Use of simple clinical signs to predict pneumonia in young Gambian children: the influence of malnutrition

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The current WHO recommendations for the case management of acute respiratory infections (ARI) in children aged 2 months to 5 years in developing countries use fast breathing (respiratory rate of ≥50 per minute in children under 12 months and ≥40 in children aged 12 months to 5 years) and lower chest wall indrawing to determine which child is likely to have pneumonia and should therefore receive antibiotics. We have evaluated these and other physical signs in 487 malnourished children and 255 well nourished children who presented with a cough or breathing difficulty. Pneumonia, defined as definite radiological pneumonia or probable radiological pneumonia associated with crackles on auscultation, was present in 145 (30%) of the malnourished children and 68 (26%) of the well nourished children. The respiratory rate predicted pneumonia equally well in the two groups, but to achieve an appropriate sensitivity and specificity the respiratory rate cut-off required in malnourished children was approximately 5 breaths per minute less than that in well nourished children. Intercostal indrawing was more common and lower chest wall indrawing was less common in the malnourished children, with or without pneumonia. These results suggest that fast breathing, as defined at present by WHO, and lower chest wall indrawing are not sufficiently sensitive as predictors of pneumonia in malnourished children. As the latter are a high-risk group, we should like to recommend that children with malnutrition who present with a cough, fast breathing or difficult breathing should be treated with antibiotics.

Introduction

Acute respiratory infections (ARI) are estimated to be responsible for about 4 million childhood deaths per year, most of them in developing countries (*1*). Malnutrition is common in most developing countries, and it has been shown to increase both the frequency and severity of ARI episodes (*2*). Indeed, malnutrition is an important determinant of mortality due to ARI (*3*).

The current WHO strategy for the control of mortality due to ARI relies heavily on standardized case management using simple clinical signs which have been shown to predict pneumonia.[a] Several studies have shown that fast breathing and lower chest wall indrawing are the best predictors of pneumonia in children with a cough or breathing difficulty (*4–7*). However, these are signs which indicate the greater workload of breathing for a young child with pneumonia and it is possible that malnourished children may not have the strength to manifest some of these physical signs in the same manner as well nourished children. The study described below was designed to evaluate the power of various widely used clinical signs as predictors of pneumonia in children presenting for the first time with malnutrition and respiratory symptoms, and to compare this with the predictive power of the same signs in well nourished children presenting with cough or breathing difficulty.

Patients and methods

The study was carried out in the outpatient department of the Medical Research Council (MRC) Hospital at Fajara in the Gambia. This clinic serves a large, predominantly urban population located about 15 km from Banjul, the capital. During the period from November 1990 to March 1992, all children aged 3 months to 5 years who arrived at the clinic for whatever reason were screened for malnutrition by being weighed and examined for oedema. All the children whose weight was less than 70% of the United States National Center for Health Statistics (NCHS) mean or who had oedema were referred to

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the study physician (AGF) for possible inclusion in the study. From April to November 1992 all children who presented at the same clinic with clinically evident malnutrition were referred directly to the study physician by the nurse in charge of the outpatient department. Children with oedema underwent urinalysis and those with the nephrotic syndrome or acute nephritis were excluded. Children who had already undergone treatment for malnutrition were also excluded. All the children underwent a full history and examination and had a chest radiograph taken. Only children whose parents stated, in response to questioning, that their children had a cough, fast breathing, breathing difficulty or chest pain were included in the analysis.

During the same period, children in the same age group who presented at the MRC Hospital with a cough or breathing difficulty and who were not malnourished, were recruited into a parallel study. On a specified day, usually once every two weeks, the first seven eligible children presenting were enrolled. They were assessed clinically using the same format as that used for the malnourished children. All the children with any auscultatory findings or fast breathing (defined as a respiratory rate of ≥50 per minute in children under 12 months and ≥40 in children aged 12 months to 5 years), and 10% of the children without these findings had a chest radiograph taken.

Respiratory rate was measured by observation of the child's chest for exactly one minute with the child either asleep, awake and quiet, or while breastfeeding. If this was interrupted by coughing the measurement was started again. Chest wall indrawing was classified as suprasternal (indrawing of the soft tissues above the clavicles and sternum with inspiration), intercostal (indrawing of the intercostal tissues with inspiration), and lower chest wall (indrawing of the bony structures of the lower chest wall with inspiration).

All chest radiographs were read in a blinded manner by a paediatric radiologist (HT), according to a format devised by the WHO/ARI Programme Radiology Working Group. Those with definite radiological consolidation were classified as having pneumonia. In addition, those with radiographs compatible with pneumonia who had crackles on auscultation were also classified as having pneumonia.

Categorical variables were compared using the chi-squared or Fisher's exact tests, as appropriate. Continuous variables were compared using the Wilcoxon rank sum test. The durations of the various symptoms and the ages were expressed as medians and interquartile ranges because the data were skewed and not well described by the ranges. Free and informed verbal consent was obtained from the parent or guardian of each child enrolled in the study, which was approved by the Gambian Government/Medical Research Council Ethical Committee.

Results

During the study period over 8000 children were screened for malnutrition; 574 were found to be malnourished and 487 of them had respiratory symptoms and were included in the analysis, of whom 145 (30%) had pneumonia as defined above. Nine (10%) of the 87 malnourished children who did not have any respiratory symptoms on presentation had pneumonia; 255 well nourished children with cough or breathing difficulty were enrolled, of whom 68 (26%) had pneumonia. There was no significant difference in age between the malnourished and well nourished children (median ages: 14 (interquartile range, 9–21) months and 13 (interquartile range, 8–21) months, respectively). Malnourished children with pneumonia were older than the well nourished children with pneumonia (median ages: 16 (interquartile range, 11–22) months and 12 (interquartile range 8–21) months, respectively; $P = 0.053$). The nutritional status of the children studied is depicted in Fig. 1.

The main symptoms on presentation are summarized in Table 1. Among the malnourished children, a history of cough, fast breathing or difficult breathing was associated significantly with the presence of pneumonia ($P < 0.001$ for each), while among the well nourished children this effect was less marked, being significant for difficult breathing only. A history of difficult breathing was found more

Fig. 1. **The nutritional state of children recruited into the study, expressed as a percent of the NCHS mean weight-for-age.** Malnourished children >70% WFA had kwashiorkor.

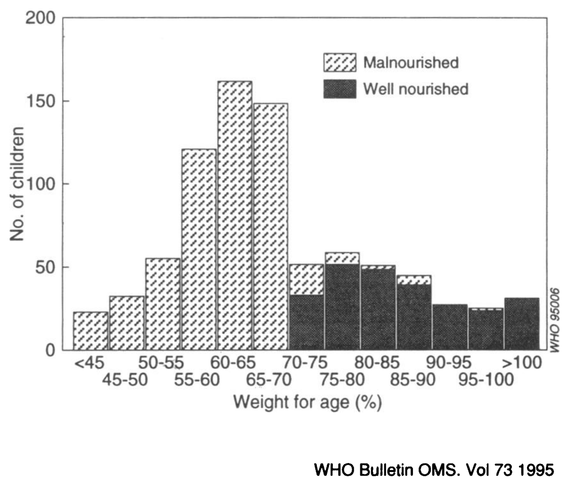


Table 1: **Presenting symptoms for malnourished and well nourished children, with or without pneumonia**

	Well nourished		Malnourished	
	No pneumonia (col. 1)	Pneumonia (col. 2)	No pneumonia (col. 3)	Pneumonia (col. 4)
Cough	183/187 (98)[a]	67/68 (99)	292/342 (85)	140/145 (97) *P* <0.001 vs col. 3
Duration[b]	3/3–5	3/3–5	5/3–7[c]	5/3–8[c]
Fast breathing	99/187 (53)	44/68 (65)	165/342 (48)	90/145 (62) *P* <0.01 vs col. 3
Duration[b]	3/2–4	3/2–4	4/3–7[c]	5/3–7[c]
Difficult breathing	87/187 (47)	47/68 (69) *P* <0.01 vs col. 1	141/342 (41)	79/145 (55) *P* <0.01 vs col. 3
Duration[b]	3/2–4	3/2–4	4/3–7[c]	4/3–7[c]
Fever	177/187 (95)	67/68 (99)	316/342 (92)	139/145 (96)
Duration[b]	3/3–4	3/3–5	5/3–7[c]	5/3–10[c]
Vomiting	90/187 (48)	43/68 (63) *P* <0.05 vs col. 1	215/342 (63) *P* <0.01 vs col. 1	91/145 (63)
Duration[b]	3/2–4	3/2–4	5/3–7[c]	5/3–7[c]
Diarrhoea	78/187 (42)	32/68 (47)	214/342 (63) P <0.001 vs col. 1	66/145 (46) P <0.001 vs col. 3
Duration[b]	3/3–4	3/3–4	5/3–7[c]	5/3–7[c]

[a] Figures in parentheses are percentages.
[b] Days: median/interquartile range.
[c] For the duration of each symptom, comparison of columns 1 & 3 and columns 2 & 4 was significant at *P* <0.001.

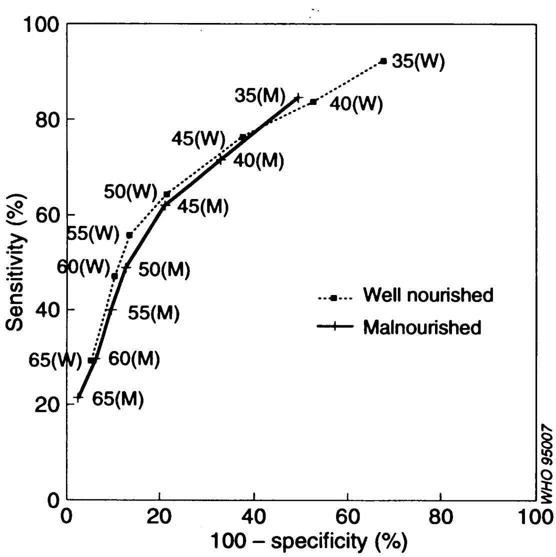
frequently in well nourished children with pneumonia than in malnourished children with pneumonia (*P* <0.05). There was a history of fever in over 90% of children in all groups. The duration of all symptoms was significantly longer in malnourished children, with or without pneumonia, than in well nourished children with or without pneumonia (*P* <0.001). However, in both groups the duration of all symptoms was not significantly different between those with pneumonia and those without.

Thirty-five percent of the malnourished children and 29% of the well nourished children had been weaned when they were seen. The symptom of reduced drinking differentiated pneumonia from no pneumonia in the well nourished group (40% vs 24% respectively; *P* <0.05), but not in the malnourished group (24% vs 22%). The Gambia Government Health Care Card was reviewed in 90% of malnourished and 93% of well nourished children. Vaccination was up to date in 60% of well nourished children and in 62% of malnourished children whose cards were seen. Measles vaccine, which normally is given at 9 months of age in the Gambia, had been received by 56% and 59% of well nourished children with and without pneumonia respectively, and by 75% and 62% (*P* <0.01) of malnourished children with and without pneumonia.

In both groups of children, the mean respiratory rate was significantly higher in children with pneumonia than in those without, but the rates were lower in malnourished children (pneumonia vs no pneumonia, 51.3 vs 37.0, *P* <0.001) than in well nourished children (58.0 vs 41.7; *P* <0.001). Thus, compared with well nourished children, malnourished children with and without pneumonia had lower respiratory rates (*P* <0.01 and *P* <0.001, respectively). As a predictor of pneumonia, fast breathing, as defined by WHO's ARI case management guidelines (respiratory rate ≥50 for children under 12 months, and ≥40 for children aged 12 months to 5 years) had sensitivities of 61% and 79%, and specificities of 79% and 65% in malnourished and well nourished children, respectively. To determine whether the power of respiratory rate to predict pneumonia was affected by malnutrition, Receiver–Operator Characteristic (ROC) curves were drawn for the two nutritional groups (Fig. 2). These curves plot the sensitivity against the specificity for various values of the continuous variable being assessed (respiratory rate). The area under the curves represents the predictive power of that variable. While the areas under the curve are similar for the two groups, the curve for malnourished children is rotated anticlockwise so that, for given values of sensitivity and specificity, the required respiratory rate for malnourished children is about 5 breaths per minute less than that for well nourished children.

The other physical signs evaluated are summarized in Table 2. Intercostal chest wall indrawing was

Fig. 2. **Receiver–Operator Characteristic (ROC) curves showing the sensitivity and specificity of respiratory rate as a predictor of pneumonia in malnourished (M) and well nourished (W) children.**



more frequent in malnourished children and was a significant predictor of pneumonia in that group. On the other hand, lower chest wall indrawing was less common in malnourished children. Thirty-two well nourished children without pneumonia had lower chest wall indrawing, of whom 16 had wheezing; of the other 16, 10 had other types of indrawing and 8 had a respiratory rate >50. Flaring of the ala nasae and grunting were specific, but relatively insensitive signs of pneumonia in both groups. Wheezing, tonsillitis, and otitis media were all more common in the well nourished group.

Discussion

The aim of this study was to compare the relative ability of simple physical signs to predict pneumonia in well nourished and malnourished children. Malnourished children can present with a variety of symptoms, but 85% of them in this study had a cough, breathing difficulty or chest problem among their symptoms. Of these, 30% were found to have pneumonia.

By conducting parallel studies of malnourished and well nourished children with symptoms of ARI we were able to calculate the relative frequency of different symptoms and signs in the two groups and to compare the predictive power of the more common symptoms and signs as predictors of pneumonia. History of cough, fast breathing and difficult breathing were better indicators of pneumonia in malnourished children than well nourished children. Vomiting and diarrhoea were more common in the

Table 2: **Physical signs found in malnourished and well nourished children with and without pneumonia**

	Well nourished		Malnourished	
	No pneumonia (col. 1)	Pneumonia (col. 2)	No pneumonia (col. 3)	Pneumonia (col. 4)
Fast breathing[a]	66/187 (35)[b]	53/67 (79)[c]	72/341 (21)[d]	89/145 (61)[c]
Temperature ≥38 °C	40/187 (21)	39/68 (57)[c]	72/342 (21)	70/145 (48)[c]
Suprasternal indrawing	19/187 (10)	15/67 (22)	30/341 (9)	35/145 (24)[c]
Intercostal indrawing	59/187 (32)	32/67 (48)	151/341 (44)[d]	103/145 (71)[c,d]
Lower chest wall indrawing	32/187 (17)	18/67 (27)	8/341 (2)[d]	25/145 (17)[c]
Flaring of alar nasae	12/187 (6)	13/67 (19)[c]	7/341 (2)	28/145 (19)[c]
Grunting	4/187 (2)	8/68 (12)[c]	5/342 (2)	18/145 (12)[c]
Observed cough	73/187 (39)	33/68 (49)	106/341 (31)	82/145 (57)[c]
Bronchial breathing	2/187 (1)	11/68 (16)[c]	5/342 (2)	26/145 (18)[c]
Wheeze	42/187 (23)	17/68 (25)	8/342 (2)[d]	6/145 (4)[c]
Hepatomegali >2 cm	53/186 (29)	29/67 (43)	83/337 (25)	60/144 (42)[c]
Otitis media	64/169 (38)	27/63 (43)	81/303 (27)	38/126 (30)
Tonsillitis or pharyngitis	21/186 (11)	7/66 (11)	5/339 (2)[d]	5/144 (4)
Poor feeding (observed)	11/175 (6)	12/66 (18)[c]	29/335 (9)	18/143 (13)

[a] Respiratory rate ≥50 if under 12 months of age and ≥40 if aged 12 months to 5 years.
[b] Figures in parentheses are percentages.
[c] Significant at $P < 0.01$ level when compared with the corresponding "no pneumonia" group.
[d] Significant at $P < 0.01$ level when compared with the corresponding "well nourished" group.

malnourished children with or without pneumonia, as these are common presenting symptoms for children with malnutrition. It is usual in the Gambia for parents to report fever in their children as was the case in this study. Thus, history of fever is not a useful finding in this community. The durations of all symptoms were significantly longer in the malnourished children since signs of clinical malnutrition represent the end state of a long period of ill-health, usually complicated by intercurrent infections.

The physical signs that predict pneumonia have been examined in a number of studies, and fast breathing and chest wall indrawing have emerged as the simple signs which best predict pneumonia (*4–7*). Each of these studies used different definitions of pneumonia, yet the conclusions drawn were similar. Radiology alone is the most objective definition of pneumonia, but many severe cases of pneumonia, particularly those associated with malnutrition, may present with vague and inconclusive radiological features (*8*). To take into account this problem we included in our pneumonia category children with abnormal radiographs which did not constitute definite radiological pneumonia, but who had crackles on auscultation. Even with this broader definition of pneumonia, there were 16 well nourished children with lower chest wall indrawing who did not have pneumonia. Of those who did not have wheezing, which is known to produce chest wall indrawing, half had fast breathing suggesting that they probably did have a significant lower respiratory tract infection, but our pneumonia definition failed to include them.

Based on the studies referred to above, fast breathing and chest wall indrawing have become the basis of the ARI case management strategy currently promoted by WHO for control of ARI-related mortality in developing countries. Malnutrition is an important cofactor in ARI mortality, yet none of the previous studies of the clinical signs predicting pneumonia examined the effect of nutritional status on these signs. In the present study we found that while fast breathing predicts the presence of pneumonia equally well in malnourished and well nourished children, the breathing rate required for a given sensitivity and specificity is about 5 breaths per minute lower in children with malnutrition. This finding could reflect ascertainment bias since all malnourished children had chest radiographs performed while only those well nourished children with some sign of pneumonia and 10% of the remainder had chest radiographs taken. In fact, only 82 of the 255 well nourished children studied did not have an indication for chest radiograph, of whom 8 were randomized to be X-rayed according to the protocol. None of the 8 were subsequently classified as having pneumonia, suggesting that few pneumonias were missed by this imperfection in the study design. It appears that, with symptoms of ARI, malnourished children do breathe at a slower rate than well nourished children. With the stress of pneumonia their breathing rate increases at a similar rate, but with malnourished children the final level reached is lower. This finding may be related to the lower temperatures found in malnourished children with pneumonia.

Indrawing of the chest wall is a manifestation of reduced lung compliance caused by pneumonic consolidation or airways obstruction. WHO recommends the use of lower chest wall indrawing, defined as an inward movement of the bony structures of the lower chest wall with inspiration, as a sign of pneumonia requiring admission to hospital. Malnourished children with little subcutaneous tissue readily demonstrate indrawing of the intercostal tissues, even in the absence of pneumonia. This is not generally thought to be as useful as lower chest wall indrawing, but in the present study this sign was a useful predictor of pneumonia in malnourished children.

The WHO case management strategy currently recommends that fast breathing (and therefore the need for antibiotics) in children with ARI be defined as ≥50 per minute for children under 12 months and ≥40 for children aged 12 months to 5 years. Our findings support the use of this definition in well nourished children, but suggest that its sensitivity to predict pneumonia in malnourished children is inadequate. This finding is of concern, given that malnourished children are more likely to die of pneumonia. Our data suggest that, if raised respiratory rate and lower chest wall indrawing are to be used to predict pneumonia in malnourished children, the respiratory rate cut-off should be 5 breaths per minute lower than that used for well nourished children. This would improve the sensitivity to 76% (117/154) while the specificity would fall to 66% (276/419), but such an adjustment is likely to be impractical in the field. As the cost of failing to treat pneumonia in a malnourished child may be considerable owing to the high mortality in that group, we should like to recommend that it may be wiser to treat all malnourished children who have a cough or breathing difficulty with antibiotics.

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Résumé

L'utilisation de critères prédictifs cliniques simples pour la pneumonie chez le jeune enfant en Gambie: influence de la malnutrition

Les recommandations OMS actuelles pour la prise en charge des infections respiratoires aiguës (IRA) chez les enfants de 2 mois à 5 ans dans les pays en développement utilisent la respiration rapide (fréquence respiratoire ≥50 par minute chez un enfant de moins de 12 mois, et ≥40 chez un enfant de 12 mois à 5 ans) et le tirage sous-sternal pour déterminer quels sont les enfants susceptibles d'être atteints de pneumonie et qui doivent par conséquent recevoir des antibiotiques. Nous avons évalué ces signes cliniques et d'autres signes chez 487 enfants dénutris et 255 enfants bien nourris atteints de toux ou de difficulté respiratoire. La pneumonie, définie comme pneumonie radiologique franche ou pneumonie radiologique probable associée à des râles crépitants à l'auscultation, a été trouvée chez 145 (30%) des enfants dénutris et 68 (26%) des enfants bien nourris. Des antécédents de toux, de respiration rapide ou de respiration difficile étaient davantage prédictifs de pneumonie chez les enfants dénutris que chez les enfants bien nourris. Les symptômes duraient plus longtemps chez les enfants dénutris. La sensibilité de la respiration rapide comme facteur prédictif de pneumonie chez les enfants des deux groupes était respectivement de 79% chez les enfants bien nourris et 61% chez les enfants dénutris, avec une spécificité respective de 65% et 79%.

Des courbes de sensibilité/spécificité pour diverses valeurs de la fréquence respiratoire ont été tracées pour évaluer la valeur prédictive de ce signe dans les deux groupes d'enfants. Cette valeur prédictive était la même dans les deux groupes, mais pour une sensibilité et une spécificité données, la fréquence respiratoire chez les enfants dénutris était plus faible d'environ 5 respirations par minute que chez les enfants bien nourris. Cela laisse à penser que, par rapport aux enfants bien nourris atteints de pneumonie, les enfants dénutris respirent plus lentement. Ce phénomène peut être dû à la plus faible incidence de la fièvre associée à la pneumonie chez les enfants dénutris (48% contre 57%) ou simplement au fait que la faiblesse des enfants dénutris les empêche de réagir convenablement au stress dû à la pneumonie. Le tirage intercostal était plus fréquent chez les enfants dénutris atteints de pneumonie que chez leurs équivalents bien nourris (71% contre 48%; p <0,01), mais était également plus fréquent chez les enfants dénutris non atteints de pneumonie que chez les enfants bien nourris également non atteints de pneumonie (44% contre 32%; p <0,01). En revanche, le tirage sous-sternal était moins fréquent chez les enfants dénutris atteints de pneumonie (17% contre 27%) ou non (2% contre 17%; p <0,01).

Ces résultats semblent montrer que la respiration rapide, telle qu'elle est actuellement définie par l'OMS, et le tirage sous-sternal ne sont pas suffisamment sensibles comme facteurs prédictifs de pneumonie en présence d'une malnutrition. Comme les enfants dénutris atteints de pneumonie constituent un groupe à haut risque, nous aimerions recommander que les enfants dénutris atteints de toux, de respiration rapide ou de respiration difficile soient traités par antibiotiques.

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