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Original Article

Is Home-Based Diagnosis and Treatment of Neonatal Sepsis Feasible and Effective? Seven Years of Intervention in the Gadchiroli Field Trial (1996 to 2003)

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OBJECTIVES:

To further evaluate our earlier findings on the feasibility and effectiveness of home-based management of neonatal sepsis by analysing 7 years data (1996 to 2003) from the field trial in Gadchiroli, India.

STUDY DESIGN:

Neonates in 39 villages were monitored by trained village health workers (VHWs) from 1995 onwards. In 1996, we trained VHWs to diagnose sepsis by using a clinical algorithm and provide domiciliary treatment using intramuscular gentamicin and oral co-trimoxazole. Health records for all neonates were kept by the VHWs, checked by field supervisors, and computerized. Live births and neonatal deaths were recorded by an independent vital statistics collection system. We evaluated the feasibility and effectiveness of this approach.

RESULTS:

During September 1996 to March 2003, VHWs monitored 93% of all neonates in 39 villages ($N = 5268$). As compared to 552 cases of sepsis diagnosed by computer algorithm, VHWs correctly diagnosed 492 cases (89%). Parents agreed to home-based treatment for the majority of infants (448, 91%), refused treatment in 31 (6.4%) cases, and hospitalized 13 infants (2.6%). VHWs treated 470 neonates with antibiotics, that is, 8.9% of all neonates in community. Of 552 cases diagnosed by computer, VHWs correctly treated 448 (81.2%) and gave unnecessary treatment to 22/470 (4.7%) of treated neonates. The case fatality (CF) was 6.9% in treated cases vs 22% in untreated or 16.6% in the pre-intervention period ($p < 0.001$). Home-based treatment resulted in 67.2% reduction in %CF among preterm and a 72% reduction among LBW neonates.

CONCLUSIONS:

Home-based management of neonates with suspected sepsis is acceptable to most parents, safe, and effective in reducing sepsis case fatality by nearly 60%. With proper selection, training, and supervision of health workers, this method may be applicable in areas in developing countries where access to hospital care is limited.

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INTRODUCTION

Neonatal infections are a major cause of morbidity and mortality worldwide. The World Health Organisation estimates that, globally, 32% of the estimated four million neonatal deaths each year are caused by infections, including sepsis, pneumonia, diarrhea, and tetanus.[1] Another global review of neonatal infections estimated that annually there are approximately 29 million neonatal infections (including 800,000 cases of sepsis and 130,000 cases of meningitis) and as many as 1.5 million neonatal deaths due to infections.[2] In Gadchiroli, India, we have studied clinical sepsis among home-based neonates in 39 villages since 1995. In our studies, the term 'sepsis' includes neonatal sepsis, pneumonia, and meningitis. In a cohort of 763 neonates prospectively observed in 1995 to 1996, we estimated the incidence of clinically suspected sepsis to be 17.0 % and the case fatality (CF) without interventions to be 18.5%.[3,4] Moreover, sepsis was the primary cause in 52.5% of neonatal deaths.[5,6]

The management of sepsis by trained village heath workers (VHWs) is one of the interventions in the home-based neonatal care package in the field trial in Gadchiroli.[5] Promising early data (1996 to 1998) on 71 cases suggested that VHWs could identify and manage neonates with suspected sepsis in the home setting, resulting in improved survival. This initial experience raised the possibility that managing neonatal infections in the community may be an intervention with broad applicability. Since then, three new field trials of community-based management of sepsis in neonates have been started in India and Bangladesh.

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We have continued the home-based interventions and monitoring in the Gadchiroli field area to date. In the current paper, we present the data and experience up to March 2003.

RESEARCH QUESTIONS

To evaluate the feasibility and effectiveness of home-based management of neonates with suspected sepsis, we asked seven questions:

1. Is it possible to monitor neonates in their community and identify suspected sepsis cases? This was evaluated using five indicators: (i) The proportion of neonates in community visited by VHWs (% coverage). (ii) The proportion of neonatal sepsis cases correctly identified (true positives), using the diagnostic guidelines given to VHWs as the gold standard. (iii) The proportion missed (false negatives). (iv) The proportion overdiagnosed (false positives). (v) The proportion correctly considered not having sepsis (true negatives).
2. What proportion of parents agree to hospitalization of neonates with suspected sepsis? What proportion accept home-based treatment by the VHWs? What proportion refuse both?
3. What proportion of neonates in community are treated for suspected sepsis?
4. How effective is home-based management in reducing case fatality in neonates with sepsis, including neonates with varying risk based on gestational age, birth weight and postnatal age (day of life)?
5. Can VHWs safely administer intramuscular injections (antibiotics and vitamin K) to newborns?
6. What are the difficulties faced by VHWs?
7. Is home-based management acceptable to the medical community, both local and national? Is it ethical?

METHODS

Data Sources

We have previously described the area, study design, methods of data collection, and the interventions in the field trial.[5,7] The data reviewed in this paper come from six sources:

(1) Maternal and neonatal health records completed by the VHWs during home visits. The date of onset of the last menstrual period was recorded from the history given by the woman at the time of registering her pregnancy, usually in the fourth month of pregnancy. The period of gestation was estimated at birth from this information. The birth weight was recorded by VHWs, usually within 6 hours after birth, by weighing the baby using a 0 to 5 kg spring balance (Salter). This printed record also included a sepsis monitoring form. From 1995 to 1998, we used six clinical criteria based on 12 signs/symptoms to diagnose presumed sepsis. In 1998, we slightly modified the diagnostic schema [seven criteria; 10 signs/symptoms (Box 1)]. The current monitoring form is given in Appendix A. Clinical sepsis was defined by the simultaneous presence of two or more criteria. Records were completed by VHW's during home visits. All neonates were visited eight times on days 1, 2, 3, 5, 7, 15, 21, and 28. High-risk neonates (birth weight <2000 g, preterm birth or difficulty in feeding on the day of birth) received additional visits on days 4, 6, 9, 13, 18, and 24 since August 1998 to date. Beginning in 2002, we reduced the number of visits to six, on days 1, 2, 3, 7, 15, and 28, to the rest of the neonates (considered low risk). If parents inform the VHW that the baby is sick, additional home visits are made.

(2) Sepsis treatment records completed by VHWs for the cases of neonatal sepsis diagnosed and treated. These records included diagnostic criteria present on various days and data on treatment and progress.

These two records were reviewed by a visiting field supervisor approximately every 15 days and verified by visiting the family. In an earlier study, we found that data recorded by VHWs showed 92% agreement with parallel observations by a visiting physician.[3] Four possible complications of antibiotic injections were specifically looked for: (i) cellulitis or abscess at the site of injection, (ii) hemorrhage at the site of injection, (iii) decreased tone and movement in the limb suggesting nerve injury, (iv) skin rash indicating possible drug allergy.

(3) Records of the supplies provided to VHWs.

(4) The field diaries maintained by the field supervisors. These provided additional clinical data, as well as the difficulties faced and community reactions.

Box 1 Clinical criteria used to diagnose neonatal sepsis*

A. Criteria used in 1995 to 98

1. Previously normal cry became weak/stopped or previously normal baby became drowsy/unconscious or previously normal sucking became weak or stopped.
2. Baby cold to touch or fever (skin temperature $>99^{\circ}$F)
3. Skin infection or umbilical infection
4. Vomitting or diarrhea or abdominal distension
5. Respiratory rate ≥ 60
6. Grunt or chest indrawing

B. Criteria used in 1998 to 2003

1. Previously normal cry became weak/stopped
2. Previously normal baby became drowsy/unconscious
3. Previously normal sucking became weak/stopped
4. Baby cold to touch or fever ($>99^{\circ}$F)
5. Skin infection or umbilical infection
6. Abdominal distension or vomiting
7. Grunt or chest indrawing

*Simultaneous presence of any two or more criteria in a neonate denoted sepsis.

(5) Meetings with VHWs, supervisors, and physician every 2 months to discuss qualitative experiences and the difficulties experienced by VHWs.
(6) Vital statistics surveillance in the study area, conducted by independent field workers and supervisors. Previously, we reported that 98% of births and child deaths were recorded by this system.[5]

Recorded data are entered onto the computer within 30 days of collection and analyzed every 6 months. A computer algorithm was written to identify cases of sepsis using the diagnostic criteria and the data in the neonatal records and sepsis monitoring forms. The incidence of sepsis was estimated from these diagnosed cases. The proportion of neonates with sepsis correctly diagnosed by VHWs (true positive), diagnoses missed by the VHW (false negative), or over-diagnosed (false positive) were estimated by comparing the VHW's sepsis diagnosis and treatment records with the cases identified by the computer algorithm of sepsis. The total live births and neonatal deaths were provided by the vital statistics surveillance. We calculated the number of vitamin K injections given from the newborn forms, and the number of gentamicin injections from the sepsis treatment forms. These were regularly matched with the supplies given to VHWs to ensure the proper use of medicines and syringes.

Home-based interventions in the field trial in Gadchiroli have been previously reported.[5] Interventions relevant to sepsis management are presented in Box 2.

Box 2 Interventions for the home-based management of neonatal sepsis

- Health education of mother and family about the five danger signs in baby. If any one of these appeared, they should immediately seek care from the VHW.
  Danger signs:
  1. Reduced sucking
  2. Drowsy or unconscious
  3. Baby cold to touch
  4. Fast breathing
  5. Chest indrawing
- VHWs monitored all neonates by making repeated home visits and recorded presence or absence of defined signs/symptoms (see appendix).
- VHWs were trained to diagnose sepsis if two or more of the signs/symptoms were simultaneously present in the baby.
- For neonates diagnosed with clinical sepsis, the VHW:
  1. Informed parents of the illness, and the threat to newborn's life.
  2. Advised parents to immediately take the baby to hospital, then the VHW offered treatment at home and obtained a written informed consent form.
  3. Maintained normal body temperature and breastmilk feeding of the baby.
  4. Administered antibiotics:
     - Gentamicin injected intramuscularly in the antero-lateral aspect of baby's thigh. The dose of gentamicin was 10 mg per day for 10 days for pre-term babies with birth weight <2500 g, and 15 mg per day for 7 days to full-term babies or to those with birth weight ≥ 2500 g. Gentamicin was given divided in two daily doses, except for a period (June 1998 to January 2001) during which it was given in once a day dosing.
     - Syrup co-trimoxazole (sulphamethoxazole 200 mg+trimethoprim 40 mg per 5 ml) 1.25 ml twice a day for 7 days.
  5. Made daily home visits to baby under treatment to administer antibiotics and record progress.
- If baby did not improve in 24 hours or if baby did not take feeds/medicines orally, or if baby was persistently hypothermic, referral to hospital was again advised.
- Recorded the outcome.

The Choice of Antibiotics

In the absence of bacterial culture and sensitivity reports, the antibiotics recommended for treating neonatal sepsis in developed countries are parenteral ampicillin and gentamicin.[8,9] This combination covers a broad spectrum of organisms that cause neonatal sepsis, including *Escherichia coli*, Klebsiella, *Streptococcus pneumoniae, Staphylococcus aureus*, Group B Streptococcus and *Hemophilus influenzae*. In the absence of community-based data on the organisms causing neonatal sepsis in Gadchiroli, we used our community-based data regarding organisms colonizing the maternal reproductive tract of rural women in Gadchiroli.[10,11] Of 280 maternal genital bacterial isolates, 93% were sensitive to co-trimoxazole, 95% to gentamicin, and 100% were sensitive to at least one of these.

For this study we chose to use parenteral gentamicin and oral co-trimoxazole (rather than parenteral ampicillin). We have previously studied the use of co-trimoxazole for pneumonia in children, including neonates, in this area[11] and reported a 40% reduction in pneumonia-specific mortality rate in neonates in the intervention area. Moreover, co-trimoxazole can be administered orally. Thus, based on this background and the recommendations of the advisory group of pediatricians, we chose injection gentamicin and oral co-trimoxazole as the antibiotic combination for treating suspected sepsis. The dose and the duration of antibiotic administration are described in Table 9.

Syringe and Needle

Gentamicin is available in India in only one strength, 40 mg/ml. As neonates in our trial needed very small doses (5 or 7.5 mg twice a day), we used disposable insulin syringes and needles to enable VHWs to accurately dispense the proper dose. These syringes, marked for insulin at 40 U/ml, match exactly with the available

strength of gentamicin, and allow precise measurement of the gentamicin dose. The small needle available with the insulin syringe ensures that the needle does not penetrate too far into neonate's thigh. Disposable syringes and needle reduce the risk of infection.

VHWs were asked to store all used syringes without washing them in a plastic box, and return these to the field supervisor. An account of syringes supplied and returned was maintained and checked with the number of neonates treated to prevent any unaccounted use to give unnecessary injections by VHWs.

Training and Supervision

We trained VHWs in stages. In 1995 they were trained to take history, examine a mother and newborn, and record data. They monitored the neonates in their village during one year (April 95 to March 96). In May 1996, we taught VHWs to give intramuscular vitamin K. When they had given 10 injections to newborns in their village in the presence of the field supervisor without any error, they were certified to give injection vitamin K independently on the day of birth. In July –August 1996, we trained VHWs to diagnose and treat sepsis (Tables 8 and 9). They were repeatedly assessed by simulated exercises and retrained, until performance was deemed satisfactory. Beginning in September 1996, we permitted them to diagnose and treat sepsis as per guidelines. Communities were informed of this new intervention, and mothers and families were given health education to recognize danger signs and seek care from the VHW. As a VHW was likely to diagnose and treat a case of sepsis only once or twice each year, continued training and drills with assessment were made in the supervisory visits and in the bi-monthly review meetings to help retain her skills. Close field supervision of VHWs, continued training, education of community and families about sepsis management, and regular uninterrupted supplies were maintained.

Communication with Medical Community

We informed and explained this intervention by visiting local private doctors. Senior pediatricians, neonatologists, and public health professionals of national standing were involved in this trial as members of an external advisory committee which met at the field site in 1995, 1996, and 1998. The committee reviewed our data, advised us about interventions, assessed the quality of training for VHWs, and gave ethical clearance.[5,7] The study director (AB) presented the findings of the trial at the annual national conferences of the Indian Academy of Pediatrics (IAP) and the National Neonatology Forum (NNF) of India. A national workshop was jointly organized by the IAP, NNF, UNICEF, and SEARCH in 1999 at the project headquarters to study the findings of the trial and discuss its significance for national policy. A consensus statement was issued on this approach by the national workshop.[12] The second national workshop was organized on 31 March 2003 at the project headquarters.[13]

Consent and ethical clearance. All neonates with suspected sepsis were advised hospitalization. If parents did not agree to it, a written consent from all families was taken before treatment at home. An external advisory committee gave ethical clearance.

RESULTS

A total of 5796 live births were recorded in 39 intervention villages from April 1996 to March 2003. Of these, 169 neonates died (neonatal mortality rate (NMR) 29.1/1000 live births). Additionally, 123 neonates from other areas were transiently in the intervention villages and were monitored by VHWs. Thus, in total 5919 neonates were present during 1996 to 2003 in the intervention villages. VHWs visited 5510 of these neonates, giving a service coverage of 93.1%.

From September 1996, when sepsis management was started, to March 2003, 5268 neonates were visited by the VHWs. Based on the data recorded by VHWs, the computer algorithm identified 552 neonates with sepsis, giving an incidence of sepsis of 10.5%. Of these 552 cases of sepsis, the VHWs correctly diagnosed 492 (89.1%). The ability of the VHWs to diagnose sepsis in comparison to the computer algorithm is presented in Table 1.

The yearly incidence of sepsis and the proportion of sepsis cases treated by VHWs is presented in Table 2. Both the incidence of sepsis and the percent treated by VHWs increased over the first few years of the study. In the last year recorded, 93/751 infants (12.4%) were diagnosed by computer algorithm and 86 of these (92.5%) were actually treated by the VHWs.

The gestational age distribution of the 552 cases was: term (462, 83.7%) and preterm (<37 weeks; 86, 15.6%). Among preterm infants, 61 (71% of all preterm infants) were 35 to 36 weeks, nine (10.5%) were 33 to 34 weeks, and 16 (18.6%) were <32 weeks gestation. Gestation was not recorded in four (0.7%) neonates. The distribution of birth weights was: 2500 g or more, 256 (46.4%) and LBW (<2500 g) 293 (53.1%). Among LBW infants 187 (63.8% of all LBW infants) were 2000 to 2499 g; 51 (17.4%) were 1750 to 1999 g; 29 (10%) were 1500 to 1749; and 26 (9%) were <1500 g. Birth weight was not recorded for three (0.5%) newborns.

Table 1 Diagnosis of Sepsis by the Trained VHWs in Comparison to Computer Algorithm

		Computer algorithm		
	Diagnosis	Sepsis	No sepsis	Total
VHW	Sepsis	492	22	514
	No Sepsis	60	4694	4754
	Total	552	4716	5268

Table 2 Number of Diagnosed* and Treated cases of Sepsis in Different Years

Time Period	Total neonates in community	Neonates diagnosed as sepsis*	Incidence (%)	Neonates treated by VHW†	% of cases treated
September, 1996 to March, 1997	443	34	7.7	18	52.9
April, 1997 to March, 1998	913	77	8.4	53	68.8
April, 1998 to March, 1999‡	669	69	10.3	60	87.0
April, 1999 to March, 2000	898	93	10.4	76	81.7
April, 2000 to March, 2001	829	105	12.7	84	80.0
April, 2001 to March, 2002	765	81	10.6	71	87.7
April, 2002 to March, 2003	751	93	12.4	86	92.5
Total	5268	552	10.5	448	81.2

*Diagnosed by computer algorithm.
†Village health worker.
‡Diagnostic criteria slightly modified to give more sensitivity from this year (see Box 1).

Table 3 Clinical Features in Neonates with Sepsis (1996 to 2003)* ($n = 552$)

Clinical features	Present in	
	n	%
Diagnostic criteria†		
Cry weak or stopped	316	57.2
Sucking reduced or stopped	375	67.9
Baby became drowsy or unconscious	212	38.4
Baby was cold to touch or had fever‡	311	56.3
Vomiting or abdominal distension	204	37.0
Grunting or chest retraction	334	60.5
Skin pustules or umbilical infection	90	16.3
Other clinical features		
Fast breathing ($\geq$60 per minute)	240	43.5

*Clinical features recorded during entire neonatal period.
†Simultaneous presence of any two criteria resulted in the diagnosis of sepsis.
‡Skin temperature >99°F.

Table 4 Feasibility of Home-Based Sepsis Management

Indicator	No./total	%
Screening for sepsis		
Coverage (% neonates visited by VHWs)	5510/5919	93.1
VHW's diagnosis compared to computer diagnosis		
True positive (Sensitivity %)	492/552	89.1
True negative (Specificity %)	4694/4716	99.5
False positive	22/514	4.2
False negative	60/552	10.9
Parental acceptance		
Agreed to hospitalise	13/492	2.6
Agreed to home-based treatment	448/492	91.1
Refused both	31/492	6.3
Proportion of total neonates in community treated by VHWs for sepsis	470/5268	8.9

Our method of diagnosing sepsis required at least two diagnostic criteria to be present simultaneously in a neonate. The clinical features present in 552 neonates with suspected sepsis are presented in Table 3. All infants had more than two diagnostic criteria, with a mean of 3.3 criteria. The most frequently recorded signs/symptoms were sucking reduced or stopped; grunting or chest indrawing (retraction), and cry became weak or stopped. For all infants with presumed sepsis, the age at diagnosis ranged from 1 to 28, with a mean of 11.1 days. For those who died with a diagnosis of sepsis, the mean age at the time of death was 7 days, and the mean age at diagnosis was 5.3 days. There was a relatively short time interval between sepsis diagnosis and death.

The feasibility of home-based diagnosis and treatment as evaluated is presented in Table 4. The vast majority of infants (93.1%) were visited by VHWs. The VHWs were likely to (89.1%) accurately diagnose a case of clinical sepsis (as defined) and only missed 10.9% cases or overdiagnosed 4.2% patients (as compared to diagnosis by computer algorithm). Of the 492 patients diagnosed by the VHW to have presumed sepsis, parents agreed to and were able to hospitalize only 13 infants (2.6%), but agreed to home-based treatment for almost all infants (91.1%). Of note, in 31 cases (6.3%), parents refused both home and hospital care. Thus, the total number of neonates treated as sepsis by VHWs (true cases treated + false positives) was 470, that is, 8.9% of the neonates in the intervention area.

Table 5 Effect of Sepsis Case Management on Case Fatality in Gadchiroli (1996 to 2003) ($n = 552$)

Treatment	Live births	Sepsis diagnoses	Deaths	% Case fatality	*p*-value
Before training of VHWs* in treatment (April 1995 to August 1996)†	1005	163	27	16.6	<0.02
After training of VHWs (September 1996 to March 2003)	5268	552	53	9.6	<0.001
Treated by VHWs	—	448	31	6.9	<0.0001
Untreated by VHWs	—	91	20	22.0	
Diagnosis missed by VHWs	—	60	15	25.0	
Parents refused treatment	—	31	5	16.1	
Hospitalized‡	—	13	2	15.4	

*Village health worker.
†Pre-intervention period.
‡Referred by VHW or self referral by parents, some received initial dose of antibiotics given by VHWs.

Table 6 Effect of Sepsis Management on the Case Fatality in Neonates by Gestation and Birth Weight (September 1996 to March 2003) (Total Sepsis Deaths: 53)

	Sepsis cases untreated* ($n = 91$)			Sepsis cases treated by VHW† ($n = 448$)				
Risk group	Cases	Deaths	% CF‡	Cases	Deaths	% CF‡	% Reduction in CF‡	*p*-value
Estimated gestational age								
<32 weeks	6	6	100.0	10	4	40.0	60.0	<0.03
33 to 34 weeks	3	2	66.7	6	2	33.3	50.0	<0.41
35 to 36 weeks	16	2	12.5	45	2	4.4	64.4	<0.28
Total preterm	25	10	40.0	61	8	13.1	67.2	<0.02
Full term	66	10	15.2	383	22	5.7	62.1	<0.02
NR§	0	0	—	4	1	25.0	—	—
Birth weight								
<1500 g	12	9	75.0	14	4	28.6	61.9	<0.05
1501 to 1749 g	7	2	28.6	21	4	19.0	33.3	<0.48
1750 to 1999 g	7	2	28.6	43	5	11.6	59.3	<0.26
2000 to 2499 g	24	5	20.8	159	11	6.9	66.8	<0.05
Total LBW	50	18	36.0	237	24	10.1	71.9	<0.001
≥2500 g	41	2	4.9	208	7	3.4	31.0	<0.46
NR§	0	0	—	3	0	0.0	—	—

*Untreated = Village health worker missed the diagnosis (60)+parents refused treatment (31).
†Village health worker.
‡Case fatality.
§Not recorded.

Home-based treatment of presumed neonatal sepsis was very effective at reducing sepsis-related deaths (Table 5). In the pre-intervention period, 16.6% of newborns with a diagnosis of clinical sepsis died. By contrast, in the post-intervention period 6.9% of those who were treated died as compared to 22% of those who were untreated (either because of missed diagnosis or parental refusal of treatment).

The effect of home-based management on the case fatality in untreated and treated neonates categorized by estimated gestational age and by birth weight is shown in Table 6. Case fatality (CF) for

Table 7 Effect of Treatment on the Case Fatality in Neonatal Sepsis by the Day of Life (1996 to 2003)

	Untreated				Treated by VHWs*				
Day of diagnosis	Diagnosed	%	Deaths	% CF†	Diagnosed	%	Deaths	% CF†	% Reduction in CF†
1 to 4 days	42	46.2	15	35.7	125	27.9	21	16.8	52.9‡
5 to 7 days	9	9.9	1	11.1	54	12.1	5	9.3	16.2
1st week	51	56.0	16	31.4	179	40.0	26	14.5	53.8‡
2nd week	11	12.1	1	9.1	114	25.4	2	1.8	80.2
3rd week	16	17.6	3	18.8	96	21.4	3	3.1	83.5‡
4th week	13	14.3	0	0.0	59	13.2	0	0.0	—
2 to 4 weeks	40	44.0	4	10.0	269	60.0	5	1.9	81.0‡
Total	91	100.0	20	22.0	448	100.0	31	6.9	68.6§

*Village health worker.
†Case fatality.
‡$p<0.05$.
§$p<0.0001$.

both treated and untreated infants was inversely related to estimated gestational age and birth weight — that is, the risk of death decreased with increasing gestational age and birth weight. Home-based management resulted in a significant reduction in the CF for both term (62.1% reduction) and preterm infants (67.2% reduction) and for those who were under 2500 g birth weight (71.9% reduction). Of note, although home-based management resulted in a 31% reduction in the CF for infants over 2500 g birth weight, this finding was not statistically significant, probably because of the already low CF for this group without treatment.

The effect of home-based management compared by age at diagnosis in those who were treated and those who were untreated (diagnosis missed or parents refused treatment) is presented in Table 7. The younger the newborn, the higher the CF. For all age groups, CF was higher in the group who were untreated. Home-based treatment significantly reduced the risk of death for neonates with both an early (first week of life) and later diagnosis of neonatal sepsis.

VHWs gave 4793 injections of gentamicin. They also gave 5069 injections of vitamin K. To date, we have not identified any neonate with injection-related complications, including infection at the injection site, hemorrhage, nerve injury, or allergic rash. We have not maintained a record of the needle injuries to VHWs. However, the prevalence of HIV-positive Elisa test in pregnant women attending the women's clinic of SEARCH in the adjacent area was less than 0.1% during this period.

The difficulties expressed by VHWs in the review meetings or observed in supervisory visits included:

1. Not able to visit a neonate due to lack of information about its birth or arrival from outside. This was more common when mothers moved to parents' home for delivery a few days before delivery.
2. Parents not informing VHWs about development of a danger sign or symptom on a non-visit day.
3. VHW misinterpreting the clinical criteria, especially when the baby was sick from birth due to asphyxia or prematurity.
4. Natural variations in the respiratory rate in a newborn, causing difficulty in correctly counting and recording respiratory rate.
5. Despite advice from the VHWs, parents refusing to take a seriously ill neonate to hospital or refusing treatment.
6. Apprehension about the possibility of death especially when treating a preterm baby of < 32 weeks gestation, or a LBW baby <1500 g, because the treatment by VHW could be blamed for death.
7. Maintenance of oral feeding and body temperature in neonates <32 weeks or <1500 g often became difficult.
8. Parents or other families in village making request to VHW to give other medicinal injections as well.

Apart from the initial surprise and skepticism in the local medical community about a VHW treating neonatal sepsis with injection gentamicin, we did not experience any opposition. The professional leadership, including the members of the external advisory group and the national office bearers of organizations such as the IAP and NNF of India, actively engaged in discussions and decisions, and approved of this approach. The national workshops passed unanimous resolutions supporting this approach.[12,13]

DISCUSSION

This analysis covering 7 years of data from the Gadchiroli trial shows that it is feasible to screen neonates in a community with 93% coverage and to identify the suspected cases of sepsis with estimated 89% sensitivity as compared to the guidelines.

The majority of parents (91.1%) accepted home-based management, and most (97.4%) refused to go to hospital. VHWs treated in total 8.9% of all neonates in community as suspected sepsis. Home-based management of sepsis, with gentamicin and co-trimoxazole, reduced the CF significantly in all risk groups assessed (gestation, weight, and day of life). Overall, CF reduced from 16.6 to 6.9% in the treated neonates. No complications of injections to neonates was recorded. The local and national medical community was highly supportive of this approach.

In many parts of the world, most births and neonatal deaths occur at home. In areas that are far from health-care facilities or when families are unable or refuse to leave their homes and villages for care, creative approaches to the delivery of health care are needed. Earlier studies in Gadchiroli suggested that trained VHWs could identify sick newborns in their homes and were able to treat neonates with presumed sepsis and pneumonia appropriately and in a timely manner, thus reducing neonatal mortality. This study extends our earlier studies, confirms the earlier findings, and presents a new evidence about feasibility, acceptance, and problems.

Infections (primarily neonatal sepsis, pneumonia, and meningitis) have been reported to be the major causes of neonatal death in many developing countries.[1,2] Untreated, neonatal infections can very quickly result in serious illness and death. They are potentially preventable causes of neonatal mortality.

In this study, VHWs used strictly defined clinical criteria to diagnose presumed sepsis in a setting where there was no laboratory to make a definitive microbiologic diagnosis. We have selected these diagnostic criteria to be able to identify all potentially fatal cases of sepsis. We acknowledge that our criteria may overdiagnose sepsis (false-positive cases). We have evaluated[14] that, using these criteria, nearly 10% neonates in rural Gadchiroli would be identified as sepsis (the yield). The ability of these trained health workers to make a diagnosis of clinical sepsis was very similar to that of a computer-based algorithm using the same criteria, confirming that it is possible to train women with limited formal education and no prior medical or nursing education to examine newborns and to decide if they are ill or not. Of note, using this computer-based comparison, VHWs missed a diagnosis of presumed sepsis in only 11% cases and only 4% of the treatment was unnecessary treatment.

The major finding of this study is that home-based treatment of presumed sepsis with intramuscular gentamicin and oral co-trimoxazole was able to markedly reduce the CF rate. While 16.6% of infants with presumed sepsis died in the pre-intervention period and 22% of those who were untreated (missed diagnosis or refused treatment) during the intervention period died, only 6.9% of those who were treated by VHWs died. Although the risk of death was greatest in neonates who were preterm and/or of low birth weight, there was a similar reduction in %CF among both term and preterm infants who were treated in the home. The preterm neonates included in this study were of 28 to 37 weeks gestation. A neonate born before 28 weeks is not considered viable in India.[15] Nearly three-fourths of the LBW neonates were full term, but intrauterine growth restricted neonates, most of them with birth weight >1500 g. Although early neonatal sepsis occurring in the first week of life had the highest CF, there was a significant reduction in CF for home-based treatment throughout the neonatal period.

A potential criticism of this approach is that diagnostic criteria are based upon nonspecific signs and symptoms that may reflect a number of pathologic neonatal conditions, in addition to sepsis (including surfactant-deficient respiratory distress of the premature infant and hypoxic–ischemic encephalopathy of the term infant). Therefore, neonatal sepsis may have been overdiagnosed in the intervention sites. However, because of the high risk of death in untreated sepsis, an accepted principle in the management of neonatal sepsis even in developed countries is to treat on the slightest suspicion of infection. Remington and Klein reported that in the neonatal nurseries in Boston, 6.5% neonates were treated with antibiotics for suspected sepsis, though of those treated only 6% turned out to be culture positive.[9] Moreover, despite possible concerns about accuracy of the diagnosis, the home-based treatment by VHWs in our study did result in a significant reduction in CF in treated cases and, as reported earlier, in the all-cause NMR by 62%.[5]

The importance of health education for mothers and families in the community must be emphasized. Despite recommendations by VHWs, the majority of families refused to take their neonates to hospital for care. Although families accepted home-based care, VHWs were concerned that parents did not always inform them about a sick infant on a non-visit day and thus treatment was delayed for some infants. Obviously, there is a great scope for improvement in parental-care-seeking behavior.

Although we were concerned about potential problems in allowing a VHW to give intramuscular injections to a sick neonate, including complications of injections and unnecessary or excessive use of injections, none of these occurred during the 7 years study period. This evidence suggests that, with proper training, motivation, supervision, and community education, potential hazards can be avoided.

A major concern about home-based care is whether it is ethical to allow a VHW, rather than a doctor, to diagnose and treat a potentially fatal disease such as neonatal sepsis. Ideally, all such neonates should be hospitalized, evaluated by a highly specialized medical team and treated. However, the ideal conditions do not exist in the real world. In areas where hospitals are not accessible, or where hospitals do not have facilities to care for a sick neonate or when parents cannot or do not want to hospitalize a sick neonate, not to treat a life-threatening condition may be considered unethical. Use of injections by nonphysicians has already been accepted and widely practiced in immunization

programs or in situations such as self-administration of insulin by insulin-dependent diabetic patients. The risk of death and hence the urgent need to treat is greater in the case of a neonate with sepsis in a rural home.

Although the local medical community was initially skeptical about the ability of VHWs to treat sick infants with antibiotics (especially injectable antibiotics) in the home, they did not oppose the program and became great supporters once the success of the intervention was established. Furthermore, national opinion leaders and decision makers (such as the successive national presidents of the IAP and the NNF) have actively supported this innovative approach.[12,13]

The unresolved issues for further research are: (1) improving methods of family education for recognition of sick neonate and better care seeking, (2) making gentamicin available in Uniject device which can be easily administered, (3) choice of antibiotics which can be administered orally, (4) interventions to prevent early-onset sepsis because it contributes most of the remaining sepsis deaths in Gadchiroli, (5) in the cases with fatal outcome, the mean duration of treatment before death was only 1.7 day. Earlier initiation of treatment will further improve the survival.

Significance

The success of the Gadchiroli trial in reducing sepsis-related neonatal mortality in a community setting with limited resources is promising for other developing countries. This intervention is currently being adapted to other settings in India and elsewhere in the developing world. If successful in replicating the findings in Gadchiroli, these studies will have broad public health implications for the prevention of neonatal mortality in developing countries.

Such innovations are not new. The history of public health in developing countries shows similar examples wherein hospital-based treatment of dreaded infections was simplified and substituted by home-based treatment. Domiciliary treatment of tuberculosis, oral rehydration therapy for cholera and other watery diarrhea, and community-based management of pneumonia in children are some such successful innovations. These have saved more lives than many other costly treatments. A similar change might occur in the public health approach to the management of neonatal infections in developing countries.

References

1. Save the children. State of the World's Newborn. Save the Children, Washington DC; 2001.
2. Stoll BJ. Neonatal infections: a global perspective in: Remington JS, Klein JO, editors. Infectious Diseases of the Fetus and Newborn Infant. 6th ed. Philadelphia: WB Saunders Company (in press).
3. Bang AT, Bang RA, Baitule SB, Deshmukh MD, Reddy HM. Burden of morbidities and the unmet need for health care in rural neonates — a prospective observational study in Gadchiroli, India. Indian Pediatr 2001;38:952–65.
4. Bang AT, Reddy HM, Baitule SB, Deshmukh MD, Bang RA. The incidence of neonatal morbidities in community: variation by season and by day of life and the scope for prevention through better home care. J Perinatol 2005;25:S18–28.
5. Bang AT, Bang RA, Baitule SB, Reddy HM, Deshmukh MD. Effect of home-based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. Lancet 1999;354:1955–61.
6. Bang AT, Paul VK, Reddy HM, Baitule SB. Why do neonates die in rural homes? (Part I): Primary causes of death assigned by neonatologist based on prospectively observed records. J Perinatol 2005;25:S29–34.
7. Bang AT, Bang RA, Reddy HM, Deshmukh MD. Methods and the baseline situation of the field trial of home-based neonatal care in Gadchiroli, India. J Perinatol 2005;25:S11–7.
8. Stoll BJ. The fetus and the neonatal infant, Part XI, Section II, Infections of the newborn infant In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson's Textbook of Pediatrics. 17th ed. Philadelphia: W.B. Saunders; 2003. p. 623–40.
9. Remington JS, Klein JO. Infectious Diseases of the Fetus and Newborn Infant. Philadelphia: WB Saunders Company; 1990. p. 641–2.
10. Bang RA, Bang AT, Baitule M, et al. High prevalence of gynaecological diseases in rural Indian women. Lancet 1989;i:85–8.
11. Bang AT, Rani RA, Morankar VP, Sontakke PG, Solanki JM. Pneumonia in neonates: can it be managed in the community? Arch Dis Childhood 1993;68:550–6.
12. Consensus Statement of the National Workshop on Home-based Neonatal Care jointly organized by the IAP, NNF, UNICEF and SEARCH, Gadchiroli, India, 1999.
13. Consensus Statement of the National Workshop on 'How to Reduce the IMR to 30?' Gadchiroli, India. 31st March to 1st April 2003.
14. Bang AT, Bang RA, Reddy HM, et al. Simple clinical criteria to identify sepsis/pneumonia in neonates in the community for treatment or referral. Ped Inf Dis J (in press).
15. Registrar General of India. Civil Registration System. Government of India, New Delhi, 2002.

Appendix A: The neonatal sepsis monitoring form in Gadchiroli

Mother's name: *Godavari Patil* Village: *Khursa* Worker's name: *Kusum Gadpayale*

Which of the following signs are present? [Mark **'Y']**

	Days														Other days
	2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**12**	**15**	**18**	**21**	**24**	**28**	
1. Previously normal cry became weak or stopped															
2. Previously normal baby became drowsy or unconscious										Y					
3. Previously normal sucking became weak or stopped										Y					
4. Mother feels that baby is cold to touch or has fever						Y	Y	Y	Y	Y					
5. Skin or umbilical infection (pus or abscess)															
6. Abdominal distension or consecutive 3 feeds led to vomiting															
7. Grunt or chest indrawing															
Total no of criteria present (On a given day)						1	1	1	1	3					

Out of above 7 criteria, simultaneous presence of two or more criteria indicate sepsis: ☐

If 'Yes' go to sepsis management form.