ORIGINAL ARTICLE

Causes and outcome of young infant admissions to a Kenyan district hospital

M English, M Ngama, C Musumba, B Wamola, J Bwika, S Mohammed, M Ahmed, S Mwarumba, B Ouma, K McHugh, C Newton

Arch Dis Child 2003;**88**:438–443

See end of article for authors' affiliations

Correspondence to: Dr M English, Centre for Geographic Medicine Research–Coast, KEMRI/Wellcome Trust Research Laboratories, PO Box 230, Kilifi, Kenya; menglish@kilifi.mimcom.net

Accepted 6 October 2002

Aims: To provide a comprehensive description of young infant admissions to a first referral level health facility in Kenya. These data, currently lacking, are important given present efforts to standardise their care through the integrated management of childhood illness (IMCI) and for prioritising both health care provision and disease prevention strategies.

Methods: Prospective, 18 month observational study in a Kenyan district hospital of all admissions less than 3 months of age to the paediatric ward.

Results: A total of 1080 infants were studied. Mortality was 18% overall, though in those aged 0–7 days it was 34%. Within two months of discharge a further 5% of infants aged <60 days on admission had died. Severe infection and prematurity together accounted for 57% of inpatient deaths in those aged <60 days, while jaundice and tetanus accounted for another 27%. *S pneumoniae*, group B streptococcus, *E coli*, and *Klebsiella* spp. were the most common causes of invasive bacterial disease. Hypoxaemia, hypoglycaemia, and an inability to feed were each present in more than 20% of infants aged 0–7 days. Both hypoxaemia and the inability to feed were associated with inpatient death (OR 3.8 (95% CI 2.5 to 5.8) and 7.4 (95% CI 4.8 to 11.2) respectively).

Conclusions: Young infants contribute substantially to paediatric inpatient mortality at the first referral level, highlighting the need both for basic supportive care facilities and improved disease prevention strategies.

It is likely that over 5 million deaths occur annually in developing countries in children during their first few months of life.[1] In Africa it has been hard to establish the cause of these deaths at the community level where the majority take place.[2 3] Sub-Saharan African hospital based data are either from tertiary referral centres, fail to distinguish perinatal mortality, or report outcome from particular disorders only.[4–7] What data are available suggest that birth asphyxia and severe prematurity are likely to be major causes of death in the first week of life while serious bacterial infections are responsible for a greater proportion of mortality as infancy progresses.[8–11] However, the current lack of data makes it unclear what impact serious illness in young infants has on first referral level health facilities where the majority of inpatient care in Africa is provided.

We have therefore investigated the cause and outcome of admission for infants aged less than 3 months of age to a Kenyan district hospital: firstly to furnish service providers with data on the problems posed by caring for young infants; secondly to include the population of sick infants (those less than 60 days) that will need to be identified by the new integrated management of childhood illness (IMCI) algorithms[12]; and thirdly to ascertain whether results of a multicentre study based largely in urban or referral hospitals on the aetiology of severe infectious disease[13] can reliably be generalised to rural African settings.

METHODS

The study was undertaken at Kilifi District Hospital on the Kenyan Coast between November 1999 and April 2001. The hospital is the main district level government inpatient facility and the majority of admissions come from a population of approximately 200 000 people living within 30 km of the hospital. Most of the adult population are subsistence farmers with families living in scattered rural homesteads. Malaria transmission occurs throughout the year with seasonal peaks in May–August and December–January following the rainy seasons. The background HIV seroprevalence is estimated to be 11% in the township surrounding the hospital and 9% in rural antenatal attendees.[14] Although approximately 1800 births a year occur in the hospital, most births (over 70%) in the district take place at home and thus most sick infants are admitted directly from the community. Recent, provincial, community based estimates suggest neonatal and under 5 mortality rates of approximately 30 and 111 per 1000 live births respectively.[15]

Sick infants brought from home were seen in the outpatient facility by government clinical officers who decided on the need for admission. Once admitted all infants less than 3 months of age were seen by a clinical member of the research staff (24 hour cover was provided) and a standardised proforma was completed detailing symptoms and signs at presentation. Examination included pulse oximetry (Nellcor, USA) with a measured oxygen saturation <90% regarded as indicative of hypoxaemia. Sick infants on the maternity unit were seen by the research staff and assessed. Those with mild illness (requiring oral or topical treatment or simply feeding assistance) were managed on the maternity ward. Infants with more serious illness were admitted to the paediatric ward; they were enrolled in the study and completed the same procedures as those admitted from home. On admission the study was explained to the parents of eligible infants in their local language by a trained project assistant and consent for inclusion was sought. Approval for the study was obtained from the national Kenyan Ethical Committee.

Abbreviations: CI, confidence interval; CSF, cerebrospinal fluid; IMCI, integrated management of childhood illness; IQR, interquartile range; OR, odds ratio; RPR, rapid plasma reagin

Table 1 Primary diagnosis of admitted infants and case fatality rates

	Number of cases (% of age group)	Deaths (case fatality)
Age 0–7 days (n=432)		
Neonatal sepsis	130 (30%)	33 (25%)
Prematurity	90 (20%)	47 (52%)
Neonatal jaundice	75 (17%)	18 (24%)
Birth asphyxia	39 (9%)	17 (44%)
Neonatal tetanus	24 (6%)	20 (83%)
Clinically apparent congenital abnormalities	19 (4%)	3 (16%)
Respiratory distress/transient tachypnoea	8 (2%)	0
Neonatal meningitis	5 (1%)	3 (60%)
Other	42 (10%)	6* (14%)
Age 8–30 days (n=260)		
Severe infection/pneumonia	157 (60%)	10 (6%)
Neonatal tetanus	17 (7%)	8 (47%)
Neonatal jaundice	12 (5%)	1 (8%)
Prematurity/very low weight	12 (5%)	3 (25%)
Meningitis	10 (4%)	1 (10%)
Other	52 (20%)	2† (4%)
Age 31–60 days (n=186)		
Pneumonia	100 (54%)	1 (1%)
Severe infection	22 (12%)	3 (14%)
Meningitis	10 (5%)	0
Other	55 (30%)	1‡ (4%)
Age 61–90 days (n=202)		
Pneumonia	106 (53%)	4 (4%)
Malaria	28 (14%)	3 (11%)
Gastroenteritis	20 (10%)	1 (5%)
Meningitis	6 (3%)	1 (17%)
Other	42 (21%)	3§ (7%)

*Two deaths from anaemia, one from congenital hepatitis, one small for gestational age, two diagnosis unknown. †Two deaths from congenital abnormalities.
‡One death attributed to severe malnutrition.
§Two deaths were in very low weight infants, one from an encephalopathic illness with a normal CSF.

Sick infants were routinely investigated according to a standard protocol with a full blood count (Coulter Electronics), blood culture (Bactec 9050, Beckton Dickinson), plasma electrolytes, creatinine (Beckman Instruments), rapid plasma reagin (RPR, Murex), and glucose (Analox Instruments, UK). Total serum bilirubin was measured in all visibly jaundiced infants. Lumbar puncture was performed as part of the routine "septic screen" in all neonatal admissions with suspected sepsis and otherwise according to locally agreed clinical criteria based on those used in the WHO multicentre study of young infants.[13] Portable chest radiography was not available during the study and it was not possible to obtain a chest *x* ray in the evening, at night, or at the weekend. The scale of this observational study meant it was not possible to routinely test infants for HIV infection. Interventions available included oxygen, antibiotics, intravenous fluids (not parenteral nutrition), nasogastric feeding of expressed breast milk, phototherapy, and exchange transfusion. During the study an incubator was not routinely available. Empiric management of suspected severe infection was with gentamicin and either benzylpenicillin, ampicillin, or cloxacillin, the latter choice being at the discretion of the admitting clinician. For eight months of the study period a randomised trial of multidose and once daily dosing of gentamicin in young infants was conducted (reported elsewhere).

The clinical care during admission was supervised by a consultant paediatrician (ME) who was also responsible for gestational age assessment[16] and assigning the final diagnosis at the end of the admission after review of the case notes and the results of all pertinent investigations. Determining the precise diagnosis in young infants is problematic and dual pathology is likely, particularly in the first week of life. Thus severe illness in a premature infant may be due entirely to immaturity (for example, the de novo development of respiratory distress) or secondary to infection to which they are predisposed on account of their immaturity. The final diagnosis assigned represents an experienced paediatrician's view of the most probable primary pathological event on which secondary pathological events might be superimposed. All infants aged less than 2 months (the target population of IMCI young infant algorithms) were invited back for a single follow up appointment 1–2 months after discharge. At follow up carers were asked about continuing problems and the infants were examined to detect gross neurological deficits. Those not attending follow up who lived within 30 km of the hospital were visited at home to establish whether the child was still alive.

Data collected throughout the study were double entered and verified using Foxpro 2.1, inconsistencies in the datasets being resolved by further examination of all available records. Data are presented as frequencies, means, and medians with 95% confidence intervals (CI) and interquartile ranges (IQR) respectively. Mantel-Haentzel odds ratios (OR), age adjusted where appropriate, were calculated to explore associations with defined outcomes, and logistic regression was used to investigate for clinical features independently associated with the presence of invasive bacterial disease. Analyses were performed using STATA 6 (Stata Corporation, USA).

RESULTS

During the study period 1080 infants less than 3 months of age (58% male) were admitted and 190 (18%) died in hospital. These children represented 14% of all paediatric admissions and 37% of paediatric deaths during this time period. Only 5% of the cohort were admitted directly from the maternity unit, the remainder being admitted from home through the outpatient department. Almost half of the mothers of admitted infants had received no primary education, 45% had to walk for at least 30 minutes to reach a place from where transport to the hospital might be found, only 15% could be described as residents of the town in which the hospital was

Table 2 Prevalence of major disease clusters in the first 60 days of life

	% of all admissions <60 days of age (rank)	% of mortality in those aged <60 days (rank)
Severe infection*	38 (1)	29 (1)
Prematurity†	11 (2)	28 (2)
Pneumonia (aged 30–59 days)‡	11 (3)	0.5 (7)
Neonatal jaundice	10 (4)	11 (4)
Neonatal tetanus	5 (5)	16 (3)
Birth asphyxia	4 (6)	10 (5)
Clinically apparent congenital abnormalities	2 (7)	2 (6)
Respiratory distress/transient tachypnoea	1 (8)	0 (8)

*Severe infection includes the clinical categories (table 1), neonatal sepsis, severe infection/pneumonia, and meningitis.
†Prematurity includes children admitted up to the age of 30 days for whom their immaturity was considered the major problem.
‡Pneumonia includes children for whom the clinician felt able to make a firm clinical diagnosis of pneumonia rather than the less specific "severe infection".

situated, and in 65% of cases the infant's delivery was attended by either a relative, a friend or no one.

Mortality and morbidity

Accepting the inherent limitations in the diagnostic process, the observed cause specific patterns of admissions and mortality are presented in tables 1 and 2. Different disease patterns and case fatality rates mean that overall mortality varies considerably across age groups, being 34% in those aged 0–7 days, 10% in those aged 8–30 days, 3% in those aged 31–60 days, and 6% in those aged 61–90 days. Of 700 infants aged less than 2 months discharged alive, 55 (8%) were excluded from follow up because their illness was considered mild or because of a large distance from the hospital. Of the remainder, 536/645 (83%) were successfully followed. Among those followed up, 30 had died at home after discharge and 48 had severe continuing problems (using the conservative denominator of 645 this gives proportions of 5% and 7% respectively). Of children dying at home, 12 (40%) had been admitted with a severe infection (of any type), five (17%) with congenital abnormalities, three (10%) with prematurity, and two (7%) with tetanus. Weight ≤2 kg was associated with an odds ratio of 3.1 (95% CI 1.3 to 7.3, p = 0.007) for death after discharge in those without congenital abnormalities. Persistent serious problems at follow up included gross neurological sequelae (n = 7), convulsions (n = 6), continued feeding difficulty with very poor weight gain (n = 6), symptomatic heart disease (n = 7), and major congenital abnormalities (n = 19).

Infectious diseases

Presumed serious infections were the commonest cause of admission among infants <2 months of age (table 2), and in the third month of life infectious diseases were responsible for more than 75% of admission episodes (table 1). No cases of malaria (congenital malaria) were observed in the first one month of life. In the majority of cases it was not possible to identify a focus of infection. However, clinicians felt more confident distinguishing pneumonia from other infections in infants older than 1 month. Among children diagnosed as having pneumonia, 44/133 (33%) had evidence of either lobar (18%) or patchy (15%) consolidation on chest *x* ray. Chest *x* rays in infants with non-specific severe infection but clinical signs compatible with pneumonia were less likely to have consolidation on chest *x* ray (8/93, 9%). Consolidation on chest *x* ray was not significantly associated with bacteraemia but was associated with the presence of hypoxaemia (OR 5.6, 95% CI 2.9 to 11.0).

Neonatal tetanus is easily distinguished clinically from other infections in early infancy and so these cases are enumerated separately. There were no characteristic cases of congenital syphillis admitted during the study period, but infants were screened to examine this possibility. Sample volumes were sufficient for RPR assay in 786 (73%) infants. Of these, 11 (1.4%) were strongly positive (titre ≥1/8) and 28 (3.6%) weakly positive (titre <1/8). The presence of a positive or strongly positive RPR was not significantly associated with a specific age group, clinical presentation, or outcome. Four of these 11 infants presented with non-specific features of severe infection, two with features of birth asphyxia, two with congenital abnormalities, two with anaemia, and one with severe skin sepsis.

Table 3 details the organisms isolated from either blood or cerebrospinal fluid (CSF) taken on admission in young infants. *Staphylococcus epidermidis* and acinetobacter species

Table 3 Isolates responsible for invasive disease

	0–7 days (n=432)	8–30 days (n=260)	31–60 days (n=186)	61–90 days (n=202)	Total
S pneumoniae	3	4	3	3	13
Group B streptococcus	6	6	0	0	12
Klebsiella spp.	10	0	1	0	11
E coli	8	1	2	0	11
Pseudomonas spp.	5	1	0	1	7
Group A streptococcus	0	5	1	0	6
S aureus	1	3	1	1	6
H influenzae	0	1	3	1	5
Enterococcus spp.	3	1	0	0	4
Proteus mirabilis	4	0	0	0	4
Others	2	1	2	2	7
Total (% of age group with invasive disease)	41* (9%)	23 (9%)	13 (7%)	7* (3%)	86

*For one individual, one culture grew two pathogens.

Table 4 Association of admission clinical features with presence of bacteriologically confirmed invasive disease

Clinical feature	OR for presence of bacteriologically confirmed invasive disease	p value
Omphalitis	2.4 (1.2 to 4.7)	0.008
Prostration	2.2 (1.3 to 3.6)	0.001
Oxygen saturation <90%	2.0 (1.2 to 3.5)	0.01
Weak or absent movements	2.9 (1.8 to 4.8)	<0.0001
Abnormally irritable or sleepy	2.3 (1.4 to 3.7)	0.005
Abnormal feeding	1.6 (1.0 to 2.6)	0.05
Inability to console infant	2.4 (1.1 to 5.1)	0.02
Bulging fontanelle	7.5 (3.1 to 18.0)	<0.0001

were considered to be contaminants. Twelve isolates were from CSF (four *Streptococcus pneumoniae*, two *Salmonella* spp., one each of *Haemophilus influenzae*, *Escherichia coli*, *Pseudomonas* spp., *Staphylococcus aureus*, *Proteus mirabilis*, and *Vibrio alginolyticus*); in 11 cases the same organism was cultured from blood. A positive blood culture (that encompasses most cases of culture proven meningitis) was associated with an odds ratio of 3.0 (95% CI 1.8 to 4.8) for death. Table 4 shows odds ratios from univariate analysis for clinical features that might predict the presence of invasive bacterial disease (positive CSF or blood culture). In a logistic regression model that included age (in four categories) constructed to examine the independent effects of these variables, only the presence of a bulging fontanelle remained significantly associated with the presence of bacteraemia (OR 4.9, 95% CI 1.5 to 16.7, $p = 0.01$). However, the sensitivity of a bulging fontanelle for detecting bacteraemia was only 12%, with specificity 98% and positive predictive value 38%. Even for bacteriologically proven or clinically defined meningitis only 3/12 (25%) and 9/28 (32%) infants had a bulging fontanelle. Signs of pneumonia, jaundice, presence of fever, the inability to cry, or the presence of apnoea were not significantly associated with documented invasive bacterial disease. (The antibiotic sensitivity of organisms responsible for invasive disease will be described elsewhere.)

Prematurity

Infants in this group accounted for 11% of admissions, but 28% of deaths in those under 2 months of age. Although 18% of all admissions less than 3 months of age were <2.0 kg, only 58% of these infants admitted in the first week of life were assigned a primary diagnosis of prematurity. Among children with a principal diagnosis of prematurity (n = 102), 15% weighed <1.0 kg while 28%, 31%, 16%, and 9% weighed 1.0–1.25 kg, >1.25 to ⩽1.50 kg, >1.50 to ⩽1.75 kg, and >1.75 to ⩽2.0 kg respectively. Eight infants who were not thought to be premature presented with clinical and radiological features most consistent with a problem in the transient tachypnoea/respiratory distress syndrome spectrum.

Neonatal jaundice

Neonatal jaundice was associated with a high mortality in the first week of life (tables 1 and 2). Of the 87 infants admitted with jaundice as a primary problem, 23 received an exchange transfusion, seven (30%) of whom died. The median bilirubin in the exchange transfusion group was 750 µmol/l (IQR 512 to 769 µmol/l). The 10 further infants who died with severe jaundice all had bilirubin values >560 µmol/l; neurological deficits at presentation precluded exchange transfusion. However, seven further exchange transfusions were performed among children with severe infection and jaundice. Phototherapy was clearly indicated in 61 children during the study period.

Problems associated with severe illness

Table 5 presents the additional problems encountered at presentation in the management of infants in the first three months of life and their association with mortality, adjusted for age category. The high prevalence of problems requiring general supportive care, including hypoglycaemia, the inability to feed, and hypoxaemia, particularly in those admitted in the first week of life, show the demands placed on limited resources by sick young infants.

DISCUSSION

Although infants in the first three months of life comprise a relatively small proportion of admissions, they contribute disproportionately to inpatient paediatric mortality. Indeed 29% of inpatient paediatric deaths occurred in children in the first week of life. In part this high mortality may be explained by

Table 5 Non-disease specific management problems affecting the young infant population

Admission status	0–7 days (n=432)	8–30 days (n=260)	31–60 days (n=186)	61–90 days (n=202)	Age adjusted OR for death (95%CI)
Reported convulsions	26/430	25/260	26/186	20/202	0.7
	6%	10%	14%	10%	(0.3 to 1.4)
Oxygen saturation <90%	87/376	36/240	25/168	16/172	3.8
	23%	15%	15%	9%	(2.5 to 5.8)
Inability to feed	125/429	30/260	21/186	14/201	7.4
	29%	12%	11%	7%	(4.8 to 11.2)
Blood glucose <2.2 mmol/l	83/363	19/208	9/134	2/115	1.5
	23%	9%	8%	2%	(1.0 to 2.4)
Sodium <130 mmol/l	20/374	21/231	13/159	11/170	1.6
	5%	9%	8%	6%	(0.9 to 3.0)
Impaired ventilation (venous pCO_2 >7.0 kPa)	18/145	1/97	3/51	0/61	5.0
	12%	1%	6%	0%	(1.8 to 14.2)
Presence of metabolic acidosis (BE <–10 mEq/l)	58/146	28/97	9/51	18/61	4.3
	40%	29%	18%	30%	(2.4 to 7.7)

the contribution of very low birthweight infants (<1.5 kg), presentation to the hospital in advanced states of illness, and the difficulties of sustaining even appropriate, basic levels of supportive care with limited personnel and resources in a setting designed to cope with less than half the number of admissions than are actually received. As well as this high inpatient mortality it seems that at least 1 in 10 infants less than 2 months old who are discharged alive either die within two months of their admission or have severe, persistent problems. One of the possible limitations of this study was the inability to assess the impact of HIV status on the observed mortality and morbidity in this age group. However, in a large community based study, maternal HIV infection did not increase the risk of neonatal death,[17] and in a study of the natural history of disease attributable to HIV infection in Rwanda the major impact of this infection appeared only after the early infant period.[18] Therefore, while it is possible that absence of this data means the "cause" of death or illness is misclassified in some cases, we feel the spectrum of disease presented here is likely to be representative of that in district hospitals in many areas of Africa with a similar background prevalence of HIV infection (~10%[14]).

There are problems in assigning a single diagnosis to sick infants, particularly where facilities for investigation are limited. While accepting that some misclassification is inevitable in our study, we believe our data provide valuable insight into the clinical challenge of caring for sick young infants faced by African district hospitals. Our findings show that prematurity and infection (which may act synergistically in many cases) are likely to be the major causes of death in such hospitals, findings in broad agreement with other recently published data from a similar type of facility in Papua New Guinea.[19] However, in contrast to the findings from Papua New Guinea, congenital syphilis did not appear to be a major cause of disease in early infancy, while jaundice and neonatal tetanus were moderately common. Birth asphyxia is a less common problem in our setting than might be anticipated from community based studies or reports from large urban hospitals. This is probably because of the high prevalence of home births and the likelihood that many asphyxiated infants die before hospital admission is possible. Even so these five conditions together comprise almost 80% of young infant admissions and should clearly be the target population for IMCI algorithms. Importantly our data show the obvious need for greater attention to illness in the first week of life. To date IMCI algorithms for use in this age group have been subject to little formal evaluation.

Perhaps the surprising finding of our study was the importance of an apparent primary diagnosis of neonatal jaundice as a cause of both admission and death (we classified infants as having severe infection if there were clinical features to support this diagnosis, even if they were jaundiced). Without better investigative facilities it is difficult to be certain of the cause of the jaundice. However, those infants assigned this primary diagnosis in general shared the following features: jaundice due almost exclusively to an unconjugated hyperbilirubinaemia, onset of jaundice described by the mother as the first symptom, lack of clinical indicators of associated severe infection, and age consistent with either haemolytic disease or physiological jaundice exacerbated by either feeding difficulty or mild infection. The high mortality occurred despite our ability to offer phototherapy and exchange transfusion (the latter undertaken if jaundice was very severe, haemolysis was considered a possible cause, and if there was not already obvious neurological impairment). However, in many cases (as evidenced by the very high bilirubin concentrations at presentation), children were already severely affected by the time they were hospitalised, many already having frank kernicterus. While conducting an exchange transfusion is an unreasonable expectation of a typical rural district hospital, providing phototherapy should be considered a priority and be combined with better education of mothers and health workers about the dangers of neonatal jaundice. The ability to provide other forms of simple supportive care (oxygen, the assessment and management of hypoglycaemia, the feeding of sick infants, and infant warming) is also clearly a critical issue for this hospital and more widely, reinforced by some evidence of their effect at improving outcome at this level.[20]

Until the publication of the WHO sponsored multicentre study in young infants,[13] there was little data from Africa on the aetiology of community acquired invasive bacterial disease in early infancy. Our data on bacterial isolates are in broad agreement with the findings of this multicentre study, with the notable exceptions of the prominent role played by group B streptococcal infection and the small number of isolates of salmonella species (n = 2) despite this being a very common pathogen in older children in our hospital (Berkley, submitted). The high prevalence of group B streptococcal infections did not seem to be explained by the inclusion of very sick infants admitted from the hospital's maternity ward as the prevalence of this infection was the same among admissions from the community. Our findings are however in keeping with the heterogeneity of reports on the prevalence of group B streptococcal disease within Africa.[4 7 21 22] Importantly our data confirm the standing of *Streptococcus pneumoniae* as a major pathogen in young infants, even in the first month of life. Thus our data support the suggestion that maternal vaccination for *S pneumoniae*, group B streptococci, or both may be worth consideration,[23] although our data do not suggest these interventions would result in major reductions in neonatal mortality. Furthermore, the effectiveness of maternal vaccination may be reduced by impaired materno-fetal antibody transfer seen in malaria endemic areas,[24] and by deficiencies in the vaccine delivery mechanism. Evidence for the latter can be seen in the persistent, major contribution to early infant mortality made by neonatal tetanus in our setting despite an active government programme of maternal, antenatal tetanus toxoid immunisation. Furthermore, it is possible that non-specific interventions that are at least as practical, or community based management, may have as significant an effect as more sophisticated intervention programmes.

The first months of life are a vulnerable time. Despite the fact that under-reporting of perinatal and neonatal deaths is likely, deaths in this age group often account for more than half of all infant deaths. Even though the majority of these deaths occur in the community, sick young infants brought for care form a significant part of the workload of rural African district hospitals. Evidence, particularly cost effectiveness data, to support policy decisions over health interventions in this age group is often lacking, while some of the data that are available, such as the lack of effectiveness of routine growth monitoring,[25] have not affected policy. Our data show that the provision of an environment suitable for care of sick young infants and adequate provision for simple supportive care (including targeted follow up of high risk groups such as those <2 kg) should be considered priorities in strategic thinking about the services and skills required at the first referral level. Examining the impact of an essential package of care in Africa, as has been done in Papua New Guinea,[20] would be of great interest. Although hospital based, our data also suggest that strategies to tackle the problem of premature birth and to prevent or treat infection may be of great benefit. In the case of infection the value of maternal immunisation should be considered alongside the possible value of community based diagnosis and care,[26] improved case management (IMCI),[12] and improved umbilical cord care,[27] among other interventions. Evidence from large, pragmatic intervention trials would be of most value.

ACKNOWLEDGEMENTS

This manuscript is published with the permission of the Director of KEMRI and was supported by KEMRI and the Wellcome Trust UK;

Mike English is a Wellcome Trust Career Development Fellow (050563) and Charles Newton (050533) is a Wellcome Trust Senior Research Fellow. The authors would like to thank the staff of Kilifi District Hospital, particularly the staff of Ward 1, and of the Centre for Geographic Medicine Research–Coast in the execution of this study.

Authors' affiliations
M English, M Ngama, C Musumba, B Wamola, J Bwika, S Mohammed, M Ahmed, S Mwarumba, B Ouma, C Newton, Centre for Geographic Medicine Research–Coast, KEMRI/Wellcome Trust Research Laboratories, PO Box 230, Kilifi, Kenya
K McHugh, Department of Radiology, The Hospitals for Sick Children, Great Ormond Street, London, UK

REFERENCES

1 **World Health Organisation**. *Perinatal mortality—a listing of available information*. Geneva: World Health Organisation, 1996.
2 **Slutsker L**, Bloland P, Steketee R, *et al*. Infant and second year mortality in rural Malawi: causes and descriptive epidemiology. *Am J Trop Med Hyg* 1996;**55**:77–81.
3 **Snow R**, Armstrong J, Forster D, *et al*. Childhood deaths in Africa: uses and limitations of verbal autopsies. *Lancet* 1992;**340**:351–5.
4 **Nathoo K**, Mason P, Chimbira T. Neonatal septicaemia in Harare Hospital: aetiology and risk factors. *Cent Afr J Med* 1990;**36**:150–6.
5 **Petit P**, Van Ginneken J. Analysis of hospital records in four African countries 1975–1990, with emphasis on infectious diseases. *J Trop Med Hyg* 1995;**98**:217–27.
6 **Meme J**. A prospective study of neonatal deaths in Nairobi, Kenya. *E Afr Med J* 1978;**55**:262–7.
7 **Owa J**, Olusanya O. Neonatal bacteraemia in Wesley Guild Hospital, Ilesha, Nigeria. *Ann Trop Paediatr* 1988;**8**:80–4.
8 **Costello A**. Perinatal health in developing countries. *Trans R Soc Trop Med Hyg* 1993;**87**:1–2.
9 **Ashworth A**, Waterlow J. Infant mortality in developing countries. *Arch Dis Child* 1982;**57**:882–4.
10 **Stoll B**. The global impact of neonatal infection. *Clin Perinatol* 1997;**24**:1–21.
11 **Leach A**, McArdle T, Banya W, *et al*. Neonatal mortality in a rural area of The Gambia. *Ann Trop Paediatr* 1999;**19**:33–43.
12 **World Health Organisation**. *Handbook IMCI—integrated management of childhood illness*. Geneva: UNICEF/WHO, 2000.
13 **The WHO Young Infants Study GroupGroup**. Bacterial etiology of serious infections in young infants in developing countries—results of a multicenter study. *Pediatr Infect Dis J* 1999;**18**(suppl):S17–22.
14 **Ministry of Health**. *AIDS in Kenya*, 6th edn. Nairobi: Ministry of Health and the National Aids Control Council, 2001.
15 **National Council for Population and Development**, Central Bureau of Statistics & Office of the Vice-President and Ministry of Planning and National Development. *Demographic and health survey*. Republic of Kenya, 1998.
16 **Parkin J**, Hey E, Clowes J. Rapid assessment of gestational age at birth. *Arch Dis Child* 1976;**51**:259–63.
17 **Bloland P**, Slutsker L, Steketee R, *et al*. Rates and risk factors for mortality during the first two years of life in rural Malawi. *Am J Trop Med Hyg* 1996;**55**:82–6.
18 **Spira R**, Lepage P, Mesellati P, *et al*. Natural history of human immunodeficiency virus type 1 infection in children: a five year prospective study in Rwanda. *Pediatrics* 1999;**104**:e56–63.
19 **Duke T**, Michael A, Mgone J, *et al*. Etiology of child mortality in Goroka, Papua New Guinea: a prospective two-year study. *Bull World Health Organ* 2002;**80**:16–25.
20 **Duke T**, Willie L, Mgone J. The effect of introduction of minimal standards of neonatal care on in-hospital mortality. *Papua New Guinea Medical Journal* 2000;**43**:127–36.
21 **Daoud A**, Abuekteish F, Obeidat A, *et al*. The changing face of neonatal septicaemia. *Ann Trop Paediatr* 1995;**15**:93–6.
22 **Omene J**. Neonatal septicaemia in Benin City, Nigeria. *Trop Goegr Med* 1978(March):35–9.
23 **Fischer G**, Ottolini M, Mond J. Prospects for vaccines during pregnancy and in the newborn period. *Clin Perinatol* 1997;**24**:231–50.
24 **Brair M**, Brabin B, Milligan P, *et al*. Reduced antibody transfer of tetanus antibodies with placental malaria. *Lancet* 1994;**343**:208–9.
25 **George S**, Latham M, Abel R, *et al*. Evaluation of effectiveness of good growth monitoring in south Indian villages. *Lancet* 1993;**342**:348–52.
26 **Bang A**, Bang R, Baitule S, *et al*. Effect of home based care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999;**354**:1955–61.
27 **Taha T**, Gray R, Abdelwahab M. Determinants of neonatal mortality in central Sudan. *Ann Trop Paediatr* 1993;**13**:359–64.