaching hospital, Peshawar Pak *J Med Sci*, 23 (2007), pp. 249-253
- [7]. I. Seoud, R. Gamal el-Din, R. Said, H. AbouHussien Predictors of neonatal mortality in intensive care unit in Children's Hospital, Cairo University Alex *J Pediatr*, 19 (2005), pp. 93-97
- [8]. A. Elwan Mortality among outborn versus inborn neonates: a retrospective comparative study *Med J Cairo Univ*, 77 (2009), pp. 209-217
- [9]. G.R. Alexander, M.D. Kogan, J.H. Himes 1994-1996 U.S. singleton birth weight percentiles for gestational age by race, Hispanic origin, and gender *Matern Child Health J*, 3 (1999), pp. 225-231

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