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ABSTRACT

Objectives: This study describes the demographic characteristics and clinical outcomes of neonates born within 7 days of public ambulance transport to hospitals across five states in India.

Design: Prospective observational study.

Setting: Five Indian states using a centralised EMS agency that transported 3.1 million pregnant women in 2014.

Participants: Over 6 weeks in 2014, this study followed a convenience sample of 1,431 neonates born to women utilizing a public-private ambulance service for a 'pregnancy related' problem. Initial calls were deemed 'pregnancy related' if categorised by EMS dispatchers as 'pregnancy', 'childbirth', 'miscarriage' or 'labour pains'. Interfacility transfers, patients absent on ambulance arrival, refusal of care, and neonates born to women beyond 7 days of using the service were excluded.

Main outcome measures: Emergency medical technician (EMT) interventions and death at 2, 7 and 42 days after delivery.

Results: Among 1,684 women, 1,411 gave birth to 1,431 newborns within 7 days of initial ambulance transport. Median maternal age at delivery was 23 years [inter-quartile range (IQR): 21-25]. Most mothers were from rural/tribal areas (92.5%) and lower social (79.9%) and economic status (69.9%). Cumulative mortality rates at 2, 7 and 42-days follow-up were 41, 53 and 62 per 1000 births, respectively. Perinatal mortality rate among enrolled cases was 53 per 1000. Preterm birth [odds ratio (OR): 2.89, 95% confidence interval (CI): 1.67-5.00], twin deliveries (OR: 2.80, 95% CI: 1.10-7.15), and cesarean section (2.21, 95% CI: 1.15-4.23) were the strongest predictors of mortality.

Conclusions: The perinatal mortality rate associated with this poor, marginalized cohort of patients with high-acuity conditions of pregnancy was nearly two times the most recent rate for

India as a whole (28 per 1000 births). Emergency medical services have the potential to reduce inequities in accessing healthcare and increase facility-based care, thereby reducing young infant mortality in India.

STRENGTHS AND LIMITATIONS

- This study is a novel, prospective assessment of perinatal mortality in India whose mothers utilized prehospital services within 7 days of delivery.
- Follow-up rates were excellent and cumulative mortality rates at 2, 7 and 42-days follow-up were 41, 53 and 62 per 1000 births, respectively.
- Generalisability may be limited as it was a convenience sample of a unique prehospital system across multiple states in India.
- Limited data regarding variability and quality of hospital management and therapeutics were collected

KEYWORDS: India, Accident and Emergency Medicine, Maternal Medicine—Obstetrics, Emergency Medical Services (EMS), Neonatal Mortality

INTRODUCTION

An estimated 2.6 million stillbirths and 2.7 million neonatal deaths occur globally each year.[1] A disproportionate percentage (approximately 99%) of these deaths occur in low and middle-income countries. [2]

India accounts for approximately one-quarter of global newborn deaths, with an estimated 760,000 neonatal deaths in 2012. While India has made laudable progress in reducing overall child mortality over the past 25 years, similar reductions in neonatal mortality have lagged. As a result, India fell short of the Millennium Development Goal (MDG-4) of a two-thirds reduction in under-five mortality from 1990-2015. [3]

Globally, the overall number of neonatal deaths has declined significantly, yet they account for an increasing proportion of under-five deaths.[4,5] Attempts to reduce deaths around the time of childbirth have been particularly challenging.[6] In 2013, India's perinatal mortality rate (PMR), or the number of third trimester stillbirths (after 28 weeks gestational age) and neonatal deaths in the first 7 days, was 28 per 1000 total births.[7]

Previous research on evidence-based approaches to reducing neonatal mortality have included efforts to increase access to preventive and curative antenatal, perinatal and postnatal care.[8] To date, however, little attention has focused on the quality of pre-hospital care and transport on neonatal outcomes in developing countries. Pre-hospital care in India has the potential to increase access to skilled birth attendants and facility-based health services, while also providing early lifesaving interventions during transport that can reduce overall neonatal mortality. Recent data from two states in India demonstrate substantial reductions in neonatal and infant mortality

rates associated with pre-hospital services.[9] This study describes the demographics, management and clinical outcomes of young infants born to laboring women in five Indian states who were transported by an ambulance service with trained emergency medical technicians (EMTs).

METHODS

Over a 6-week period, from February-April 2014, research assistants enrolled a convenience sample of neonates born to women in their third trimester of pregnancy who called for GVK Emergency Management and Research Institute (GVK EMRI) ambulance transport for pregnancy-related complaints. Neonates were enrolled from one of five participating Indian states: Andhra Pradesh, Assam, Gujarat, Karnataka, and Meghalaya (Figure 1).

GVK EMRI

GVK EMRI is a not-for-profit, public-private partnership that provides free ambulance transport and pre-hospital stabilization care that can be accessed using a three-digit, toll-free phone number. Launched in 2005, GVK EMRI is currently the largest provider of emergency medical services in India (and in the world), operating in 17 of 28 Indian states and union territories and representing a catchment population of 750 million people. Obstetric emergencies comprise the single largest category of GVK EMRI's pre-hospital transports, with upwards of 30% of all calls being pregnancy-related, totaling 3.1 million calls for pregnancy-related complaints in 2014.[10]

Call management, dispatch, and online medical direction are provided by central state-based, emergency call centers that support a fleet of ambulances, strategically distributed to optimize

response times. Individual ambulance providers are dispatched based on availability and distance to the patient. EMTs provide basic emergency obstetric and neonatal care, including resuscitation and administration of life-saving medications, under the oversight of real-time physician-guided medical direction. Patients are transported to the nearest appropriate public or private care facility unless they request an alternate facility.

Enrollment Process

Patients were enrolled six days a week, Monday through Saturday, during daytime hours for six hours per day. Any woman in her third trimester of pregnancy who called for a pregnancy-related complaint was eligible for enrollment. A call was considered "pregnancy-related" if it was categorized by the dispatch officer as a call for "pregnancy", "childbirth", "miscarriage", or "labor pains". Exclusion criteria included calls for inter-facility transfers, patients who were absent upon EMT arrival, and patients who refused care. Newborns of women callers were enrolled if born to a mother within seven days of the initial call.

Data Collection

EMTs collected demographic, historical and current clinical data related to both maternal and neonatal care during and after ambulance transport. This information was relayed and categorized by research assistants via telephone in real time.

Neonates were matched to maternal demographic, prenatal characteristics and pre-hospital care. Demographic data included geography, economic status (defined by maternal possession of the low-income government health insurance programme white ration card), prior maternal

education, and current employment. Social status was classified by maternal self-identified caste; Lower social classes included 'scheduled caste' (lowest, most socially disadvantaged group), 'scheduled tribe' (socially and geographically disadvantaged), and 'backward caste' (intermediary group socially). 'Other caste' included refers to those with the highest social status.

Among the subset of neonates delivered either prior to ambulance arrival or in the pre-hospital setting (under the care of an EMT), direct neonatal clinical care data was also recorded. Newborn infant gestational age was determined by maternal report often based on last menstrual period.

Two separate telephone numbers, the mother's and a friend's or relative's, were collected at the time of enrollment to facilitate patient follow-up. All patients who delivered prior to emergency medical services (EMS) arrival through 7 days after the dispatch call, were followed up by phone at 48 hours, 7 days and 42 days postpartum.[11] The 42-day follow-up period was utilized to capture maternal mortality as well as young infant outcomes.

Per GVK EMRI's standard protocol, all patients were verbally consented by responding EMTs for treatment, data collection, and follow-up at the time of enrollment. The study was approved by the Institutional Review Board at Stanford University (IRB#18185) and the Ethics and Research Committee at GVK EMRI.

Data Analysis

Initial patient data was recorded securely online using REDCap (Stanford University).[12] All data analysis was conducted via SAS Enterprise Guide for Windows, V.4.3 (SAS Institute Inc., Cary, NC, USA). Both maternal and patient data was cleaned and de-identified for analyses. Descriptive demographic and maternal clinical data was provided as numbers and percentages where appropriate. In addition to descriptive data, main outcomes included medical interventions in the pre-hospital setting and mortality at each stage of follow-up. We were unable to differentiate stillbirths versus neonatal deaths that occurred on the day of delivery.

Wilcoxon rank sum and Chi-square tests were used to compare cases of early infant deaths to those that survived to 2, 7 and 42 days. Variables analysed included demography, items in the maternal prenatal and past medical history and in the medical care history in the pre-hospital setting, and delivery characteristics.

A multivariate model was constructed using variables that were significant from the Chi-square tests. State was not included in initial multivariate models, though it was controlled for in iterative analysis given the proportional variability in early infant death from state to state. Odds ratios (ORs) and 95% confidence intervals (CI) were used to assess the association of individual variables with infant death.

RESULTS

A total of 1,411 (83.8%) of the 1,684 women enrolled gave birth to a total of 1,431 newborns (including 40 twins, 2.8%) within 7 days of calling for ambulance services (Table 1*).* This represents approximately 1.7% of all pregnancy-related calls to GVK EMRI across the five states

during the study period.

Table 1. Demographic and maternal health characteristics among neonates born to mothers using Emergency Medical Services (EMS) in five states in India, February-April, 2014.

	N=1431	%
Maternal Demographic Characteristics		
Age		
Median (Intra-quartile range, IQR)	23	21-26
15-19	70	4.9
20-24	809	56.5
25-29	434	30.3
30-34	92	6.4
35-39	23	1.6
40-44	3	0.2
State		
Andhra Pradesh	381	26.6
Assam	201	14.0
Gujarat	477	33.3
Karnataka	342	23.9
Meghalaya	30	2.1
Geographic location		
Rural/Tribal	1323	92.5
Urban	108	7.5
Social status *		
Backward caste	508	35.5
Other caste	284	19.8
Scheduled caste	254	17.7
Scheduled tribe	381	26.6
Economic Status**		
Pink ration card	422	29.5
White ration card	987	69.0
Education level completed		
None	528	36.9
Primary	357	24.9
Secondary	381	26.6
Intermediate	81	5.7
Graduate degree	37	2.6
Occupation		
Homemaker	1079	75.4
Other	352	24.6
Medical history		
Anemia	99	6.9
Hypertension	10	0.7
Pulmonary disease	4	0.3
HIV	2	0.1
Antenatal care visits (ANC)		
1-3	732	51.2
>3	671	46.9
≥1 visit with a physician	1,111	77.6
Iron supplementation	1197	83.6

Parity		
Multiparous	818	57.2
Nulliparous	613	42.8
Age at first pregnancy***		
Median (IQR)	21	20-22
15-19	197	24.1
20-24	550	67.2
25-29	65	7.9
30-34	3	0.4
Years since prior pregnancy***		
<2	364	44.5
2-3	211	25.8
>3	237	29.0

* Self-identified caste is used as a proxy for social status and in India and is often used in national population health level monitoring. Scheduled caste is the lowest, most socially disadvantaged group. 'Scheduled tribe' is also a disadvantaged group. 'Backward caste' is an intermediary group socially; and 'other caste' includes all those who do not belong to the aforementioned group and have the highest social status.
** Economic status is defined by whether patients were dependent on the low-income government health insurance program (white ration card).
***Of multiparous mothers only (n=818).

Most neonates were born to mothers from rural or tribal areas (n=1,323, 92.5%), lower economic status (n=987, 69.0%) and lower social class (n=1,143, 79.9%); and the majority had less than a secondary education (n=885, 61.8%).

At the time of initial ambulance call, 82.5% (n=1,180) of women were term gestation (37-42 weeks), 97.2% (n=1391) reported contractions or abdominal pain, 31.0% (n=443) had rupture of membranes (ROM) with contractions and 7.9% (n=113) had vaginal bleeding (Table 2*)*.

Table 2. Characteristics of neonates peri-EMS transport in five states in India, February-April, 2014

	N=1431	%
Prehospital Characteristics		
Gestational age (weeks) at transport		
Median (IQR)	39.7	38.4-40.0

<32	32	2.2
32-36	164	11.5
37-42	1180	82.5
>42	38	2.7
Receiving hospital type		
Government	1181	79.7
Private/Paid	187	13.2
Trust/NGO	50	3.5
Distance from scene to facility (km)	15	9-23
Time from call to facility (min)	65	50-84
Presentation		
Contractions	1391	97.2
Rupture of membranes	443	31.0
Vaginal bleeding	113	7.9
Abnormal maternal vital recorded	301	22.1
HR ≥100	112	7.8
SBP<90	16	1.2
SBP≥140 AND <160 or DBP ≥90 AND <110	192	13.4
SBP ≥160 or DBP≥110	20	1.4
RR≥30	1	0.1
Emergency Medical Technician (EMT) actions		
Left lateral positioning	1364	95.3
Oxygen provided	331	23.1
IV placed	165	11.5
Delivery Characteristics		
When delivered		
Prior to ambulance arrival	37	2.6
After ambulance arrival and prior to hospital admission	45	3.1
Within 48 hours	1285	89.8
Within 7 days	64	4.5
In-hospital	1274	89.1
Term (>37 week gestation)	1223	85.5
Vaginal	1170	81.8
Twin	40	2.80

Abnormal pre-hospital vital signs (pulse rate >99, respiratory rate>29, systolic blood pressure<90 or >140, or diastolic blood pressure>90) were documented in 22.1% (n=301) of women. Of those women with tachycardia (n=112), 89.3% (n=100) were placed in the left lateral position and 10.7% (n=12) received intravenous (IV) fluids. Among those women with documented hypotension (n=16) 75.0% (n=12) were placed in the left lateral position, and 37.5% (n=6) received intravenous (IV) fluids. In sum, four women died during this study, and all within 48 hours after hospital arrival.

Prior to hospital admission, 82 (5.7%) neonates were delivered from 80 distinct mothers. Thirty-seven delivered prior to ambulance arrival. EMTs assisted in the delivery of 45 neonates, either on scene (where the ambulance picked up the patient), during transport or immediately on hospital arrival. Another 1,349 (94.3%) deliveries occurred after EMS transport, with the majority (n=1,285, 89.8%) occurring within 2 days of EMS dispatch. Of the deliveries that followed EMS transport, 1,274 (94.4%) occurred in the hospital and another 74 (5.5%) followed hospital discharge.

The median distance from the scene to the hospital was 15 km [Inter-quartile range (IQR): 9-23]. The median time from initial call to hospital arrival was 65 minutes (IQR: 50-84).

The overall follow-up rates at 2, 7 and 42 days were 99.8%, 99.3% and 94.1%, respectively. In sum, 62 died by day 2, 76 neonates had died by day 7 and a total of 84 young infants had perished by day 42 (Table 3). Cumulative mortality rates were 53 and 62 per 1000 births at 7 and 42-day follow-up, respectively. The calculated PMR was 53 deaths per 1000 births. The highest

7-day mortality rate was in the state of Meghalaya (200 per 1000, p =0.019). Other demographic indicators, including economic, social (caste status), education or occupational status of the mother were not significantly related to mortality in univariate analysis.

Table 3. Characteristics and factors associated with perinatal mortality in five states in India, February-April, 2014.

	Alive		Dead		
	N=1345	%	N=76	%	P-value
Maternal Demographic Characteristics					
Rural or tribal geography	1243	92.4	72	94.7	0.652
Gujarat state	444	33.0	31	40.8	0.162
Meghalaya state	25	1.9	5	6.6	**0.019**
Social status					
Other caste	270	20.1	12	15.8	0.356
Non-other caste	1071	79.6	64	84.2	
Economic status					
Pink ration card	396	29.4	24	31.6	0.639
White ration card	930	69.1	50	65.8	
Education level					
No prior schooling	489	36.4	32	42.1	0.332
Attended school	811	60.3	42	55.3	
Homemaker	1014	75.4	59	77.6	0.658
≥2 years since prior delivery	423	31.4	23	30.3	0.802
Maternal Prenatal Characteristics					
Prenatal iron supplementation	1129	83.9	60	78.9	0.248
≥1 visit with a physician	1046	77.8	57	75.0	0.532
<4 ANC visits	677	50.3	49	64.5	**0.019**
Current Maternal and Neonatal Care					
Any abnormal maternal vital sign	264	19.6	27	35.5	**0.019**
C-section	107	8.0	13	17.1	**0.005**
Delivery prior to hospital admission	73	5.4	6	7.9	0.361
In-hospital	1197	89.0	68	89.5	0.911
IV placed in mother	148	11.0	13	17.1	0.103
Maternal tachycardia (HR≥100)	102	7.6	10	13.2	0.081
Left lateral position during transport	1287	95.7	69	90.8	**0.047**
Premature rupture of membranes	62	4.6	8	10.5	**0.021**
Preterm (<37 weeks)	167	12.4	18	23.7	**0.005**
Twin	33	2.5	7	9.2	**0.001**

Univariate analysis among all mothers identified the following maternal risk factors for elevated neonatal mortality at 7 days: less than four antenatal care (ANC) visits (p=0.019), abnormal vital signs (p=0.049), IV placement (p=0.007) and mother not placed in left lateral position during transport (p=0.047). Of those infants delivered in the presence of pre-hospital care providers, the cumulative mortality rate at 42 days was 122 per 1000 (n=5) with 4 infants lost to follow-up.

The association between maternal and infant characteristics and death at 7 and 42-day follow-up was also assessed through multivariate logistic regression (Table 4). At 42-day follow-up, preterm birth (OR = 2.89, 95% CI = 1.67-5.00) and twin deliveries (OR = 2.80, 95% CI = 1.10-7.15) were the strongest predictors of mortality. Other maternal risk factors raising the likelihood of young infant death included not being placed in the left lateral position en-route to the hospital (OR = 2.44, 95% CI = 1.06-5.61), heart rate greater than 100 (OR = 2.21, 95% CI = 1.13-4.35), or having a caesarean section delivery (OR = 2.21, 95% CI = 1.15-4.23). The risk of death was nearly two-fold higher for young infants born to mothers who went to fewer than four ANC visits (OR = 1.89, 95% CI = 1.14-3.14).

Controlling for geographic (state-to-state) variability led to some changes in the multivariate regression model for 42-day mortality. Prematurity (OR = 3.08, 95% CI = 1.77-5.35), twin delivery (OR = 2.79, 95% CI = 1.07-7.23), fewer than four ANC visits (OR = 1.72, 95% CI = 1.03-5.89), and caesarean section delivery (OR = 2.20, 95% CI = 1.09-4.45) continued to be independent predictors of overall young infant mortality, while maternal tachycardia (OR = 1.76, 95% CI = 0.86-3.62) and maternal positioning (OR = 2.05, 95% CI = 0.87-4.85) were no longer statistically significant.

Table 4. Predictors of young infant mortality at 7- and 42-day follow-up by multivariate logistic regression models

	7 Days		42 Days	
	OR	95 % CI	OR	95 % CI
Prematurity (<37 weeks)	2.21	1.19-4.09	2.89	1.67-5.00
Twin delivery	3.87	1.56-9.64	2.80	1.10-7.15
C-section	1.93	0.92-4.03	2.21	1.15-4.23
<4 ANC visits	1.76	1.02-3.02	1.89	1.14-3.14
Not placed in left lateral position*	1.67	0.62-4.46	2.44	1.06-5.61
Maternal HR ≥100*	1.57	0.70-3.52	2.21	1.13-4.35

*When controlled by state these variables were no longer statistically significant.

DISCUSSION

Reducing the equity gap

Elevated neonatal mortality has been shown globally to be associated with various forms of marginalisation, including poverty, low maternal education, and low social standing.[13] Previous programs to reduce neonatal mortality have focused on reducing the equity gap—reaching women and newborn infants in greatest need and those with limited access to formal healthcare services.[14-16] This prospective study suggests EMS plays an important, but under-appreciated role in reducing the equity gap and adds to prior data supporting the the role of centralized EMS services in maternal and neonatal health policy.[9] Pre-hospital interventions and rapid transport when coupled with current data on known community and hospital-based risks has the potential to lead to development of interventions aimed at further reducing neonatal deaths.[17-19]

Ambulance services cared for a population—93% from lower social or economic strata— that historically has had less timely access to formal medical services. EMTs performed essential pre-hospital services, including assisting with the delivery of newborns in the field and during transport to the hospital. In 94% of all transports, EMTs connected women and neonates to

health facilities offering obstetric care in less than two hours.

The absence of an association between mortality and social determinants of health, such as socioeconomic status or education level, was unexpected. However, the overwhelmingly high number of neonates from lower socioeconomic classes in our study cohort decreased our ability to detect the impact of these demographic characteristics on mortality. Furthermore, the impact of socioeconomic status on neonatal mortality may be very closely linked to the lack of access to care customary to these populations. In our study, this link did not exist, as EMS overcome many factors limited healthcare access for poor and marginalized populations; thus, access to care was broadly provided for all populations by the responding EMTs and subsequent ambulance transport. This suggests that delivery of EMS may be an important means to achieving greater equity in healthcare delivery.

Quality of Pre-hospital Care

Deficits in the quality of India's pre-hospital care of pregnant women persist. Maternal haemodynamic instability has significant risks for neonatal health,[20,21] and subsequent maternal resuscitation, whether through positioning or administration of fluids, has been shown to increase cardiac output and stroke volume—effectively improving maternal and, by-proxy, neonatal haemodynamics.[22,23] Continued training aimed at EMT recognition of high-risk patients and treatment with simple interventions based on vital signs abnormalities is imperative. Ongoing quality assurance and training efforts are now aimed at increasing EMT recognition of high-risk patients, rates of fluid resuscitation and proper positioning during pre-hospital maternal resuscitation.

Helping a high-risk population

In developing countries, most perinatal deaths occur at home.[24] Estimates suggest that transitioning to institutional deliveries with a skilled birth attendant in lieu of traditional home deliveries could prevent over 500,000 stillbirths and 1.3 million annual neonatal deaths by 2020.[25,26] Yet, even with transport to healthcare facilities, the estimated PMR of 53 deaths per 1000 births is nearly double the reported PMR for all of India of 28 per 1000 births.[27]

This discrepancy in PMR rates is likely multifactorial. Prematurity (based on maternal report of gestational age) was found to be one of the strongest predictors of death. This relationship is consistent with global data identifying this as the number one cause of neonatal death.[28] Moreover, many deaths in preterm infants occur early in the neonatal period, and rapid intervention, made possible through transport under the care of an EMT to health care facilities with the capabilities to provide neonatal intensive care is critically important for survival.

The natural twinning rate in the study was 14.0 per 1,000 births, almost double the estimated 7.2 per 1,000 births reported across India.[29] Twin births were a significant predictor of death in this study (OR 2.8) and thus another important factor in the increased PMR.

The relationship between initial maternal hemodynamic instability and mortality of their infants suggests that the level of acuity of our maternal cohort was high. Women may not recognize the need to seek emergent care and are calling EMS only when they are in a very critical condition.

Finally, almost half (47.4%) of women enrolled in our study attended less than the recommended four ANC visits, a factor which proved to also be an important predictor of young infant

mortality in this study. These women may have had complications that went unrecognized in the perinatal period and that presented as emergencies necessitating the use of EMS.

Notably, the PMR associated with this cohort of patients was significantly higher than the state averages and associated with risk factors that, when addressed in future efforts, will be important in reducing neonatal mortality. In this study, however, we were unable to link records from care pre-hospital care with those for hospital-based care, and thus we cannot comment on the relationship between mortality and variability in post-transport facility-based care in India, including treatments, disease course and cause of death in hospital.

Emergency response services have the potential to promote equity in access to healthcare services, and improve perinatal survival in India. The elevated PMR in this large patient cohort is reflective of the high-risk nature of this population and the need for further attention to coverage of these services, provision of high-quality tailored interventions and focused investigations to inform continuous improvement in EMS.

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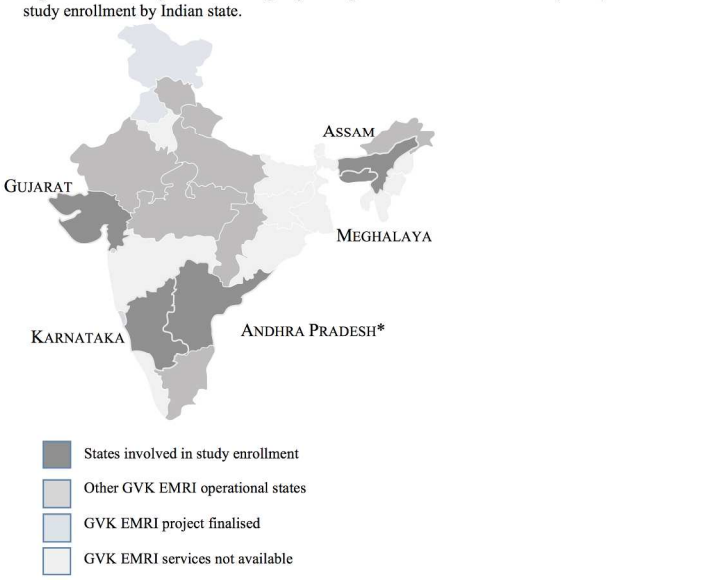
Figure 1. Availability of GVK Emergency Management and Research Institute (EMRI) services and study enrollment by Indian state.



*After the study's conclusion Andhra Pradesh was partitioned into two separate states: Telengana and Andhra Pradesh

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Reducing early infant mortality in India: results of a prospective cohort of pregnant women utilizing emergency medical services

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ABSTRACT

Objectives: To describe the demographic characteristics and clinical outcomes of neonates born within 7 days of public ambulance transport to hospitals across five states in India.

Design: Prospective observational study.

Setting: Five Indian states using a centralised EMS agency that transported 3.1 million pregnant women in 2014.

Participants: Over 6 weeks in 2014, this study followed a convenience sample of 1,431 neonates born to women utilizing a public-private ambulance service for a 'pregnancy related' problem. Initial calls were deemed 'pregnancy related' if categorised by EMS dispatchers as 'pregnancy', 'childbirth', 'miscarriage' or 'labour pains'. Interfacility transfers, patients absent on ambulance arrival, refusal of care, and neonates born to women beyond 7 days of using the service were excluded.

Main outcome measures: Death at 2, 7 and 42 days after delivery.

Results: Among 1,684 women, 1,411 gave birth to 1,431 newborns within 7 days of initial ambulance transport. Median maternal age at delivery was 23 years (IQR: 21-25). Most mothers were from rural/tribal areas (92.5%) and lower social (79.9%) and economic status (69.9%). Follow-up rates at 2, 7 and 42 days were 99.8%, 99.3% and 94.1%, respectively. Cumulative mortality rates at 2, 7 and 42-days follow-up were 41, 53 and 62 per 1000 births, respectively. The perinatal mortality rate (PMR) was 53 per 1000. Preterm birth [OR: 2.89, 95% CI: 1.67-5.00], twin deliveries (OR: 2.80, 95% CI: 1.10-7.15), and cesarean section (2.21, 95% CI: 1.15-4.23) were the strongest predictors of mortality.

Conclusions: The perinatal mortality rate associated with this cohort of patients with high-acuity conditions of pregnancy was nearly two times the most recent rate for India as a whole (28 per 1000 births). EMS data has the potential to provide more robust estimates of PMR, reduce

inequities in timely access to healthcare, and increase facility-based care through service of marginalized populations.

STRENGTHS AND LIMITATIONS

- This study is a novel, prospective assessment of perinatal mortality in India whose mothers utilized prehospital services within 7 days of delivery.
- Follow-up rates were excellent, with over 99% of patients followed at 7 days.
- Overall cumulative mortality rates at 2, 7 and 42-days follow-up were 41, 53 and 62 per 1000 births, respectively.
- Generalisability may be limited as it was a convenience sample of a unique prehospital system across multiple states in India.
- Limited data regarding variability and quality of hospital management and therapeutics were collected

KEYWORDS: India, Accident and Emergency Medicine, Maternal Medicine—Obstetrics, Emergency Medical Services (EMS), Neonatal Mortality

INTRODUCTION

An estimated 2.6 million stillbirths and 2.7 million neonatal deaths occur globally each year.[1] A disproportionate percentage (approximately 99%) of these deaths occur in low and middle-income countries. [2]

India accounts for approximately one-quarter of global newborn deaths, with an estimated 760,000 neonatal deaths in 2012. While India has made laudable progress in reducing overall

child mortality over the past 25 years, similar reductions in neonatal mortality have lagged. As a result, India fell short of the Millennium Development Goal (MDG-4) of a two-thirds reduction in under-five mortality from 1990-2015. [3]

Globally, the overall number of neonatal deaths has declined significantly, yet they account for an increasing proportion of under-five deaths.[4,5] Attempts to reduce deaths around the time of childbirth have been particularly challenging.[6] In 2013, India's perinatal mortality rate (PMR), or the number of third trimester stillbirths (after 28 weeks gestational age) and neonatal deaths in the first 7 days, was 28 per 1000 total births.[7] Most agree that this likely underestimates the overall perinatal mortality given the difficulty in capturing stillbirths and deaths that occur at home. [8]

Previous research on evidence-based approaches to reducing young infant mortality have included efforts to increase access to preventive and curative antenatal, perinatal and postnatal care.[9] To date, however, little attention has focused on the role and quality of pre-hospital care and transport on describing neonatal outcomes in developing countries. Pre-hospital care in India has the potential to capture those deaths that occur at home and are not transferred to the hospital. At the same time, prehospital care increases access to skilled birth attendants and facility-based health services, while also providing early lifesaving interventions during transport that can reduce overall neonatal mortality. Recent data from two states in India demonstrate substantial reductions in neonatal and infant mortality rates associated with pre-hospital services.[10] This study aims to report the perinatal mortality among a cohort of young infants, born to laboring women in five Indian states who were transported by an ambulance service with

trained emergency medical technicians (EMTs). Secondarily we report on the demographic, maternal indicators and clinical management associated with increased rates of perinatal death.

METHODS

Over a 6-week period, from February-April 2014, research assistants enrolled a convenience sample of neonates born to women in their third trimester of pregnancy who called for GVK Emergency Management and Research Institute (GVK EMRI) ambulance transport for pregnancy-related complaints. Neonates were enrolled from one of five participating Indian states: Andhra Pradesh, Assam, Gujarat, Karnataka, and Meghalaya (Figure 1).

GVK EMRI

GVK EMRI, named after Gunupati Venkata Krishna, is a not-for-profit, public-private partnership that provides free ambulance transport and pre-hospital stabilization care that can be accessed using a three-digit, toll-free phone number. Launched in 2005, GVK EMRI is currently the largest provider of emergency medical services in India (and in the world), operating in 17 of 28 Indian states and union territories and representing a catchment population of 750 million people. Obstetric emergencies comprise the single largest category of GVK EMRI's pre-hospital transports, with upwards of 30% of all calls being pregnancy-related, totaling 3.1 million calls for pregnancy-related complaints in 2014.[11] This is in comparison to the US and European countries where maternal and pregnancy calls are often <1% of total.[12]

Call management, dispatch, and online medical direction are provided by central state-based, emergency call centers that support a fleet of ambulances, strategically distributed to optimize

response times. Individual ambulance providers are dispatched based on availability and distance to the patient. The majority of ambulances are staffed by both a driver and a single emergency medical technician (EMT). EMTs are trained to provide basic emergency obstetric and neonatal care, including resuscitation and administration of life-saving medications, with oversight from real-time physician-guided medical direction available by phone. EMTs scope of practice around obstetric, gynecologic and neonatal care are driven by standard protocols (see online supplementary material 1) Patients are transported to the nearest appropriate public or private care facility unless they request an alternate facility.

Enrollment Process

Patients were enrolled six days a week, Monday through Saturday, during daytime hours for six hours per day. Enrollment was limited to this time frame given constraints of research assistant availability, safety and cost. Any woman in her third trimester of pregnancy who called for a pregnancy-related complaint was eligible for enrollment. A call was considered "pregnancy-related" if it was categorized by the dispatch officer as a call for "pregnancy", "childbirth", "miscarriage", or "labor pains". Exclusion criteria included calls for inter-facility transfers, patients who were absent upon EMT arrival, and patients who refused care. Newborns of women callers were enrolled if born to a mother within seven days of the initial call.

Data Collection

EMTs collected demographic, historical and current clinical data related to both maternal and neonatal care during and after ambulance transport. This information was relayed and categorized by research assistants via telephone in real time.

Neonates were matched to maternal demographic, prenatal characteristics and pre-hospital care. Demographic data included geography, economic status (defined by maternal possession of the low-income government health insurance programme white ration card), prior maternal education, and current employment. Social status was classified by maternal self-identified caste; Lower social classes included 'scheduled caste' (lowest, most socially disadvantaged group), 'scheduled tribe' (socially and geographically disadvantaged), and 'backward caste' (intermediary group socially). 'Other caste' included refers to those with the highest social status.

Among the subset of neonates delivered either prior to ambulance arrival or in the pre-hospital setting (under the care of an EMT), direct neonatal clinical care data was also recorded. Newborn infant gestational age was determined by maternal report often based on last menstrual period.

Two separate telephone numbers, the mother's and a friend's or relative's, were collected at the time of enrollment to facilitate patient follow-up. All patients who delivered prior to emergency medical services (EMS) arrival through 7 days after the dispatch call, were followed up by phone at 48 hours, 7 days and 42 days postpartum.[13] The 42-day follow-up period was utilized to capture maternal mortality as well as young infant outcomes.

Per GVK EMRI's standard protocol, all patients were verbally consented by responding EMTs for treatment, data collection, and follow-up at the time of enrollment. The study was approved by the Institutional Review Board at Stanford University (IRB#18185) and the Ethics and Research Committee at GVK EMRI.

Data Analysis

Initial patient data was recorded securely online using REDCap (Stanford University).[14] All data analysis was conducted via SAS Enterprise Guide for Windows, V.4.3 (SAS Institute Inc., Cary, NC, USA). Both maternal and patient data was cleaned and de-identified for analyses. Descriptive demographic and maternal clinical data was provided as numbers and percentages where appropriate. In addition to descriptive data, main outcomes included medical interventions in the pre-hospital setting and mortality at each stage of follow-up. We were unable to differentiate stillbirths versus neonatal deaths that occurred on the day of delivery.

Wilcoxon rank sum and Chi-square tests were used to compare cases of early infant deaths to those that survived to 2, 7 and 42 days. Variables analysed included demography, items in the maternal prenatal and past medical history and in the medical care history in the pre-hospital setting, and delivery characteristics.

A multivariate model was constructed using variables that were significant from the Chi-square tests. State was not included in initial multivariate models, though it was controlled for in iterative analysis given the variability in enrollment and proportional variability in early infant death from state to state. Odds ratios (ORs) and 95% confidence intervals (CI) were used to

assess the association of individual variables with infant death.

RESULTS

A total of 1,411 (83.8%) of the 1,684 women enrolled gave birth to a total of 1,431 newborns (including 40 twins, 2.8%) within 7 days of calling for ambulance services (Table 1*).* This represents approximately 1.7% of all pregnancy-related calls to GVK EMRI across the five states during the study period.

Table 1. Demographic and maternal health characteristics among neonates born to mothers using Emergency Medical Services (EMS) in five states in India, February-April, 2014.

	N=1431	%
Maternal Demographic Characteristics		
Age		
Median (Intra-quartile range, IQR)	23	21-26
15-19	70	4.9
20-24	809	56.5
25-29	434	30.3
30-34	92	6.4
35-39	23	1.6
40-44	3	0.2
State		
Andhra Pradesh	381	26.6
Assam	201	14.0
Gujarat	477	33.3
Karnataka	342	23.9
Meghalaya	30	2.1
Geographic location		
Rural/Tribal	1323	92.5
Urban	108	7.5
Social status *		
Backward caste	508	35.5
Other caste	284	19.8
Scheduled caste	254	17.7
Scheduled tribe	381	26.6
Economic Status**		
Pink ration card	422	29.5
White ration card	987	69.0
Education level completed		
None	528	36.9
Primary	357	24.9
Secondary	381	26.6
Intermediate	81	5.7
Graduate degree	37	2.6

Occupation		
Homemaker	1079	75.4
Other	352	24.6
Medical history		
Anemia	99	6.9
Hypertension	10	0.7
Pulmonary disease	4	0.3
HIV	2	0.1
Antenatal care visits (ANC)		
1-3	732	51.2
>3	671	46.9
≥1 visit with a physician	1,111	77.6
Iron supplementation	1197	83.6
Parity		
Multiparous	818	57.2
Nulliparous	613	42.8
Age at first pregnancy***		
Median (IQR)	21	20-22
15-19	197	24.1
20-24	550	67.2
25-29	65	7.9
30-34	3	0.4
Years since prior pregnancy***		
<2	364	44.5
2-3	211	25.8
>3	237	29.0

* Self-identified caste is used as a proxy for social status and in India and is often used in national population health level monitoring. Scheduled caste is the lowest, most socially disadvantaged group. 'Scheduled tribe' is also a disadvantaged group. 'Backward caste' is an intermediary group socially; and 'other caste' includes all those who do not belong to the aforementioned group and have the highest social status.
** Economic status is defined by whether patients were dependent on the low-income government health insurance program (white ration card).
***Of multiparous mothers only (n=818).

Most neonates were born to mothers from rural or tribal areas (n=1,323, 92.5%), lower economic status (n=987, 69.0%), lower social class (n=1,143, 79.9%), and had less than a secondary education (n=885, 61.8%).

At the time of initial ambulance call, 82.5% (n=1,180) of women were term gestation (37-42 weeks), 97.2% (n=1391) reported contractions or abdominal pain, 31.0% (n=443) had rupture of membranes (ROM) with contractions and 7.9% (n=113) had vaginal bleeding (Table 2*).*

Table 2. Characteristics of neonates peri-EMS transport in five states in India, February-April, 2014

	N=1431	%
Prehospital Characteristics		
Gestational age (weeks) at transport		
Median (IQR)	39.7	38.4-40.0
<32	32	2.2
32-36	164	11.5
37-42	1180	82.5
>42	38	2.7
Receiving hospital type		
Government	1181	79.7
Private/Paid	187	13.2
Trust/NGO	50	3.5
Distance from scene to facility (km)	15	9-23
Time from call to facility (min)	65	50-84
Presentation		
Contractions	1391	97.2
Rupture of membranes	443	31.0
Vaginal bleeding	113	7.9
Abnormal maternal vital recorded	301	22.1
HR ≥100	112	7.8
SBP<90	16	1.2
SBP≥140 AND <160 or DBP ≥90 AND <110	192	13.4
SBP ≥160 or DBP≥110	20	1.4
RR≥30	1	0.1
Emergency Medical Technician (EMT) actions		
Left lateral positioning	1364	95.3
Oxygen provided	331	23.1
IV placed	165	11.5
Delivery Characteristics		
When delivered		
Prior to ambulance arrival	37	2.6
After ambulance arrival and prior to hospital admission	45	3.1
Within 48 hours	1285	89.8
Within 7 days	64	4.5
In-hospital	1274	89.1
Term (>37 week gestation)	1223	85.5
Vaginal	1170	81.8
Twin	40	2.80

Abnormal pre-hospital vital signs (pulse rate >99, respiratory rate>29, systolic blood pressure<90 or >140, or diastolic blood pressure>90) were documented in 22.1% (n=301) of women. Of those women with tachycardia (n=112), 89.3% (n=100) were placed in the left lateral position and 10.7% (n=12) received intravenous (IV) fluids. Among those women with documented hypotension (n=16) 75.0% (n=12) were placed in the left lateral position, and 37.5% (n=6) received intravenous (IV) fluids. In sum, four women died during this study, and all within 48 hours after hospital arrival (for further discussion of this high risk group see reference 13).

Prior to hospital admission, 82 (5.7%) neonates were delivered from 80 distinct mothers. Thirty-seven delivered prior to ambulance arrival. EMTs assisted in the delivery of 45 neonates, either on scene (where the ambulance picked up the patient), during transport or immediately on hospital arrival. Another 1,349 (94.3%) deliveries occurred after EMS transport, with the majority (n=1,285, 89.8%) occurring within 2 days of EMS dispatch. Of the deliveries that followed EMS transport, 1,274 (94.4%) occurred in the hospital and another 74 (5.5%) followed hospital discharge.

The median distance from the scene to the hospital was 15 km [Inter-quartile range (IQR): 9-23]. The median time from initial call to hospital arrival was 65 minutes (IQR: 50-84).

The overall follow-up rates at 2, 7 and 42 days were 99.8%, 99.3% and 94.1%, respectively (Table 3).

Table 3. Follow-up and cumulative mortality stratified by Indian state, February-April, 2014.

	Andhra	Assam	Gujarat	Karnataka	Meghalaya

	Pradesh									
	N	%	N	%	N	%	N	%	N	%
N	381		201		477		342		30	
Follow-up										
2 Day	379	99.5	201	100	477	100	341	99.7	30	100
7 Day	378	99.2	199	99.0	475	99.6	339	99.1	30	100
42 Day	359	94.2	180	89.6	444	93.1	334	97.7	30	100
Cumulative Mortality										
2 Day	13	3.4	7	3.5	18	3.8	13	3.8	5	16.7
7 Day	14	3.7	12	6.0	31	6.5	14	4.1	5	16.7
42 Day	14	3.9	13	7.2	37	8.3	14	4.2	6	20.0

In sum, 62 neonates died by day 2, 76 neonates died by day 7 and a total of 84 young infants perished by day 42 (Table 4). Cumulative mortality rates were 53 and 62 per 1000 births at 7 and 42-day follow-up, respectively. The calculated PMR was 53 deaths per 1000 births. There was variation in state PMR with he highest 7-day mortality rate was in the state of Meghalaya (166 per 1000, p =0.019). PMRs in Andhra Pradesh, Assam, Gujarat and Karnataka were 37, 60, 65 and 41 per 1000, respectively. Other demographic indicators, including economic, social (caste status), education or occupational status of the mother were not significantly related to mortality in univariate analysis.

Table 4. Characteristics and factors associated with perinatal mortality in five states in India, February-April, 2014.

	Alive		Dead		
	N=1345	%	N=76	%	P-value
Maternal Demographic Characteristics					
Rural or tribal geography	1243	92.4	72	94.7	0.652
State					
Andhra Pradesh	364	27.1	14	18.4	0.972
Assam	187	13.9	12	15.8	0.645
Gujarat	444	33.0	31	40.8	0.162
Karnataka	325	24.2	14	18.4	0.253
Meghalaya	25	1.9	5	6.6	**0.019**
Social status					
Other caste	270	20.1	12	15.8	0.356
Non-other caste	1071	79.6	64	84.2	

Economic status					
Pink ration card	396	29.4	24	31.6	0.639
White ration card	930	69.1	50	65.8	
Education level					
No prior schooling	489	36.4	32	42.1	0.332
Attended school	811	60.3	42	55.3	
Homemaker	1014	75.4	59	77.6	0.658
≥2 years since prior delivery	423	31.4	23	30.3	0.802
Maternal Prenatal Characteristics					
Prenatal iron supplementation	1129	83.9	60	78.9	0.248
≥1 visit with a physician	1046	77.8	57	75.0	0.532
<4 ANC visits	677	50.3	49	64.5	**0.019**
Current Maternal and Neonatal Care					
Any abnormal maternal vital sign	264	19.6	27	35.5	**0.019**
C-section	107	8.0	13	17.1	**0.005**
Delivery prior to hospital admission	73	5.4	6	7.9	0.361
In-hospital	1197	89.0	68	89.5	0.911
IV placed in mother	148	11.0	13	17.1	0.103
IV fluids given to mother	56	4.2	9	11.8	**0.018**
Maternal tachycardia (HR≥100)	102	7.6	10	13.2	0.081
Left lateral position during transport	1287	95.7	69	90.8	**0.047**
Premature rupture of membranes	62	4.6	8	10.5	**0.021**
Preterm (<37 weeks)	167	12.4	18	23.7	**0.005**
Twin	33	2.5	7	9.2	**0.001**

Univariate analysis among all mothers identified the following maternal risk factors for elevated neonatal mortality at 7 days: less than four antenatal care (ANC) visits (p=0.019), abnormal vital signs (p=0.049), maternal IV placement (p=0.007) and IV fluids given (p = 0.018), and mother not placed in left lateral position during transport (p=0.047). Of those infants delivered in the presence of pre-hospital care providers, the cumulative mortality rate at 42 days was 122 per 1000 (n=5) with 4 infants lost to follow-up.

The association between maternal and infant characteristics and death at 7 and 42-day follow-up was also assessed through multivariate logistic regression (Table 5). At 42-day follow-up, preterm birth (OR = 2.89, 95% CI = 1.67-5.00) and twin deliveries (OR = 2.80, 95% CI = 1.10-7.15) were the strongest predictors of mortality. Other maternal risk factors raising the likelihood

of young infant death included not being placed in the left lateral position en-route to the hospital (OR = 2.44, 95% CI = 1.06-5.61), heart rate greater than 100 (OR = 2.21, 95% CI = 1.13-4.35), or having a caesarean section delivery (OR = 2.21, 95% CI = 1.15-4.23). The risk of death was nearly two-fold higher for young infants born to mothers who went to fewer than four ANC visits (OR = 1.89, 95% CI = 1.14-3.14).

Controlling for geographic (state-to-state) variability in overall PMR led to some changes in the multivariate regression model for 42-day mortality. Prematurity (OR = 3.08, 95% CI = 1.77-5.35), twin delivery (OR = 2.79, 95% CI = 1.07-7.23), fewer than four ANC visits (OR = 1.72, 95% CI = 1.03-5.89), and caesarean section delivery (OR = 2.20, 95% CI = 1.09-4.45) continued to be independent predictors of overall young infant mortality, while maternal tachycardia (OR = 1.76, 95% CI = 0.86-3.62) and maternal positioning (OR = 2.05, 95% CI = 0.87-4.85) were no longer statistically significant.

Table 5. Predictors of young infant mortality at 7- and 42-day follow-up by multivariate logistic regression models

	7 Days		42 Days	
	OR	95 % CI	OR	95 % CI
Prematurity (<37 weeks)	2.21	1.19-4.09	2.89	1.67-5.00
Twin delivery	3.87	1.56-9.64	2.80	1.10-7.15
C-section	1.93	0.92-4.03	2.21	1.15-4.23
<4 ANC visits	1.76	1.02-3.02	1.89	1.14-3.14
Not placed in left lateral position*	1.67	0.62-4.46	2.44	1.06-5.61
Maternal HR ≥100*	1.57	0.70-3.52	2.21	1.13-4.35

*When controlled by state these variables were no longer statistically significant.

DISCUSSION

Reducing the equity gap

Elevated neonatal mortality has been shown globally to be associated with various forms of marginalisation, including poverty, low maternal education, and low social standing.[15] Previous programs to reduce neonatal mortality have focused on reducing the equity gap—reaching women and newborn infants in greatest need and those with limited access to formal healthcare services.[16-18] This prospective study suggests EMS plays an important, but under-appreciated role in reaching women from a lower socioeconomic strata and adds to prior data supporting the role of centralized EMS services in maternal and neonatal health policy.[10] Pre-hospital interventions and rapid transport when coupled with current data on known community and hospital-based risks has the potential to lead to development of interventions aimed at further reducing neonatal deaths.[19-21]

Ambulance services cared for a population—93% from lower social or economic strata— that historically has had less timely access to formal medical services. EMTs performed essential pre-hospital services, including assisting with the delivery of newborns in the field and during transport to the hospital. In 94% of all transports, EMTs connected women and neonates to health facilities offering obstetric care in less than two hours.

The absence of an association between mortality and social determinants of health, such as socioeconomic status or education level, was unexpected. However, the overwhelmingly high number of neonates from lower socioeconomic classes in our study cohort decreased our ability to detect the impact of these demographic characteristics on mortality. Furthermore, the impact of socioeconomic status on neonatal mortality may be very closely linked to the lack of access to care customary to these populations. In our study, where the majority of mothers were from disadvantaged backgrounds, this link did not exist. EMS may serve to overcome many factors that have traditionally been thought to limit healthcare access for poor and marginalized

populations; thus, access to care was broadly provided for all populations by the responding EMTs and subsequent ambulance transport. This suggests that delivery of EMS may be an important means to achieving greater equity in healthcare delivery.

Quality of Pre-hospital Care

Deficits in the quality of India's pre-hospital care of pregnant women persist. Maternal haemodynamic instability has significant risks for neonatal health,[22,23] and subsequent maternal resuscitation, whether through positioning or administration of fluids, has been shown to increase cardiac output and stroke volume—effectively improving maternal and, by-proxy, neonatal haemodynamics, even among those women who deliver after hospital arrival.[24,25] Continued training aimed at EMT recognition of high-risk patients and treatment with simple interventions based on vital signs abnormalities is imperative. Ongoing quality assurance and training efforts are now aimed at increasing EMT recognition of high-risk patients, rates of fluid resuscitation and proper positioning during pre-hospital maternal resuscitation. Lastly prehospital interventions whether through patient positioning, fluid resuscitation, or timely diversion of high-risk patients to facilities with trained providers suggestive of a higher level of care all serve to affect births that occur after delivery.

Helping a high-risk population

In developing countries, most perinatal deaths occur at home.[26] Several studies suggest that the reported PMR for all of India of 28 per 1000 births is also an underestimate given the difficulty in capturing stillbirths occurring at home.[8, 27] Estimates suggest that transitioning to institutional deliveries with a skilled birth attendant in lieu of traditional home deliveries could prevent over 500,000 stillbirths and 1.3 million annual neonatal deaths by 2020.[28,29] Yet, even

with transport to healthcare facilities, the estimated PMR of 53 deaths per 1000 births is nearly double the reported national average. While PMR varied considerably by state, all, except for Karnataka, had reported PMRs greater than previously reported averages for the year 2013. [7] Comparatively the PMR in our study ranged from 37-167 per 1000 in the five states, while published PMRs for Andhra Pradesh, Assam, Gujarat, and Karnataka ranged from 24-30 per 1000.

The high PMR is likely multifactorial. Prematurity (based on maternal report of gestational age) was found to be one of the strongest predictors of death. This relationship is consistent with global data identifying this as the number one cause of neonatal death.[30] While the proportion of prematurity in this study was similar to reported rates of India as a whole, the proportion of infants born premature who died within the first 7 days of life was higher than previous hospital-based studies. [31] Moreover, many deaths in preterm infants occur early in the neonatal period, and rapid intervention, made possible through transport under the care of an EMT to health care facilities with the capabilities to provide neonatal intensive care is critically important for survival.

The natural twinning rate in the study was 14.0 per 1,000 births, almost double the estimated 7.2 per 1,000 births reported across India.[32] Twin births were a significant predictor of death in this study (OR 2.8) and thus another important factor in the increased PMR.

The relationship between initial maternal hemodynamic instability and mortality of their infants suggests that the level of acuity of our maternal cohort was high. Women may not recognize the need to seek emergent care and are calling EMS only when they are in a very critical condition.

Finally, almost half (47.4%) of women enrolled in our study attended less than the recommended four ANC visits, a factor which proved to also be an important predictor of young infant mortality in this study. Population based data for India shows similar ANC visitation rates at around 51%. [1] The risk associated with a lack of ANC visits supports consensus based recommendations emphasizing the importance of family planning and antenatal care, as women in this study may have had complications that went unrecognized in the perinatal period and that presented as emergencies necessitating the use of EMS.

Notably, the PMR associated with this cohort of patients was significantly higher than known state averages and associated with risk factors that, when addressed in future efforts, will be important in reducing neonatal mortality. In this study, however, we were unable to link records from care pre-hospital care with those for hospital-based care, and thus we cannot comment on the relationship between mortality and variability in post-transport facility-based care in India, including treatments, disease course and cause of death in hospital.

Additionally we were unable to differentiate stillbirths vs deaths that occurred on day one of life and while this may serve to limit our recommendations we believe emergency response services have the potential to improve data quality while at the same time promote equity in access to healthcare services, and improve perinatal survival in India no matter the cause. The elevated

PMR in this large patient cohort is reflective of the high-risk nature of this population and the need for further attention to coverage of these services, provision of high-quality tailored interventions and focused investigations to inform continuous improvement in EMS.

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Figure 1 Legend. Availability of GVK Emergency Management and Research Institute (EMRI) services and study enrollment by Indian state.

States involved in study enrollment

Other GVK EMRI operational states

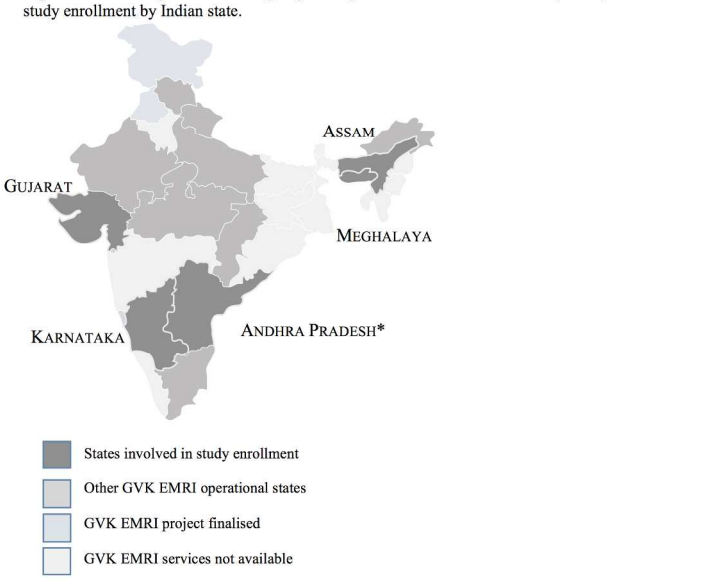
GVK EMRI project finalised

GVK EMRI services not available

*After the study's conclusion Andhra Pradesh was partitioned into two separate states: Telengana and Andhra Pradesh

1

Figure 1. Availability of GVK Emergency Management and Research Institute (EMRI) services and study enrollment by Indian state.



*After the study's conclusion Andhra Pradesh was partitioned into two separate states: Telengana and Andhra Pradesh

215x279mm (300 x 300 DPI)

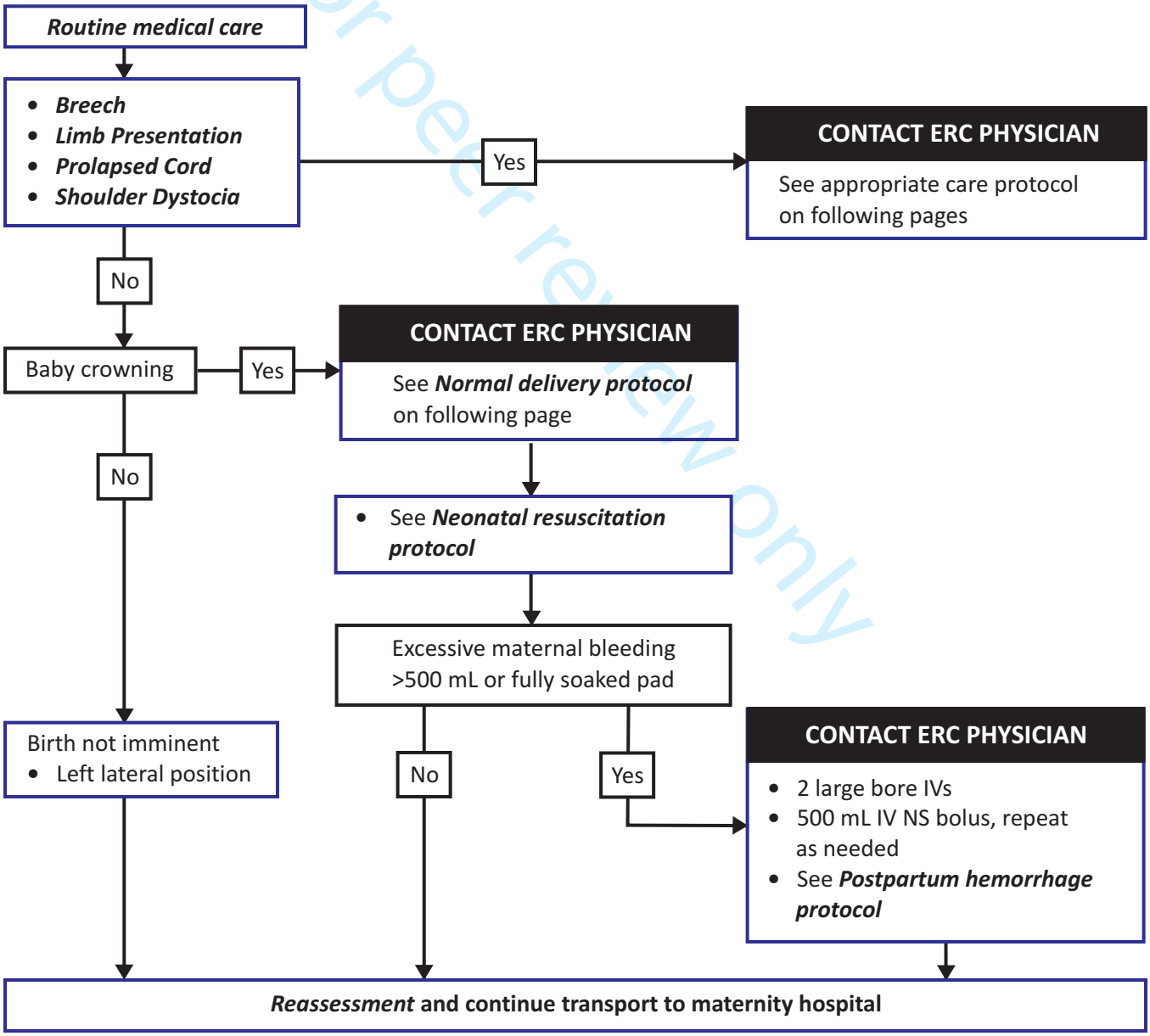
CHILDBIRTH (Uncomplicated/Complicated)

Key points

- Symptoms: Abdominal/back pain, vaginal bleeding/gush of fluid, minutes between contractions
- History of current pregnancy: Antepartum care, estimated gestational age, complications
- OB history: Number of pregnancies and c-sections, prior complications during pregnancy
- Physical exam: Inspecting external vaginal area for crowning/presenting part if patient feels like she wants to push or if she feels there is something protruding from her vagina
- *DO NOT* pull/push baby

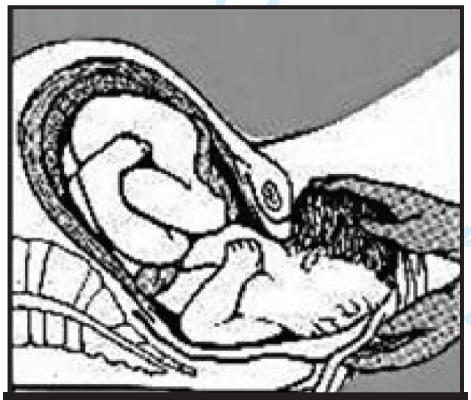
Serious signs and symptoms

- Part other than head presenting from vagina (arm, leg, umbilical cord)
- Excessive maternal bleeding
- Prolonged contractions (>6 contractions in 10 minutes or duration >2 minutes)
- Shortness of breath
- Altered mental status

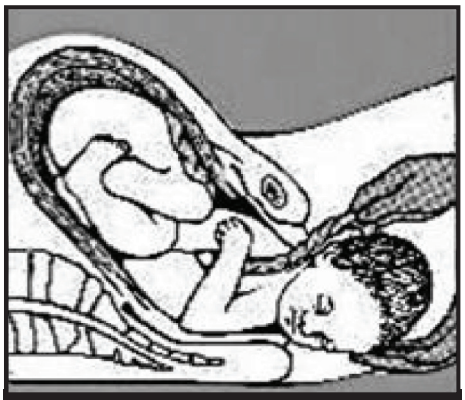


Normal Delivery

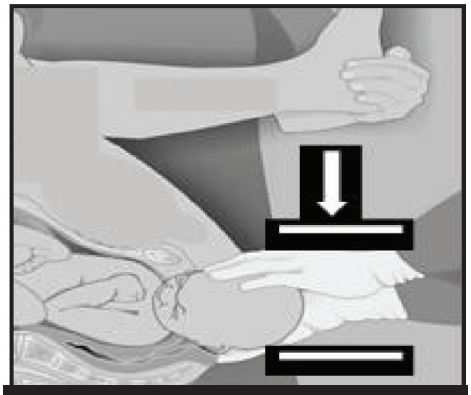
- Position patient
- Prepare OB kit
- As head delivers, suction with bulb syringe (only if not spontaneously breathing)
- Check for cord wrapped around neck
- If cord around neck, slip over shoulders/head of baby
  - If unable to unwrap cord, place umbilical clamps 5 cm apart and cut cord between clamps
- Support head, deliver body
- Place baby next to mother; dry baby and keep warm (see ***Neonatal resuscitation protocol***)
- See ***Post delivery care*** on last page



Step 1: Support head and let head turn to side to align with body



Step 2: Check for cord and slip over head if present



Step 3: Keeping hands parallel to floor, apply downward pressure to deliver shoulder

Step 4: Support body and place next to mother

Shoulder Dystocia

Definition

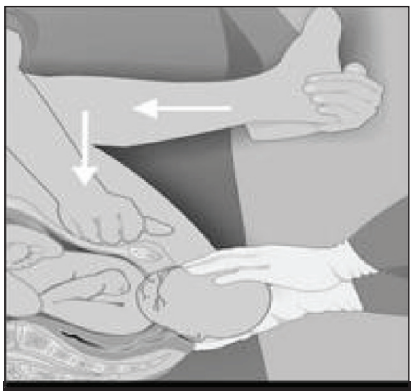
- Inability to deliver either shoulder within 60 seconds of delivery of head

Key points

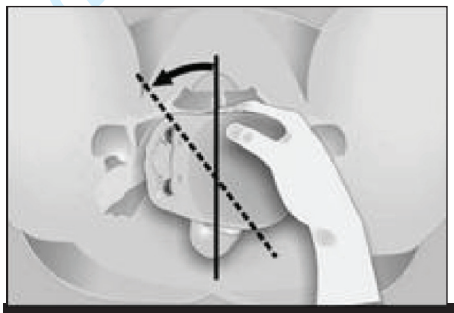
- Complications
  - Severe hypoxia, traumatic brachial plexus injuries and humerus/clavicle fractures
- *Turtle sign:* when fetal head moves back into the mother's perineum
- ***HELPERR (HeLP-R*** for BLSO provider denoted by *below) mnemonic can assist with recall of correct actions

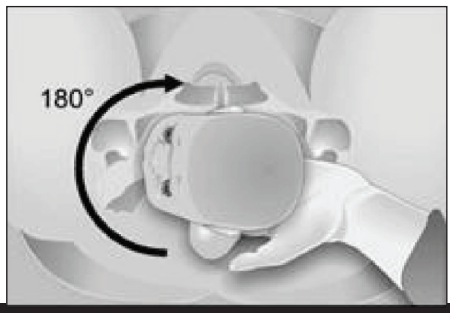
Prehospital management options

- H: Call for **H**elp*
- E: Consider **E**pisiotomy (only if additional space needed for hands to complete maneuvers below)
- L: Position **L**egs, pull knees to chest*
- P: Suprapubic **P**ressure (not fundal)*
- E: **E**nter vagina with hands to push on posterior aspect of anterior shoulder and other maneuvers
- R: **R**oll patient to knee to chest position, then deliver the posterior shoulder*
- R: **R**emove the arm, sweep posterior arm across chest

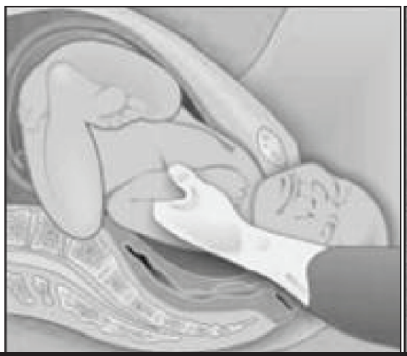


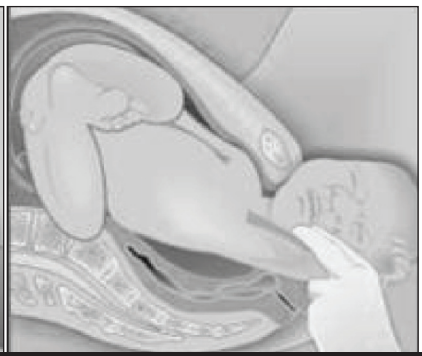
Legs: Pull knees up
Pressure: Push down in suprapubic area (not fundal)



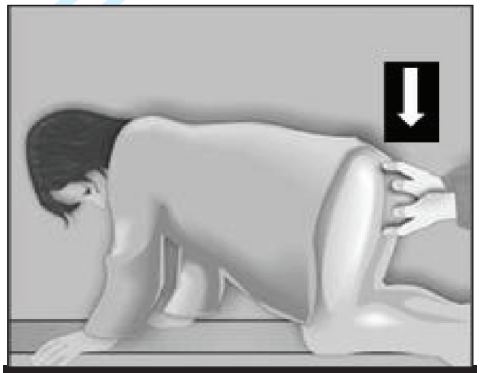


Enter maneuvers:
1) Push anterior shoulder forward
2) Pressure: Push anterior shoulder backward and posterior shoulder forward





Remove posterior arm by bending at elbow and sweeping across chest and out



Roll on to knee chest position and deliver posterior shoulder first by gentle downward pressure on fetal head

Breech Presentation

Definition

- When buttocks (or legs) deliver first

Key points

- Transport immediately
- *AVOID* delivery in ambulance if possible. Tell patient not to push.

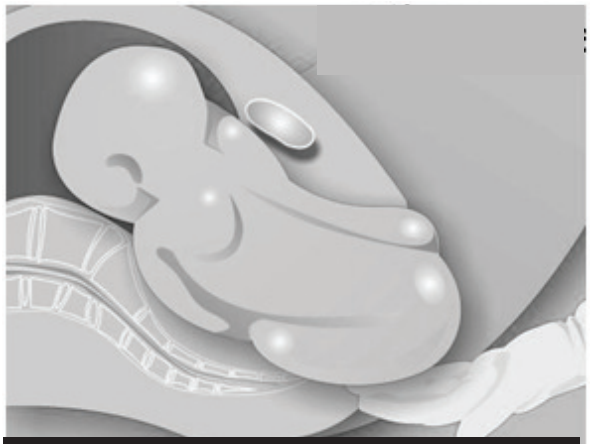
Prehospital management options

- Determine if buttocks or limb is presenting first
  - If limb (leg or arm) is presenting first, see ***Limb presentation*** section on the following page
- Delivery of breech presentation
  - Step 1
    - Support baby and allow delivery to proceed passively until base of umbilical cord is seen
    - *DO NOT* pull baby
  - Step 2
    - Grab the bony pelvis and femurs and apply gentle traction
    - *DO NOT* grab the abdomen as you may injure abdominal organs
  - Step 3
    - Once the wing-like scapulae are visible, rotate the fetus until a shoulder is anterior and deliver the arm. Rotate 180 degrees and deliver the other arm. Position the fetus so that the back is facing anteriorly.
  - Step 4
    - Anteriorly place a gloved middle finger on the fetus's occiput. The index and ring finger rest on the shoulders. Place a hand posteriorly sliding the index and middle finger into a V shape along the baby's face. Gently place pressure on the cheek bones.
    - Performing these maneuvers at the same time causes the fetal head to flex.
    - Additionally, one assistant can apply suprapubic pressure to help with flexion of the head. Another assistant can support the body.
  - See ***Post delivery care*** section on last page

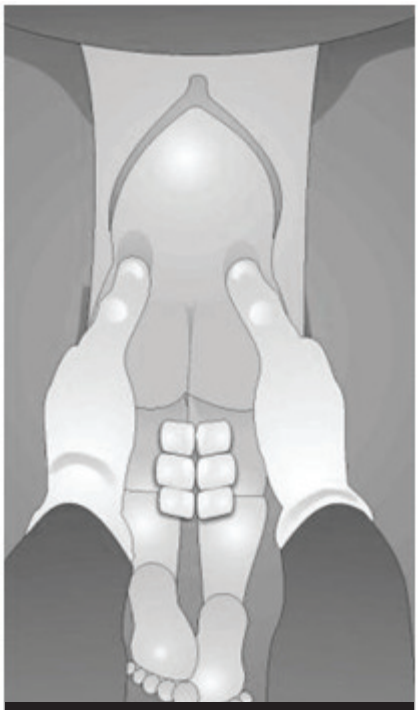
Frank breech Complete breech Footling breech

Presentation is the part of the fetus that is coming out of birth canal first

Delivery Steps for Breech Presentation



Step 1: Support the body



Step 2: Gentle traction on bony pelvis

Step 3: Rotate each shoulder anteriorly and deliver arms

Step 4: Flex the fetal head by placing the middle finger on the occiput and the other middle and index finger on the cheek bones

Cord Presentation (Prolapsed Cord)

Definition

- Umbilical cord presents/is seen before the head or other part of the baby

Key points

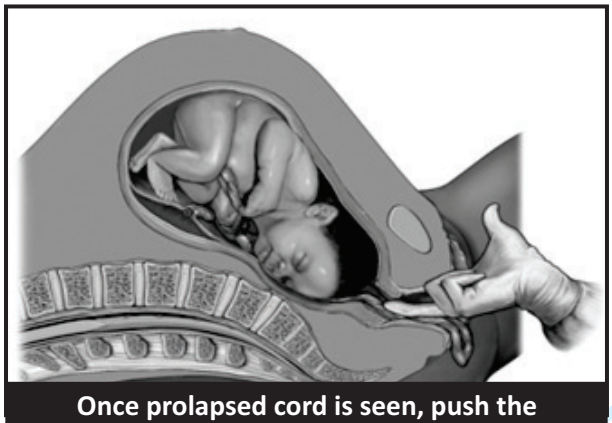
- If the umbilical cord is compressed, blood flow and oxygen don't reach the baby
- Transport immediately and try to avoid delivery in the ambulance
- Tell the patient *NOT* to push

Prehospital management options

- With two fingers of your gloved hand, gently push the presenting part of baby (not the cord) back up into the vagina until the presenting part no longer presses on the cord
  - *DO NOT* remove your hand (after elevating the presenting part of the baby) until arriving at the hospital and being relieved by other hospital personnel
- With your other hand, palpate the cord and feel the fetal HR. If <110 bpm, consider rolling the patient over and placing her in the *knee-chest position.* This may relieve pressure on the cord.

Prolonged transport or in hospital management options

- Place a Foley (urinary) catheter in the bladder and fill with 500 mL of NS. Clamp the Foley.
- Wrap the cord loosely with a moist, warm dressing



Once prolapsed cord is seen, push the presenting part (not the cord) gently back up

Knee chest position

Limb Presentation

Definition

- When one limb of the baby delivers first

Key points

- Nearly all of these patients will require delivery by caesarean-section
- Transport immediately. Avoid delivery in the ambulance if possible.
- Tell the patient *NOT* to push.

Prehospital management options

- Oxygen
- *DO NOT* attempt to deliver the baby
- *DO NOT* pull on the presenting limb
- *DO NOT* place your hand into the vagina unless there is a prolapsed cord (see ***Cord presentation*** section on previous page)

Multiple Births

Key points

- Usually both babies are born before the first placenta is delivered
- In order to prevent bleeding from the 2nd twin, carefully inspect the cord and apply a second clamp if leaking blood (oozing)
- Contractions usually restart within 5-10 minutes after the first baby is born; the second baby usually delivers within 30-45 minutes of the first baby

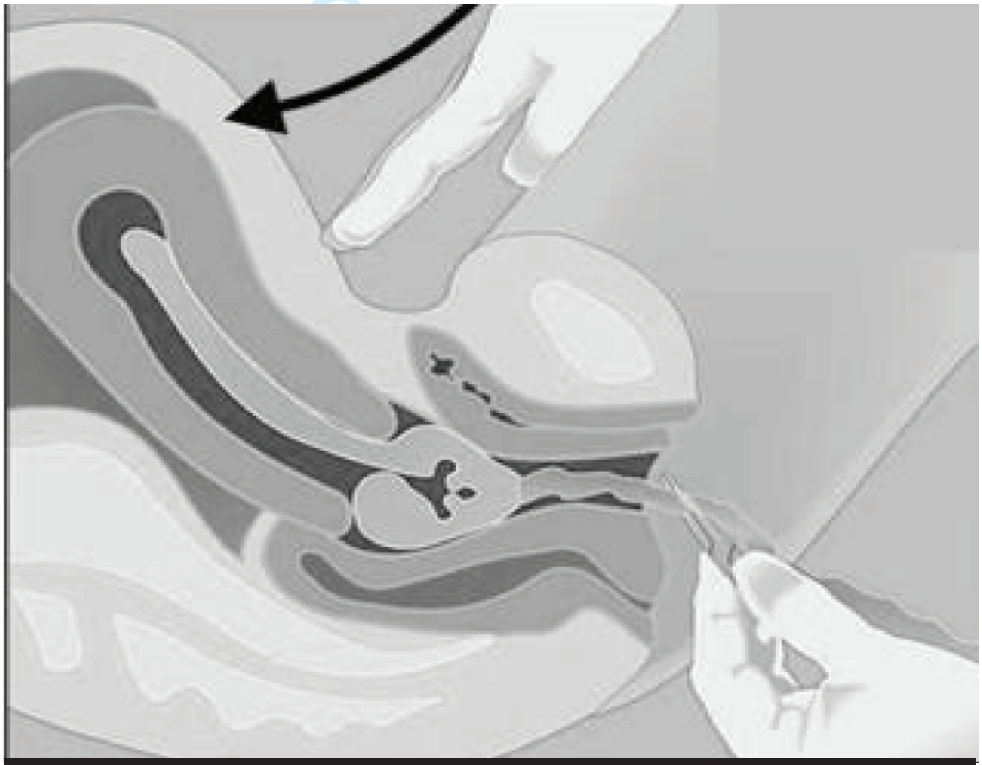
Limb presentation with prolapsed umbilical cord

Twin gestations may present with the fetuses lying in multiple positions

Post Delivery Care

Active management of 3rd stage of labor (following delivery of all fetuses)

- See ***Neonatal resuscitation protocol***
- **Oxytocin 10 Units IM** to mother immediately following delivery
  - Consider multiple fetuses and do not give until all babies are delivered
- Record time of birth
- Assess APGAR scores at 1 and 5 min after birth
- Wait until cord pulsations have stopped or 5 minutes have passed. Then, place two clamps on the cord at least 4-10 cm from the baby and cut between the clamps.
- Gently pull on the umbilical cord while providing suprapubic pressure (see below)
- Once the placenta delivers, place the placenta in a bag and give it to hospital staff
- Externally massage the uterus
- If significant ongoing bleeding or signs of maternal shock, see ***Postpartum hemorrhage protocol***



Placenta delivery: Gently pull on cord while applying pressure to suprapubic area

References

- Advanced Life Support in Obstetrics (ALSO) Provider Course Syllabus Fourth Edition, Copyright 2009, American Academy of Family Physicians

POSTPARTUM HEMORRHAGE (PPH)

Definition

- Greater than 500 mL of blood loss following delivery
- Severe PPH is >1000 mL of blood loss following delivery

Key points

- Most common cause of maternal death in developing nations
- Active management of the third stage of labor can prevent 60% of PPH
- Rapidly evaluate for and correct possible causes
- Uterine atony (soft, boggy uterus) is the most common cause of PPH

Serious signs and symptoms

- SBP <90
- HR >100
- Shortness of breath (RR >30)
- Altered mental status
- Cool or moist skin

Routine medical care

Active management of 3rd stage of labor

>500 mL of blood loss -*OR*-
Serious signs and symptoms

No

Yes

CONTACT ERC PHYSICIAN

- **Oxytocin 20 Units** in 500 mL NS (IV bolus over 20 minutes)
- 2nd IV as needed

Uterus firm

No

Yes

- Bimanual uterine massage
- Continue IV oxytocin infusion
- **Misoprostol 1000 mcg PR** *AND/OR* **Methylergonovine 0.2 mg IM** (do not give Methylergonovine if SBP >140 mmHg or known preeclampsia or chronic hypertension)

CONTACT ERC PHYSICIAN

- Perform vaginal exam for signs of uterine inversion, lacerations, and ongoing bleeding
- Consider appropriate treatment options

***Reassessment* and continue transport**

Active management of 3rd stage of labor

- Following delivery of all fetuses provide:
  - **Oxytocin 10 Units IM** to mother (immediately following delivery)
  - Gentle traction on umbilical cord while providing suprapubic pressure (see below)
  - External massage of uterus (see below)

ERC Physician

Key points

- Decisions on management options should be based on the expected time to hospital arrival

4 T's	Causes	Prehospital treatment
Tone	Decreased uterine tone	1. Uterine massage 2. Oxytocin 3. Misoprostol 4. Methylergonovine
Trauma	1. Cervical/perineal lacerations 2. Uterine inversion	1. Apply direct pressure 2. Restore uterus (see below)
Tissue	Placenta retained	Manual removal
Thrombin	Decreased clotting	Supportive measures

Bimanual uterine massage

Placental tissue removal

Inversion and restoration of uterus

References

- Advanced Life Support in Obstetrics (ALSO) Provider Course Syllabus Fourth Edition, Copyright 2009, American Academy of Family Physicians

PREECLAMPSIA/ECLAMPSIA

Key points

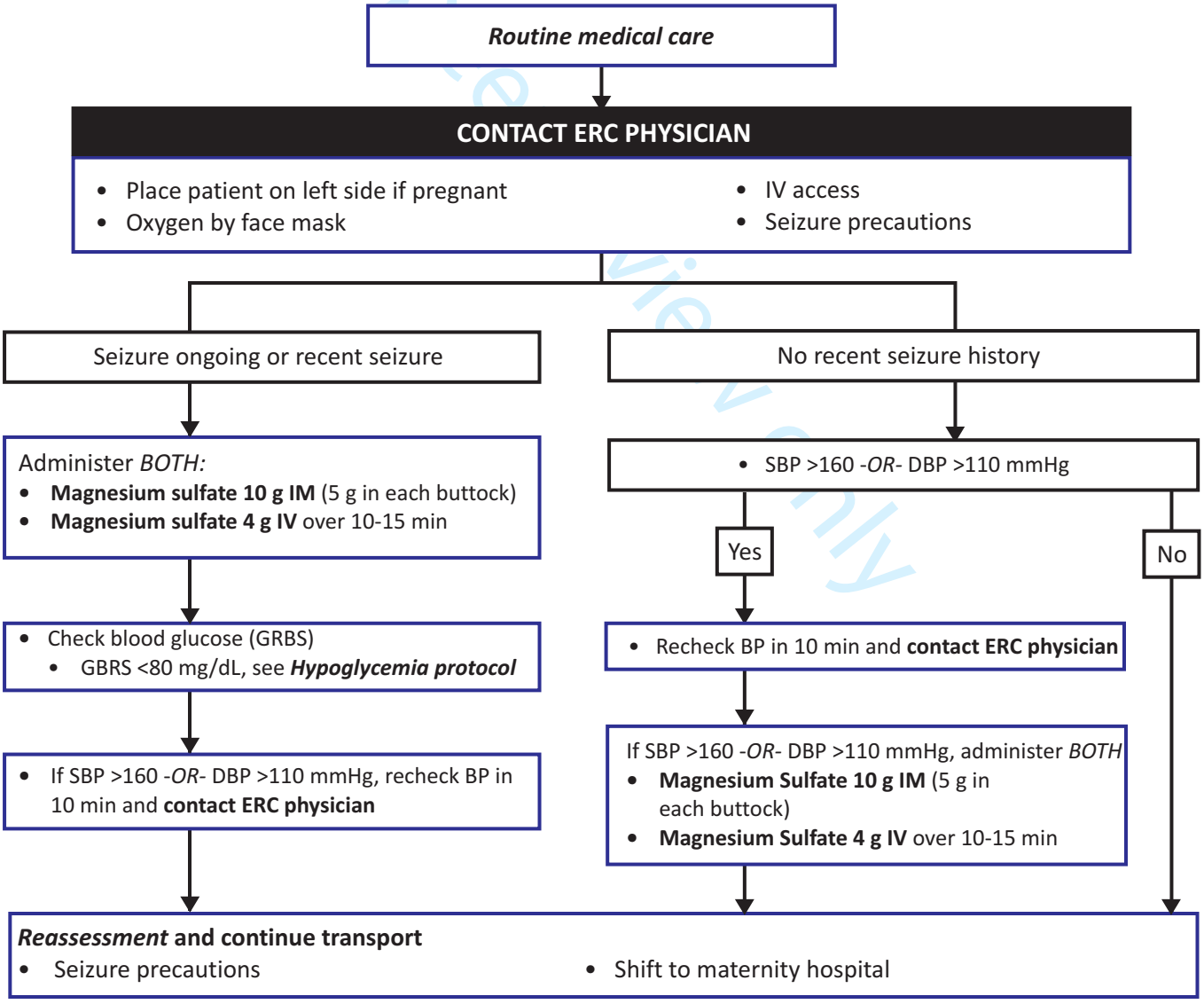
- Preeclampsia and eclampsia can occur from the 20th week of pregnancy until 6 weeks after delivery
- Preeclampsia is a BP >140/90 on >2 readings >6 hours apart *AND* significant protein in the urine
- Severe preeclampsia signs/symptoms include altered mental status, blurred vision and persistent headache
- Eclampsia is preeclampsia with seizures
- Obtain past medical history: medications, last menstrual period, gestational age (trimester)
- Magnesium toxicity manifests as loss of deep tendon reflexes and respiratory depression

Differential diagnosis

- Epilepsy
- Hypoglycemia
- Trauma/head injury
- Alcohol withdrawal
- Toxins/poisoning/overdose
- Chronic hypertension

Serious signs and symptoms

- Hypoxia/cyanosis
- Shortness of breath
- Seizures
- Altered mental status



ERC Physician

Key points

- The definitive treatment for eclampsia is delivery
- Magnesium should not be used to control hypertension
- Epigastric pain may be a sign of severe preeclampsia (also consider gallbladder disease)

Prehospital management options

- If repeat seizure occurs more than 10 minutes after the initial IV loading dose of magnesium, administer **Magnesium sulfate 2 g IV** over 10-15 minutes
- Respiratory depression may occur with magnesium toxicity
  - **Calcium gluconate 1 g IV** can be given for significant respiratory depression

Prolonged transport or in hospital management options

- If the patient continues to seize after repeat magnesium administration, consider **Midazolam 2-4 mg IV/IM**; may repeat x 1 for ongoing seizure
  - Alternate medications:
    - **Diazepam 5 mg IV/IM**; may repeat x 1 for ongoing seizure
- Antihypertensive medications
  - Treat persistent SBP >160 or DBP >110 mmHg (Goal: SBP <160 and DBP <110 mmHg)
    - **Nifedipine 20 mg PO** *(DO NOT* give sublingual)
      - **Nifedipine 10 mg PO** may be repeated every 30 min to a max of 40 mg
    - Alternate medications:
      - **Labetalol 10 mg IV**
        - If BP remains elevated above goal after 10 min, then administer **Labetalol 20 mg IV** every 10 minutes as needed to a max of 110 mg
      - **Labetalol 200 mg PO**
        - If BP remains elevated above goal after 30 min, then administer **Labetalol 200 mg PO** x 1 additional dose

How to mix and infuse Magnesium sulfate

- **Magnesium sulfate 4 g**: Mix 4 ampules of 50% $MgSO_4$ (1 g/ampule) in 100 mL NS
  - Infuse over 10 minutes, 100-150 drops per minute
- **Magnesium sulfate 2 g**: Mix 2 ampules of 50% $MgSO_4$ (1 g/ampule) in 100 mL NS
  - Infuse over 10 minutes, 100-150 drops per minute

Monitor the patients' vital signs, oxygen saturation, deep tendon reflexes, and level of consciousness every 15 minutes for the first hour, and every 30 minutes for the second hour.

Assess for signs of *magnesium toxicity* (e.g., visual changes, somnolence, flushing, muscle paralysis, loss of patellar reflexes) or pulmonary edema.

References

- Advanced Life Support in Obstetrics (ALSO) Provider Course Syllabus Fourth Edition, Copyright 2009, American Academy of Family Physicians

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***
Title: Reducing early infant mortality in India: results of a prospective cohort of pregnant women utilizing emergency medical services

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Page 2, line1
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 4, line 1
Objectives	3	State specific objectives, including any prespecified hypotheses Page 5, line 1
Methods		
Study design	4	Present key elements of study design early in the paper Page 5, line 11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 5, line 11-15
Participants	6	*(*a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Enrollment: Page, line 18. Follow-up: Page 7, line 22
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 7, line 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 7, line 5-16
Bias	9	Describe any efforts to address potential sources of bias Page 6, line 18
Study size	10	Explain how the study size was arrived at NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 8, line 11
Statistical methods	12	*(*a) Describe all statistical methods, including those used to control for confounding Page 8, line 19
		(*b*) Describe any methods used to examine subgroups and interactions Page 9, line 2
		(*c*) Explain how missing data were addressed

		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 12, line 20
		(b) Give reasons for non-participation at each stage Page 12, line 20
		(c) Consider use of a flow diagram NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page 10, line 2
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount) Page 12, line 20
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Page 13, line 9
		(*b*) Report category boundaries when continuous variables were categorized NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Page 14, line 19
Discussion		
Key results	18	Summarise key results with reference to study objectives Page 15, line 25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 19, line 7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 17, line 4
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 3, line 11
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 20, line 6

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.