

## Maternal reports of child illness and the biochemical status of the child: the use of morbidity interviews in rural Bangladesh

E. K. Rousham<sup>1\*</sup>, C. A. Northrop-Clewes<sup>2</sup> and P. G. Lunn<sup>3</sup>

<sup>1</sup>Department of Human Sciences, Loughborough University, Loughborough LE11 3TU, UK

<sup>2</sup>School of Biomedical Sciences, University of Ulster at Coleraine, Coleraine BT52 1SA, UK

<sup>3</sup>MRC Dunn Nutrition Unit, Milton Road, Cambridge CB4 1XJ, UK

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In a longitudinal study of child growth and nutritional status in Bangladesh, child morbidity was recorded using health interviews with the mother. The aim of the present study was to establish whether maternal reports of child illness were associated with the biochemical health status of the child. Children aged 2–5 years ( $n$  117) took part in the study and their mothers were interviewed every fortnight by Bangladeshi fieldworkers. Maternal reports of diarrhoea were associated with significantly lower plasma albumin concentrations ( $P < 0.001$ ), poorer intestinal permeability ( $P < 0.001$ ), higher plasma immunoglobulin A levels ( $P < 0.005$ ) and higher  $\alpha$ -1-antichymotrypsin (ACT) levels ( $P < 0.05$ ) compared with children reported to be healthy. Children with fever had significantly higher ACT ( $P < 0.001$ ) and lower albumin ( $P < 0.05$ ) levels compared with their healthy counterparts. Respiratory infections (RI) were not associated with any significant changes; however, reports of RI with fever were associated with significantly higher levels of ACT than either illness individually (interaction  $P < 0.05$ ). These highly significant associations between maternal reports of illness and biochemical profiles of child health support the use of health interviews in developing countries.

### Morbidity interviews: Childhood: Nutritional status

Child morbidity is important in the assessment of health because of the close association between infection and malnutrition. On the one hand, infectious disease may precipitate the onset of malnutrition and, on the other hand, malnourished children are more likely to experience morbidity from infection (Tomkins *et al.* 1989).

Morbidity interviews are often used in conjunction with anthropometry and dietary information in community-based surveys of nutritional status. Morbidity surveys which employ maternal recall, however, have been used with mixed success. The methodological difficulties associated with morbidity surveys in developing countries have been reviewed at length (Kroeger, 1983; Ross & Vaughan, 1986). These include establishing, first, whether maternal reports of illness correspond with a clinically defined illness, and second, whether the reported prevalence of infectious diseases represents the 'true' prevalence rate. Discrepancies between medical examinations and health surveys may occur because the former identify many chronic symptoms which are not commonly self-reported (e.g. malnutrition, parasitic infection, anaemia; Kroeger, 1983). Conversely, individuals who perceive themselves or their children to be ill may not display the set of symptoms required for a

clinical diagnosis of infection. Other confounding factors in morbidity surveys lie in cultural differences in the definitions and interpretations of illness (Martorell *et al.* 1976) and the varying responses of mothers according to the professional status of the interviewer (Ross & Vaughan, 1986).

Simple morbidity surveys do have certain advantages over detailed clinical or epidemiological surveys in that a large sample can be assessed in a short time, at a low cost and without the need for medical staff or equipment (Ross & Vaughan, 1986). However, the value of such surveys depends on demonstrating a significant relationship between the reported information and the health status of the population.

More recently, interest has developed in the effect of mild or sub-clinical infections on the biochemical status of the host; in particular, the use of acute-phase proteins to indicate the immune response to infection, the presence of inflammation, and its extent or severity (Filteau *et al.* 1993, 1995). Filteau *et al.* (1993) observed elevated levels of acute-phase proteins among asymptomatic children, suggesting that sub-clinical infections have a significant effect on the biochemical status of the host. Wasunna *et al.* (1995)

**Abbreviations:** ACT,  $\alpha$ -1-antichymotrypsin; IgA, immunoglobulin A; RI, respiratory infections.

\*Corresponding author: Dr Emily Rousham, fax +44 (0)1509 223940, email e.k.rousam@lboro.ac.uk

suggested that acute-phase proteins may be useful as non-invasive markers for monitoring disease activity, response to therapy and relapse in the case of visceral leishmaniasis. Of the commonly detected acute-phase proteins,  $\alpha$ -1-antichymotrypsin (ACT) has been shown to be the most sensitive and has a superior predictive value compared with other tests of the inflammatory response (Calvin *et al.* 1988). It has the added advantage in community-based surveys that it remains elevated for longer than other acute-phase proteins and is of use when the time of onset of inflammation is unknown (Thompson *et al.* 1992).

Rather than focus on the comparison of morbidity surveys with clinical examinations, the aim of the present paper was to examine the degree of association between maternal reports of child illness and several biochemical indicators of child health.

### Materials and methods

The study was conducted in a poor and remote, rural area of northern Bangladesh. The local population depends on subsistence agriculture with some cash-cropping of jute and sugar cane. The area is subject to seasonal changes in climate and experiences annual flooding during the monsoon. Severe floods are responsible for land erosion, loss of rice crops, damage to property and widespread homelessness. The population is serviced by a non-government maternal and child health centre which records the dates of all births in the region and provides free medical consultation and treatment to children under 15 years of age. Ethical permission for the study was granted by the Ministry of Health of Bangladesh. The study sample was selected using the birth records of the maternal and child health centre. The four villages closest to the health centre were selected to minimize the distance required for study participants to travel on assessment days. Approximately 20% of the total number of children aged 2–5 years were recruited by selecting every fifth child on the records. Parents were invited to let their child participate in a 12-month longitudinal study of growth and nutritional status and were requested to sign or fingerprint a letter of informed consent.

#### Data collection

Biochemical and morbidity data were collected on five assessment days during the study at 2-monthly intervals (April, June, August, October) with the final assessment in February after a slightly longer interval of 4 months. On each assessment day, the mother and child attended the health centre at a pre-arranged time for a duration of 5 h. To ensure that all women and children attended on the correct day, a household visit was made to every subject on the day before assessment requesting their attendance. Assessment days were scheduled when the health centre was closed in order to avoid any confounding effects of women attending in order to seek medical advice and treatment. The study did not provide any medication or treatment to subjects but advised them to return to the health centre on one of the opening days, if necessary.

On the assessment day, each child participated in a test of

intestinal permeability and provided a fingerprick blood sample. No food was eaten during the first 2 h of the test, but after this all children and caregivers were provided with a meal of rice, meat and lentils. During this time, mothers took part in the morbidity interview.

#### Morbidity survey

The caregiver, usually the mother, was interviewed by local field assistants who had received basic training as health workers. On each occasion the mother was asked whether the child was ill on the day of the assessment, or had been ill in the previous 2 weeks. Illnesses were recorded according to the common descriptive terms used by parents rather than medical definitions of infection. For example, fever was referred to as *gor*, a term which has been reported in previous epidemiological studies in Bangladesh (Becker *et al.* 1991). Diarrhoeal diseases were described using three terms; *patla paikhana*, meaning watery stools or diarrhoea; *amasha* meaning dysentery and *rokto amasha* meaning blood dysentery. As the local terms for dysentery and diarrhoea did not correspond with biomedical definitions of these diseases they were included under the same heading. Diarrhoea was generally defined as having three or more loose, watery stools daily. Parents used two terms to describe respiratory infections (RI), which translate as 'cough' and 'pneumonia'. However, the two terms were not clearly differentiated and, furthermore, the number of reports of 'pneumonia' was small. For these reasons, the terms were grouped together as RI. There was no evidence that the respondents were biased in their reporting of information according to the sex of the child (Rousham, 1996).

#### Biochemical survey

Intestinal permeability tests and fingerprick blood samples were collected on each of the five assessment days. Intestinal permeability was assessed through an orally ingested sugar solution of lactulose and mannitol followed by a 5 h urine collection. The differential uptake of these two sugars indicates the function and structural integrity of the gut mucosa. The lactulose : mannitol ratio is used as an index of mucosal integrity (Travis & Menzies, 1992) such that a high value is indicative of impaired gut function.

Subjects were given a solution containing 4 g lactulose and 1 g mannitol made up to 20 ml with drinking water. Total urine volume was measured after the 5 h collection period. Two 1.8 ml portions of urine and a sample of the original dosing solution were frozen at  $-20^{\circ}$ . Urinary lactulose and mannitol were measured by enzymic assay on the Cobas Bio (Roche, Welwyn Garden City, Herts., UK) centrifugal analyser at the Dunn Nutrition Centre, Cambridge (Northrop *et al.* 1990; Lunn & Northrop-Clewes, 1992).

A fingerprick blood sample of approximately 600  $\mu$ l was collected into lithium-heparinized microtainers with separators (Becton-Dickinson, Cowley, Oxford, UK), spun in a battery driven centrifuge and frozen at  $-20^{\circ}$ . Plasma albumin was measured by an immunonephelometric method described by Northrop *et al.* (1987) using the Cobas Bio centrifugal analyser. ACT was measured by a modification

**Table 1.** Frequency of child illnesses reported by mothers in Bangladesh

Illness reported	<i>n</i>	%
Diarrhoea, fever and RI	7	1.3
Diarrhoea and fever	21	4.0
Diarrhoea and RI	1	0.2
Diarrhoea only	25	4.7
Fever only	89	16.7
Fever and RI	13	2.4
RI only	23	4.3
None, 'healthy'	352	66.4
Total	531	100

RI, respiratory infections.

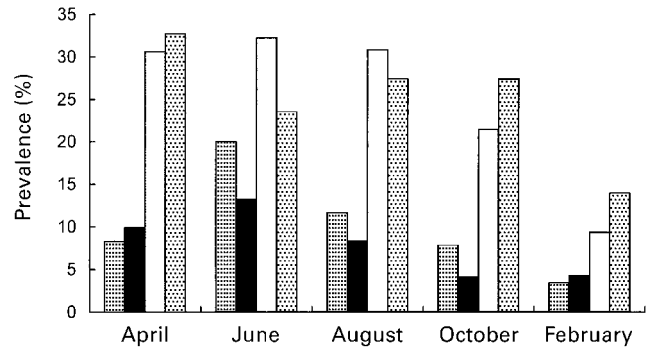
of the immunonephelometric method described by Calvin & Price (1986). Serum immunoglobulin A (IgA) was measured using an immunoturbidimetric method based on that by Dako (High Wycombe, Bucks., UK) for use on the Cobas Bio.

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 6.1 for Windows (SPSS Inc., Chicago, IL, USA). The lactulose : mannitol values were transformed to natural logarithms in order to normalize the distribution. The values were transformed back to the anti-log values after statistical analysis.

## Results

A total of 117 out of 123 children completed the study. Four children withdrew because of relocation outside the study site and two children were withdrawn by their mothers, who did not provide a reason. A total of 531 observations were made on the 117 children who completed the study. Eighty-eight children (75 %) attended all five assessment days with a further twenty-three (20 %) attending four of the five assessment days. The remaining six children (5 %) attended three out of five assessment days. Of the subjects, therefore, 95 % completed four or more of the assessments. Table 1 shows the number of reported episodes of diarrhoea, fever and RI reported either alone or in combination with another illness. Diarrhoea (alone or in combination) was reported on 10 % of observations, fever on 24 % of observations and RI on 8 % of observations.

The biochemical values obtained from the first collection of blood and urine were examined for age-related differences within the study sample. Albumin and ACT levels and intestinal permeability showed no correlation with age. Plasma IgA, which is known to increase with age, was



**Fig. 1.** The reported prevalence of diarrhoea (■), fever (□) and respiratory infections (■) and percentage of children with elevated plasma  $\alpha$ -1-antichymotrypsin levels (▨) on each assessment day.

significantly higher among older children ( $r$  0.24,  $P$  < 0.05,  $n$  117).

### Seasonal variation in biochemical status and infection

Fig. 1 shows the reported prevalence of illness on each of the assessment days, together with the proportion of children with ACT levels greater than the normal range (> 0.6 g/l). The highest proportion of children with elevated ACT levels was observed on the first assessment day (33 %). This measurement coincided with a period of prolonged drought and severe food shortages in the area. The prevalence of illness and elevated ACT levels was also high during the monsoon months (24 % and 27 % in June and August respectively). Although illnesses were less common at the end of the monsoon (October), 27 % of children still had elevated ACT levels. In February, after the favourable months of winter, the prevalence of illness and the proportion of infants with elevated ACT levels was markedly lower (14 %).

Table 2 provides the mean values of biochemical indicators on each of the assessment days for healthy children only. Although the mean values for all cases do not vary substantially, paired  $t$  tests on children who were reported to be healthy on two consecutive assessments showed evidence of seasonal variation in biochemical status. Biochemical status deteriorated significantly between August and October among children who were reported to be healthy on both occasions, for albumin (35.8 v. 34.1 g/l, paired  $t$  2.46,  $P$  = 0.017); IgA (1.25 v. 1.44 g/l, paired  $t$  2.55,  $P$  = 0.014) and lactulose : mannitol (0.25 v. 0.35, paired  $t$  2.94,  $P$  = 0.005). Similarly, there were significant

**Table 2.** Biochemical status of Bangladeshi children on each assessment day (healthy children only)  
(Mean values and standard deviations)

	April ( <i>n</i> 56)		June ( <i>n</i> 59)		August ( <i>n</i> 62)		October ( <i>n</i> 81)		February ( <i>n</i> 100)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Albumin (g/l)	38.2	3.26	36.2	3.56	35.7	2.90	35.7	4.19	39.3	3.09
ACT (g/l)	0.53	0.11	0.49	0.10	0.50	0.11	0.53	0.11	0.49	0.10
IgA (g/l)	1.33	0.59	1.21	0.42	1.28	0.42	1.29	0.58	*	*
L : M	0.25	0.13	0.27	0.12	0.23	0.11	0.31	0.20	0.23	0.13

ACT,  $\alpha$ -1-antichymotrypsin; IgA, immunoglobulin A; L : M, lactulose : mannitol.  
\* Data unavailable due to damage to samples at the analysis stage.

**Table 3.** Biochemical indicators in Bangladeshi children according to illnesses reported by the mothers\*  
(Mean values and 95 % confidence intervals)

Reported illness	Albumin (g/l)		ACT (g/l)		IgA (g/l)		L : M	
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI
Diarrhoea, fever, RI (n 7)	30.79	24.94, 36.65	0.67	0.48, 0.86	1.81	1.04, 2.59	0.30	0.16, 0.57
Diarrhoea + fever (n 21)	34.33	32.88, 35.78	0.60	0.54, 0.66	1.53	1.25, 1.81	0.33	0.26, 0.43
Diarrhoea only (n 25)	33.76	31.28, 36.30	0.56	0.51, 0.61	1.63	1.39, 1.87	0.32	0.24, 0.43
Fever only (n 89)	35.73	34.92, 36.53	0.59	0.56, 0.62	1.44	1.32, 1.56	0.26	0.23, 0.29
Fever and RI (n 13)	36.16	34.22, 38.10	0.72	0.58, 0.85	1.35	1.03, 1.67	0.26	0.18, 0.38
RI only (n 23)	37.68	35.82, 39.54	0.53	0.49, 0.56	1.29	1.08, 1.51	0.22	0.18, 0.28
'Healthy' (n 352)	36.97	36.57, 37.38	0.51	0.50, 0.52	1.33	1.27, 1.39	0.23	0.22, 0.24

ACT,  $\alpha$ -1-antichymotrypsin; IgA, immunoglobulin A; L : M, lactulose : mannitol; RI, respiratory infections.  
\* Results for diarrhoea and RI are not shown as only one case was reported.

improvements in biochemical status between October and February among children without any reported illnesses. Albumin increased from 34.4 to 39.5 g/l (paired  $t = -8.09$ ,  $P < 0.001$ ); ACT decreased from 0.53 to 0.49 g/l (paired  $t = 2.57$ ,  $P = 0.12$ ); and lactulose : mannitol decreased from 0.36 to 0.21 (paired  $t = 6.87$ ,  $P < 0.001$ ).

#### Relationship between morbidity reports and biochemical status

Table 3 shows the mean value of each variable according to the illnesses described by the mothers. Children who were reported to have concurrent infections of diarrhoea, fever and RI had the lowest plasma albumin level (30.8 g/l). Low albumin values were also observed in children reported to have diarrhoea either alone (33.8 g/l) or in combination with fever (34.3 g/l). Intestinal permeability was poorest (highest) in children reported to have diarrhoea and fever (0.33) or diarrhoea alone (0.32). Plasma IgA level was highest among children reported to have diarrhoea, fever and RI (1.81 g/l). ACT levels were highest in the children reported to have more than one illness, with the highest mean ACT level in children who had RI and fever (0.72 g/l).

Regression analysis was used to examine the effect of one

particular illness after removing the effects of concurrent illnesses. The dependent variable was the biochemical variable and the independent variable was the presence or absence of illness (coded 1,0). Interactions between diarrhoea, fever and RI were tested for and non-significant interactions were eliminated progressively. Age was included in the regression analysis for IgA because of the age-related increase in IgA concentration. Table 4 presents the mean value of each variable among healthy children and the change in value associated with each illness (B and 95 % CI).

After removal of the effect of other illnesses, fever was associated with a significantly elevated mean level of ACT ( $P < 0.001$ ) and significantly reduced plasma albumin concentration ( $P < 0.01$ ). Reported episodes of diarrhoea were associated with significantly elevated IgA ( $P < 0.005$ ) and ACT ( $P < 0.05$ ) levels, reduced plasma albumin concentration ( $P < 0.001$ ) and significantly worse (higher) permeability ( $P < 0.001$ ).

Reports of RI were not associated with any significant changes in ACT, IgA, albumin or lactulose : mannitol. However, there was a statistically significant interaction between fever and RI ( $P < 0.05$ ), such that the effect of fever with RI was significantly worse than the effect of either illness alone.

**Table 4.** Regression analysis of the effect of illness on mean values of plasma  $\alpha$ -1-antichymotrypsin (ACT), albumin and immunoglobulin A (IgA) and intestinal permeability in Bangladeshi children

	Healthy children (mean value)	Change in value with fever		Change in value with diarrhoea		Change in value with RI		Interactions
		B	95 % CI	B	95 % CI	B	95 % CI	
Albumin (g/l)	36.43	-1.10**	-1.92, -0.28	-2.82***	-3.99, -1.64	0.06	-1.19, 1.31	RI + fever; 0.122* (0.04, 0.20)
ACT (g/l)	0.54	0.08***	0.06, 0.10	0.05*	-0.02, 0.09	0.02	-0.04, 0.08	
IgA (g/l)	1.38	0.09	-0.03, 0.21	0.23**	0.07, 0.39	-0.02	-0.20, 0.16	
L : M	0.24	1.10	-0.96, 3.16	1.33***	-0.79, 3.45	1.02	-1.10, 3.14	

L : M, lactulose : mannitol; RI, respiratory infections.  
\* $P < 0.05$ , \*\* $P < 0.005$ , \*\*\* $P < 0.001$ .

## Discussion

The aim of this paper was not to establish the effect of fever or diarrhoea *per se* on the biochemical status of children in Bangladesh since this would be far better determined through clinical studies. Rather, the present study aimed to examine whether a mother's subjective account of child morbidity was related to other biochemical indicators of child health. Such associations between maternal reports of morbidity and biochemical status of the child have not been previously demonstrated in a population from a developing country.

Diarrhoea was reported by mothers more often than RI. This concurs with the independent clinic records for the region which recorded diarrhoea as the most prevalent infection followed by RI (Save the Children Fund, 1990).

The values for biochemical variables of children reported to be ill or healthy were in accord with values obtained in clinical studies. Bangladeshi children reported to have diarrhoea had slightly lower mean albumin levels than Gambian children with persistent diarrhoea and protein-energy malnutrition (mean 34.3 g/l) (Sullivan *et al.* 1991), whereas albumin values of the 'healthy' Bangladeshi children fell within the normal range for the UK (36–52 g/l; Belfast City Hospital, UK). The mechanism leading to lower albumin levels is difficult to identify since this can be an indication of protein-losing enteropathy, protein malnutrition or albumin acting as a negative acute-phase protein. Whichever the responsible mechanism, the findings demonstrate that children reported to have diarrhoea had a significantly poorer albumin status than children reported to be healthy.

Bangladeshi children with fever and RI had ACT levels greater than the normal range (mean 0.65 g/l; normal range 0.2–0.6 g/l; Calvin & Price, 1986), as did children with fever only (0.62 g/l). As one might expect, these values are not as high as those observed in hospitalized children in the Gambia (0.9 g/l) (Sullivan *et al.* 1991).

Comparison of the intestinal permeability values with those of other populations is hindered by the lack of reference values for children 2–6 years of age. The 'healthy' Bangladeshi children had poorer permeability values than UK infants (0.12; Lunn *et al.* 1991) and children (0.15; Noone *et al.* 1986), but better values than healthy 6-month-old infants in the Gambia (0.42; Behrens, 1987). Deterioration of intestinal permeability among Gambian infants has been demonstrated in the first year of life (Weaver, 1988), raising the question of whether there is long-term damage to the small intestine. This may also occur in Bangladesh and would be worthy of further investigation.

Finally, the mean IgA concentration of 'healthy' Bangladeshi children was within the normal range for the UK (0.3–1.3 g/l for 2–3 years of age, 0.4–2.0 g/l for 3–6 years of age; Royal Belfast Hospital for Sick Children, UK).

The limitations of morbidity interviews must be recognized in that there is no indication of the severity of illness; the specific pathogens responsible for illness are unknown, and only crude prevalence rates can be estimated. In addition, the study does not answer the question of whether children had a poor biochemical status before an episode of

infection, or whether the deterioration in biochemical status was a result of infection. Comparisons of children who were reported to be ill on the day of the visit with those who were ill in the 2 weeks before the visit did not reveal any consistent differences. Finally, the maternal responses to interviews may be different in another study depending on the social and cultural characteristics of the population. Although the majority of women in this study had no education and were illiterate, the health of their children was a high priority and hence poor health was a salient feature of their life.

Seasonal variation in biochemical status is a topic worthy of further investigation. Since this was not the primary aim of the present study, the assessment days were not timed to coincide with the main seasons and larger sample sizes on each occasion would have been required to look at changes in the effect of illness across seasons. However, the reported prevalence of illness and the proportion of children with abnormal levels of ACT were markedly higher after food shortages (April) and during the monsoon (June to October). These periods were associated with high unemployment, high food prices and a high prevalence of wasting malnutrition (Rousham & Mascie-Taylor, 1995). Even children without any reported illnesses showed a deterioration in biochemical status during the monsoon season, with the worst values being observed in October, at the end of the monsoon. Between October and February there were significant improvements in biochemical status of healthy children which corresponded with a decline in infectious illnesses, increased food availability and the favourable conditions of winter.

Detailed studies of seasonal variation in the biochemical status of children with clinical or sub-clinical infections would shed further light on the inter-relationships between nutrition, infection and biochemical status of the host.

Certain features of the study design may have contributed to the strong association between maternal morbidity reports and child health status. The recall period of 2 weeks was selected as the best compromise between over- and under-reporting (Martorell *et al.* 1976; Kroeger, 1983; Ross & Vaughan, 1986). In addition, the fieldworkers were from the local community, they were of similar socio-economic status to the respondents and the interviewer was always female. The study did not offer any treatment for illness which may have deterred mothers from over-reporting symptoms. Instead, free medical treatment was available independently of the study.

In sum, this study provides evidence of highly significant associations between maternal reports of illness and the biochemical status of their child. These findings add to the mounting body of data demonstrating the usefulness of biochemical status as an indicator of clinical and sub-clinical infections in developing country populations (Filteau *et al.* 1993, 1995; Wasunna *et al.* 1995). Furthermore, this study supports the use of maternal interviews as a means of collecting data on child morbidity or as crude indicators of health status. In terms of public health nutrition, this is valuable information that can be obtained at low cost, on large samples and over a relatively short period of time.

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