Causes of early neonatal respiratory distress in the former Venda — a community-based study

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Objective. To determine in a rural black population the incidence of common forms of respiratory distress (RD) and low birth weight (LBW), the mortality from RD and the perinatal mortality rate (PMR).

Design. A prospective study in a context in which about 90% of the community's births take place within the health service and unwell neonates are transferred to hospital.

Setting. The Donald Fraser health ward, Northern Province (then Venda), which serves a population of about 180 000 through 21 clinics and health centres and a 450-bed hospital.

Subjects. 7 539 infants born alive between 1 February 1992 and 31 January 1993, of whom 48 developed RD.

Outcome measures. Hjalmarson's classification of RD, modified for local conditions. Criteria depended on clinical signs, chest radiography, neutrophil count in blood and gastric aspirate, blood cultures and postmortem examination.

Results. RD 6.4/1 000 livebirths (95% CI 4.6 - 8.2); infection 2.6/1 000 livebirths (95% CI 1.4 - 3.7); hyaline membrane disease (HMD) 0.9/1 000 livebirths (95% CI 0.2 - 1.6); pulmonary maladaptation (transient tachypnoea) 0.8/1 000 livebirths (95% CI 0.2 - 1.4); mortality from RD 2.1/1 000 livebirths (95% CI 1.1 - 3.2); incidence of LBW 7.9% (95% CI 7.3 - 8.5); PMR 19.8/1 000 livebirths (95% CI 17 - 23).

Conclusion. A strikingly low incidence of neonatal RD in general and of HMD in particular was found in a rural black population, probably related to a low LBW incidence. Infection was the commonest cause of RD.

S Afr Med J 1996; **86:** 1413-1416.

Respiratory diseases are a major cause of neonatal morbidity and mortality.[1] The commonest causes of respiratory distress in the newborn in Western Europe among predominantly white populations are hyaline membrane disease (HMD), transient tachypnoea (also called

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wet lung syndrome or respiratory distress syndrome type 2), meconium aspiration syndrome and congenital pneumonia.[1] Of these, HMD is the most important, occurring in 0.5 - 1.0% of all deliveries.[1] Among black neonates, a high incidence of respiratory disease might be expected since prematurity is their commonest problem.[2,3] Quantitative information is scanty and usually hospital-based. Of eight studies obtained through Medline, only two were community-based.[4,5] None was of an entirely black rural population.

This study of neonatal respiratory distress was carried out in the Donald Fraser health ward (DFHW), which is situated in what was then the independent homeland of Venda in the north-east corner of South Africa adjoining the Kruger National Park. This health ward serves a population of approximately 180 000 black people with a population growth rate of 2.7%.[6]

Nineteen clinics, one health care centre and one maternity centre provide primary care. A 450-bed hospital provides primary and secondary care. The only referral hospital for tertiary care is 450 km away at Ga-Rankuwa.

The aims of the study were to determine: (*i*) the incidence of common forms of respiratory distress in neonates; (*ii*) the mortality rate from respiratory distress; (*iii*) the low-birth-weight incidence; and (*iv*) the perinatal mortality rate.

Three features of the health service favoured the study design. Firstly, the average distance from home to the nearest health facility for a Venda citizen is 3.6 km.[6] Secondly, all low-birth-weight and ill infants delivered at the clinics are transferred to the hospital.

Thirdly, a very high proportion of infants born in the health ward are delivered at the health ward facilities. In 1982 3.5% of deliveries in the DFHW took place at home.[7] In 1988 5% of deliveries took place at home, 87% at health ward facilities, 3% in another health ward in Venda and 5% outside Venda (D. M. Schoor, N. D. Carlier, M. E. Edginton — unpublished observations). In 1993 about 96% of deliveries took place in health service facilities (A. C. Hereward — unpublished observations).

Method

All infants born between 1 February 1992 and 31 January 1993 in the facilities of the DFHW, including those born before arrival, who developed respiratory distress in the first 24 hours of life were studied.

Respiratory distress is defined as tachypnoea with one of the following: central cyanosis, grunting, nasal flaring, or subcostal or intercostal retractions.[1] Tachypnoea in the newborn is defined as a respiratory rate persistently greater than 60/min.[8,9] Hjalmarson's classification used procedures commonly used in neonatal wards, but in the Donald Fraser Hospital C-reactive protein, micro-analysis of blood and oxygen need could not be measured. Culturing was limited to aerobic bacteria only. Hjalmarson's classification was therefore adapted as follows.

Pulmonary maladaptation, i.e. transient tachypnoea, respiratory distress syndrome type 2 and wet lung syndrome. These infants have non-infectious respiratory disorders and pathological chest radiographs, and improve clinically during the first day of life.

Extreme prematurity. Immature infants below 28 weeks of gestation who die within a few hours of birth. Chest radiographs are normal and there is no evidence of infection.

HMD. Infants of at least 26 weeks' gestation who develop respiratory distress during the first day of life. Chest radiographs show reduced air content, variably prominent air bronchograms and a characteristic reticulogranular pattern (which is also characteristic of group B streptococcal pneumonia but which can be excluded by blood culture).[9]

Infection. Infants with positive blood cultures or chest radiographs that indicate infection (often unilateral coarse mottling[8] and sometimes air brochograms), or with at least either positive clinical findings or a positive maternal history and either an abnormal gastric aspirate or an abnormal white cell count. Positive clinical findings are an enlarged liver or spleen, skin petechiae or blisters, or a positive rapid plasma reagin (RPR) test. A positive maternal history features intrapartum fever above 37.5°C, rupture of membranes for more than 18 hours, or a fetal heart rate above 180/min. An abnormal gastric aspirate has more than 5 neutrophils per high-power field on microscopy.[8] An abnormal white blood cell count is below 5 x 10^9/l or above 30 x 10^9/l.

Meconium aspiration. Infants who have meconium in amniotic fluid and gastric aspiration. Chest radiographs show bilateral, massive, patchy infiltrates and coarse streaking of both lung fields, increased anteroposterior diameter, and flattening of the diaphragm.[10,11]

Miscellaneous conditions. Infants with respiratory distress not classifiable as above. This group includes those infants with congenital abnormalities, hypoglycaemia and asphyxia. Hypoglycaemia is defined as a blood sugar concentration below 1.4 mmol/l,[12] or below 2.2 mmol/l if symptoms disappear after administration of glucose.[8,12]

Every day one of the hospital's doctors (usually P.v.R.) inspected the neonatal ward for infants with respiratory problems. For the rest of the 24 hours, identification and reporting depended on the nursing staff, who received extra training in the identification of respiratory problems.

A maternal and obstetric history was taken. Physical examination was performed, and the rectal temperature recorded. The infants' gestational age was assessed by Dubowitz score. The following investigations were performed: chest radiograph, blood culture, RPR test, blood glucose measurement using Dextrostix with a glucometer, gastric aspirate assessment for the presence of meconium, and neutrophil count. Laboratory confirmation of low blood glucose readings was obtained.

Chest radiographs were reported on by two paediatricians who were provided with the other findings. When infants died before this full assessment could be undertaken, consent was requested for postmortem examination. Lung specimens were examined by the Department of Pathology, Medical University of Southern Africa. Dr J. B. Ellis, the late Head of the Department of Neonatology at MEDUNSA, helped to finalise classification.

All infants with respiratory distress received benzylpenicillin 50 000 U/kg/day and gentamicin 5 mg/kg/day in 12-hourly doses, started after blood culture specimens had been taken. Further supportive treatment was given, but equipment for ventilation was not available. Ninety-five per cent confidence intervals appear in brackets after estimates. Epi-Info[13] was used for calculation of odds ratios and their confidence intervals and Confidence Interval Analysis[14] for the confidence intervals of proportions.

The project was approved by the Research Ethics and Publications Committee of MEDUNSA.

Results

During the study period there were 7 539 livebirths. The mean time in which respiratory distress manifested itself was 8 hours after birth with a range of 1 - 20 hours. Forty-eight infants with respiratory distress were identified, of whom 16 died (33%). Two infants died before full assessment, but postmortem examination was performed on both. The assessments of the other 46 infants were complete.

There were 594 low-birth-weight infants, 101 stillbirths and 48 early postnatal deaths. The incidence of respiratory distress was 6.4 per 1 000 livebirths (range 4.6 - 8.2). The respiratory distress mortality rate was 2.1 per 1 000 livebirths (range 1.1 - 3.2). The incidence of low birth weight was 7.9% (range 7.3 - 8.5). The perinatal mortality rate was 19.8 per 1 000 livebirths (range 17 - 23).

The frequency of respiratory distress syndromes (Table I)

Pulmonary maladaptation (12.5%). Five infants had abnormal chest radiographs, no signs of infection, and recovered within the first day of life. One, with a normal chest radiograph, had meconium in the liquor and gastric aspirate but recovered within 12 hours.

Table I. Frequency of causes of respiratory distress

Cause	Frequency	%
Pulmonary maladaptation	6	12.5
HMD	7	14.6
Infection	20	41.7
Meconium aspiration	5	10.4
Miscellaneous		
Hypoglycaemia	3	6.3
Congenital abnormality	2	4.2
Hypothermia	1	2.1
Anaemia (hypovolaemia)	1	2.1
Asphyxia	1	2.1
Extreme prematurity	0	
Unclassified	2	4.2
Total	48	100.2

HMD (14.6%). All 7 chest radiographs were diagnostic. The mean gestational age of these infants was 30 weeks (range 28.3 - 32.4 weeks). All infants in this group died.

Infection (41.7%). There were 10 infants with pneumonia; in 9 this was diagnosed by chest radiograph and in 1 at postmortem examination. There were 4 infants with proven septicaemia (*Klebsiella, Acinobacter calcoaceticum, Streptococcus epidermis*, streptococcus group B) and one of these 4 had a reticular pattern on chest radiograph but was classified by positive blood culture for streptococcus group B. Six infants had other evidence of infection; 2 had abnormal neutrophil counts (4.1 and 38 x 10^9/l) and gastric aspirate neutrophil counts above 100/high-power field (HPF); 3 had mothers with chorio-amnionitis, abnormal gastric aspirate neutrophil counts and 2 of these 3 had skin petechiae and blisters; 1 had only an abnormal gastric aspirate neutrophil count of more than 300/HPF. All 20 infants with pneumonia, septicaemia or other evidence of infection showed signs of respiratory distress for more than 48 hours. None showed signs of congenital syphilis. All RPR tests were negative. Eight infants died (42%).

Meconium aspiration (10.4%). All 5 infants had meconium in liquor and gastric aspirate, and massive patches on chest radiograph. All were above 39 weeks' gestation. All recovered.

Miscellaneous (16.8%). Three infants were hypoglycaemic with blood sugar levels of 0.9, 1.9 and 1.9 mmol/l respectively; all 3 responded to intravenous glucose. Two had congenital abnormalities; 1 of them, with bradycardia and an enlarged heart, died soon after birth; the other had reduced muscle tone, wide skull sutures and poor ossification of the bones on the chest radiograph suggestive of osteogenesis imperfecta. One infant was hypothermic (35°C) and recovered in the incubator within 8 hours. One infant was anaemic (haemoglobin concentration 9.4 g/dl, haematocrit 30.4%) and, in view of the haemotocrit reading, may have been hypovolaemic. This infant responded well to blood transfusion. One had an Apgar score of 4 after 5 minutes at the clinic and came into the hospital with opisthotonos, fitting and an absent Moro reflex. Lumbar puncture showed predominantly red cells. A diagnosis of asphyxia was made.

Extreme prematurity. No infant was classified in this group.

Unclassified (4.2%). Two infants had normal chest radiographs, no signs of infection and recovered within 24 hours. One of them was the second of twins. Meconium aspiration and pulmonary maladaptation occurred only among infants ⩾ 2 500 g birth weight (Table II). HMD occurred only among infants < 2 500 g birth weight. Infection was strongly associated with low birth weight (OR 17.9 (6.8 - 48)). The only normal-birth-weight infant who died had a congenital cardiac abnormality.

Table II. Comparison of the incidence of RD syndromes among low-birth-weight infants and normal-birth-weight infants

	Weight < 2 500 g (*N* = 594)		Weight ⩾ 2 500 g (*N* = 6 945)	
Cause	No.	Incidence*	No.	Incidence†
PMA	0	—	6	0.9
HMD	7	11.8	0	—
Infection	12	20.2	8	1.2
Meconium aspiration	0	—	5	0.7
Miscellaneous	4	6.7	4	0.6
Unknown	2	3.4	0	—
All causes	25	42.0	23	3.2

* per 1 000 low-birth-weight infants.
† per 1 000 infants weighing 2 500 g and above.
PMA = pulmonary maladaptation.

Discussion

Strengths of the study were that it was prospective and used predefined criteria for classification. The validity of its claim to be community-based depends on a delivery rate within health service facilities of between 87% and 96%. The study was handicapped by limited diagnostic, postmortem and X-ray facilities. Over-penetration (2 radiographs) and rotation (4 radiographs) made radiological diagnoses difficult in 3 infants.

Table III compares the results of the study with those of the community-based studies of Hjalmarson[4] and Field *et al.*[5] Hjalmarson[4] reported an average incidence of respiratory distress for the different participating hospitals of 29 per 1 000 livebirths (range 12 - 40); Field *et al.*[5] reported 20.8. In comparison the study's figure of 6.4 is low. These differences are only partly accounted for by the differences in the incidence of HMD.

Table III. Comparison of the incidence per 1 000 livebirths of causes of respiratory distress with other community-based studies (95% confidence intervals)

Cause	This study (African) (*N* = 7 539)	Field *et al.* (English)[5] (*N* = 7 557)	Hjalmarson (Swedish)[4] (*N* = 32 281)
PMA	0.8 (0.2 - 1.4)	3.6 (2.2 - 4.9)	9.3 (8.2 - 10.3)
Extreme prematurity	0.0	1.6 (0.6 - 2.5)	0.4 (0.1 - 0.5)
HMD	0.9 (0.2 - 1.6)	9.6 (7.5 - 11.9)	3.3 (2.6 - 3.9)
Infection	2.6 (1.4 - 3.7)	0.5 (0.01 - 1.1)	1.7 (1.3 - 2.2)
Meconium aspiration	0.7 (0.1 - 1.8)	0.5 (0.01 - 1.1)	0.9 (0.5 - 1.2)
Miscellaneous	1.1 (0.3 - 1.8)	2.6 (1.4 - 3.6)	2.4 (1.9 - 2.9)
Unclassified	0.4	—	0.1
All causes	6.4 (4.6 - 8.2)	20.8 (17.7 - 24.1)	29.0 (27.0 - 30.7)

PMA = pulmonary maladaptation.

The incidence of pulmonary maladaptation was also low in comparison. This may be because the definition of respiratory distress used excluded milder forms, which are likely to be subclassified as pulmonary maladaptation.

The incidence of HMD was 0.9/1 000 livebirths. This is 3.6 times (1.7 - 7.7) lower than that reported by Hjalmarson[4] and 10.4 times (4.8 - 22.6) lower than the findings of Field *et al.*[5] It is unlikely that infants with HMD were missed, because the distress it causes is severe.

Field *et al.*[5] reported 22% of infants with HMD to be of > 33 weeks' gestation; Hjalmarson[4] reported a proportion of 56%. In the study there were none > 33 weeks' gestation. We think this is the main reason for the low incidence of HMD. In infants < 33 weeks, De Wilde[15] found an incidence of 6.8/1 000 livebirths in the DFHW in 1993. Because of lack of facilities for ventilation of the newborn the general policy at the hospital is to 'keep the baby *in utero*' until matured. Such conservative management of complicated pregnancies tends to lower the incidence of prematurity. In Hjalmarson's study the incidence of infants < 33 weeks' gestation was 10/1 000 livebirths.

At least 95% of infants < 33 weeks weigh < 2 500 g. If De Wilde's incidence is applied to the 594 low-birth-weight infants in the study we arrive at an approximately 13.7% incidence of HMD among infants < 33 weeks. This corresponds with Hjalmarson's proportion of 13.9% and reassures us that misclassification of premature infants is not a reason for the low incidence of HMD found.

The absence of infants with extreme prematurity may have been because women with pregnancies < 26 weeks in whom abortion was anticipated were delivered in a surgical ward. Given the distance to ventilation and incubation in the maternity ward, the tachypnoea of respiratory distress may not have developed because of respiratory weakness; deaths would have been due to hypothermia and recurrent apnoea.[16]

The low-birth-weight rate of 7.9% that was found concurs with a rate of 8.4% (7.9 - 9.2) in the DFHW in 1993.[14] Stein and Ellis[17] found a rate of 19.5% in Johannesburg. Belizán *et al.*[18] and the World Health Organisation[19] reported rates between 16% and 19% in other African studies. The low rate may partly explain why the incidence of respiratory distress was low.

The incidence of infection was 5.0 times (1.7 - 14.7) higher than that found by Field *et al.*,[5] but not significantly higher than Hjalmarson's figure.[4] Blood cultures were performed on all children in the study. The descriptions of culture protocols in the other studies were insufficient to allow comparison.

Conclusion

The community-based study showed a strikingly low incidence of neonatal respiratory distress in general and of HMD in particular among a rural black population, probably related to a low low-birth-weight incidence (which is closely linked to prematurity) in the same community. Infection was the commonest cause of respiratory distress.

We are indebted to the late Dr J. B. Ellis for his advice and support; to him and Dr P. Gwamanda for reporting on radiographs; and to Professors A. F. Malan and D. L. Woods for much helpful comment on the MS. We wish to thank the many nurses, radiographers and laboratory workers of Donald Fraser Hospital, upon whom so much depended and who made the study possible.

This research comprised P. van Rijswijk's dissertation for the M.Fam.Med. degree at the Medical University of Southern Africa.

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Accepted 4 June 1996.