European Journal of Clinical Nutrition (1997) 51, 302–307

Impact of a single megadose of vitamin A at delivery on breastmilk of mothers and morbidity of their infants

SK Roy[1], A Islam[1], A Molla[2], SM Akramuzzaman[1], F Jahan[1] and G Fuchs[1]

[1]*Clinical Sciences Division, International Centre for Diarrhoeal Disease Research, Bangladesh, GPO Box 128, Dhaka 1000, Bangladesh;* [2]*Kuwait University, Kuwait*

Objectives: To evaluate the effect of vitamin A supplementation 24 h after delivery on breastmilk retinol concentration.
Methods: Fifty low income women were randomly assigned to a single oral dose of 209 μmol of Vitamin A or none at delivery. Maternal serum and breastmilk retinol levels and infant morbidity and anthropometry were serially assessed.
Results: Mean (95% CI) serum retinol levels increased in the supplemented mothers at 2.77 (2.3, 3.2) compared to 1.15 (0.9, 1.4) μmol/l in controls ($P < 0.05$) and remained at a significantly higher level of 1.59 (1.4, 1.8) μmul/l compared to 1.33 (1.8, 1.5) μmol/l in the control group ($P < 0.001$) up to a period of three months. Breastmilk retinol concentration was also greater at 24 h after supplementation, mean (CI) 11.34 (9.0, 13.7) μmol/l, compared to 2.95 (2.3, 3.6) μmol/l in the control group ($P < 0.0001$), and remained higher for the next six months at 1.06 (0.9, ,1.3) μmol/l compared to 0.73 (0.6, 0.8) μmol/l in the control group ($P < 0.02$). Infants of the supplemented mothers had reduced mean duration of respiratory tract infection of 3.1 (2.7, 3.5) days compared to 3.7 (3.3, 4.2) days ($P < 0.03$) and mean incidence of febrile illness 0.1 (0.1, 0.1) compared to control infants 0.3 (0.3, 0.3) days, ($P < 0.002$).
Conclusion: Vitamin A supplementation of malnourished mothers maintains higher breastmilk retinol concentration for at least six months and reduces the duration of respiratory tract infection and febrile illness in their breastfed infants.
Sponsorship: The study was supported by the International Centre for Diarrhoeal Disease Research and the United States Agency for International Development.
Descriptors: vitamin A deficiency; postpartum; retinol; breastmilk; children; morbidity

Introduction

A close relationship exists between vitamin A deficiency and increased diarrhoeal morbidity and mortality in children (Sommer *et al*, 1983). Moreover, vitamin A status may be affected adversely by high incidence of diseases such as diarrhoea, dysentery, measles and acute respiratory tract infection (Sommer *et al*, 1987). Women in developing countries have an average daily intake of vitamin A that is less than half and average serum retinol that is less than 70% of the women in the developed countries respectively (Newman, 1993). The vitamin A status of most newborn is marginal, and those whose mothers have inadequate vitamin A intake appear to be at particular risk (Shilali *et al*, 1989; Greene, 1991).

In a recent study of 85 primarily breastfed Bangladesh infants 60% and 65% were observed to have a low vitamin A status according to serum retinol and relative dose response respectively (Wahed *et al*, 1996). In Bangladesh, a significant proportion of children suffer from moderate to severe malnutrition (UNICEF, 1996) and a large proportion (1.1%) of young children six months to 59 months suffer from vitamin A deficiency such as night blindness (HKI, 1995). Nearly 50% of the newborns in Bangladesh are of low birth weight (Hassan *et al*, 1995) and are therefore likely to be vitamin A deficient as measured by hepatic stores (Robinson *et al*, 1977). Protection of infants from vitamin A deficiency may be ensured by breast feeding when there is adequate retinol concentration in the breastmilk. The retinol concentration of mothers' milk is adversely affected by a poor maternal nutritional status and dietary intake. In this context, even breastfed infants may not be protected from vitamin A deficiency because of a lower vitamin A content of their mothers milk. Malnourished Bangladesh mothers have reduced breastmilk output and a breastmilk of lower nutritive values including reduced retinol concentration (Brown *et al*, 1986). It is not known whether vitamin A supplementation to malnourished mothers at delivery can improve retinol content of breastmilk or result in any other benefits to the mothers or their breasted infants. To examine the impact of postpartum supplementation of a single megadose of vitamin A on breastmilk, we conducted the following prospective, randomized controlled trial with or without 209 μmol (200 000 I.U.) of Vitamin A in a group of mothers from a low-income peri-urban village near Dhaka city.

Materials and methods

Description of the study population

Nandipara is a densely populated peri-urban village situated ten kilometer northeast of Dhaka city with a popula-

Correspondence: Dr SK Roy.
Received 21 August 1996; revised 30 December 1996; accepted 7 January 1997

tion of approximately 3000 in an area of about four square kilometers. The number of under-five children is about 500. Among the inhabitants, 70% of men were day laborers, 20% were rickshaw pullers, 5% were carpenters and 5% were service holders. Fifteen percent of the women were day laborers and 85% were housewives. The average income of a family was 1500 taka per month (1 US$ = Taka 42). Ninety percent of the women had no formal school education and most of the houses had earthen walls with thatched roofs. The average family size was 4.5. Water and sanitation systems were poor with only 20% of the people having hand-pump tube well water for drinking and cooking, while the rest of the population used water from ditches. Excreta disposal was indiscriminate.

Study groups A cohort of 50 pregnant women in their last trimester aged 16–35 yr. from a low socioeconomic environment were selected for the study. Informed and written consent were obtained after explanation of the study procedure. Antenatal evaluation was conducted and tetanus toxoid vaccine was given to all mothers by trained health workers. Free delivery kits containing antiseptic devices and the services of traditional birth attendants were made available for the subjects in the study. Women were randomly allocated to either the intervention or control group. Subjects of the intervention group were supplemented with 209 μmol retinol at 24 h after delivery by a trained health worker. Iron syrup was given (60 mg elemental iron daily) to both treatment and control groups for a period of nine months after delivery. Details of baseline information of the mothers were collected by home visits in the beginning of the study.

Collection of data

Anthropometry and morbidity Body weight and height of the mothers were measured at delivery followed by monthly weighing for the next nine months. Weight of the women was taken by a Seca Balance (Seca Corp. Columbia, MD, USA) with 100 g sensitivity and body weights of the newborn babies and infants were taken with a Salter scale (Salter Industrial Measurement Limited, UK) with 100 g divisions. Body mass index of the women (BMI) was calculated using the formula:

$$= \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

For collection of data on morbidity and taking anthropometric measurements, one male and one female worker (called health assistants) were previously trained in ICDDR,B on accuracy in data collection, on morbidity and anthropometry. They were again standardized by the Principal Investigator and were rehearsed in the field prior to commencement of study. Local traditional birth attendants were trained for providing antenatal, natal and post natal care to the study participants. They were also trained how to collect cord blood in dark glass tubes for the purpose of retinol estimation. They collected the cord blood only when the delivery was at home during very late or early hours of the day (10 pm to 5 am). At all other times the cord blood was collected by health workers and sent to central laboratory at ICDDR,B. Venous blood samples were always collected by the investigators. The morbidity data on diarrhoea, fever, respiratory tract infections and other illnesses were recorded through alternate-day home visits by health workers. Subjects were asked about the presence of illness or that of infants. The health workers recorded the presence of illness by examination at each visit. Clinical services were made available for necessary treatment of the study subjects through a weekly clinic and when necessary.

Definitions of illness: (Rahamatullah et al, 1991)

Episode of diarrhoea ≥ 1 d in which ≥ 3 stools of watery or lose consistency or any loose stool with blood.

Episode of upper respiratory infection (URI) ≥ 1 d of cough or nasal discharge or purulent ear drainage.

Episode of lower respiratory infection (LRI) ≥ 1 d of combination of cough with indrawing of the lungs. Three or more symptom-free days differentiate episodes of diarrhoea or respiratory tract infections.

Measles Clinical signs of maculopapular skin rash with its typical distribution, and fever with cough, coryza or conjunctivitis was defined as measles.

Fever Rise of body temperature above 39°C axillary for a period of 48 h or more was defined as fever.

Vitamin A deficiency (VAD) Vitamin A deficiency in mothers was regarded with the presence of night blindness, bitot's spot, corneal xerosis or corneal ulcer. In infants up to nine months, conjunctival xerosis, bitot's spots or corneal ulcers were regarded as VAD.

Ear infection (a) Acute: serous/suppurative was characterized by presence of earache (or persistent crying on tugging at the ears) and examination with the otoscope reveals a hyperemic, opaque bulging tympanic membranae or purulent discharge. (b) Chronic: serous/mucoid/purulent: Symptoms of dull pain for a long period, fever with purulent discharging or otoscopic examination reveals perforation of tympanic membrane with or without purulent discharge.

Laboratory procedures

Three ml of cord blood was collected for pre-dose estimation of retinol and retinol binding protein (RBP) approximately 24 h after delivery. Women randomized to the intervention group were given a vitamin A capsule 24 h after delivery and after the pre-dose collection of venous blood. Post dose venous blood and breastmilk samples were obtained after 24 h, one month, three months and nine months for determination of retinol and retinol binding protein. Breastmilk was collected at the middle of breastfeeding between 9 and 11 am. Test tubes containing breastmilk and blood samples were protected from exposure to light, placed in a cool box, and transferred within four hours to the central laboratory and stored at −20°C for laboratory estimation at a later date. Dietary intake of energy and vitamin A was estimated by a 24 h recall method before collection of blood and breast-milk samples of vitamin A. Food content of retinol equivalents and energy were estimated from the Indian Food Tables (Gopalan *et al*, 1982). Retinol concentrations of serum and breastmilk were estimated by spectrophotometry with standard precautions to prevent decomposition of retinol in presence of oxygen and ultraviolet rays. The retinol standard was furnished as the USP reference standard. Retinol in serum and breastmilk was quantitated according to the modified method of Neeld and Pearson, (1963) in which vitamin A rests with a chromogenic solution (chloroform: TFA, 2:1). Serum RBP was estimated by the gel diffusion method in Partigen plates (Boehringer, Germany). A standard curve was prepared for each batch of samples. The curve was linear and the intraassay variation was between 98–102%. To check the within batch variation, a pool serum was used in seven different batches, and the coefficient of variation was 4.2%. The reproducibility of the assay was assessed using a serum of known value mixed with a standard. The recovery percentage was between 95–105%.

Data analysis
Data were checked by the investigators before entry into a microcomputer and analyzed using SPSS/PC+ software package (USA). Group means were compared with the student's *t*-test when distribution was normal and by a Mann-Whitney U test when data was non-normally distributed. Statistical significance was accepted at 5% probability.

Table 1 Comparison of baseline data between the supplemented and control mothers†

	Supplemented n = 25	*Control n = 25*
Age (y)	24.8 (22.7, 26.9)	22.7 (21.1, 24.3)
Body weight (kg)	41.1 (38.9, 43.3)	39.3 (37.4, 41.2)
BMI {Wt/Ht(m)^2}	18.5 (18.2, 18.8)	18.0 (18, 18)
Income (Taka/month)[a]	1546 (1423, 1669)	1701 (1537, 1865)
Family size	5.0 (4.68, 5.32)	4.3 (3.9, 4.7)
Body Wt. (kg) of the newborn	2.6 (2.4, 2.8)	2.7 (2.5, 2.9)

[a] Taka 42 = US$ 1.0.
†Mean (95% confidence interval).

Results

The supplemented and control groups were comparable with respect to age, body weight, nutritional and socioeconomic status (Table 1). Study mothers were malnourished as indicated by a mean body mass index of 18.3. Infants born to mothers of both groups had comparable birth weights (2.6 *vs* 2.7 kg, $P = 0.08$). The median dietary intake of retinol equivalent before the collection of blood samples was comparable between the control and supplemented groups (39 *vs* 43 μmol; $P = 0.53$) except at delivery when the supplemented group had lower dietary intake due to reduced intake by a larger proportion of subjects. Dietary intake was substantially less during the delivery period and there was a wide variation in dietary intake within the groups. Mean cord blood retinol level was low at delivery (0.72 *vs* 0.66 μmol/l) and increased at 24 h after delivery (1.38 *vs* 1.18 μmol/l, $P = 0.8$) before supplementation. After 24 h of supplementation, mean serum retinol levels increased significantly (2.77 *vs* 1.15 μmol/l; $P < 0.0001$) and then gradually decreased. The mean increase of serum retinol level remained significantly higher up to a period of three months in the supplemented group (1.59 *vs* 1.33 μmol/l, $P < 0.05$). After three months of supplementation, serum retinol levels remained comparable between the groups (Table 2).

Breastmilk retinol concentration increased significantly to a higher concentration in supplemented mothers at 24 h after the dose and was significantly greater than the control group. A gradual decline of retinol was observed in both groups of mothers after birth, although in the supplemented groups the mean retinol level in breastmilk was maintained at a significantly higher level until six months compared to the unsupplemented women (Table 3). The body mass index of the supplemented mothers remained comparable with those of the unsupplemented mothers during the nine month follow-up period (data not shown). Mean body weight after delivery was 41.1 *vs* 39.3 kg ($P = 0.8$) respectively for supplemented and control groups. There was no significant difference in body weights during the subsequent 9 months of follow-up. Serum retinol binding protein

Table 2 Comparison of serum vitamin A levels (μmol/l) between the supplemented and control mothers

	Supplemented (n = 25)	*Control (n = 25)*	*Statistical significance (P value)*
Prior to supplementation	1.38 (1.22, 1.55)	1.18 (0.94, 1.41)	0.26
24 h after supplementation	2.77 (2.34, 3.20)	1.15 (0.92, 1.38)	0.0001
1 Month	1.97 (1.76, 2.18)	1.35 (1.12, 1.58)	0.001
3 Months	1.59 (1.43, 1.76)	1.33 (1.17, 1.49)	0.05
6 Months	1.54 (1.27, 1.80)	1.36 (1.22, 1.50)	0.24
9 Months	1.29 (1.13, 1.46)	1.35 (1.20, 1.50)	0.77

Mean (95% confidence interval).

Table 3 Breastmilk retinol levels (μmol/l) of supplemented and control mothers

	Supplemented (n = 25)	*Control (n = 25)*	*Statistical significance (P value)*
Prior to supplementation	3.20 (2.53, 3.88)	3.08 (2.24, 3.92)	0.99
24 h after supplementation	11.34 (8.95, 13.71	2.96 (2.29, 3.64)	0.0001
1 Month	1.92 (1.64, 2.20)	1.24 (0.99, 1.48)	0.001
3 Months	1.34 (1.12, 1.57)	1.12 (0.91, 1.34)	0.01
6 Months	1.06 (0.87, 1.27)	0.73 (0.64, 0.83)	0.02
9 Months	0.94 (0.76, 1.13)	1.09 (0.73, 1.46)	0.31

Table 4 Comparison of cumulative morbidity between vitamin A supplemented and control mothers

	No. of cumulative episodes (Cumulative duration of illness in days)		
	Diarrhoea	*RTI*	*Fever*
1 Month preceding delivery			
supplemented	Nil	8 (18)	2 (5)
control	Nil	7 (53)	1 (8)
After supplementation			
0–1 month			
supplemented	3 (12)	15 (66)	6 (23)
control	2 (15)	11 (87)	4 (12)
0–3 months			
supplemented	10 (27)	23 (82)	10 (30)
control	2 (15)	25 (125)	10 (28)
0–6 months			
supplemented	12 (36)	39 (126)	17 (54)
control	5 (27)	49 (177)	19 (72)
0–9 months			
supplemented	13 (42)	61 (261)	27 (162)
control	8 (52)	68 (262)	28 (110)

(RBP) concentration in both the groups were comparable at delivery (data not shown) and a gradual fall after the first month was noticed in both groups. As with body weight, there were no significant differences in RBP levels between the groups during the nine month follow up period.

No significant differences were observed in either the number of episodes or in total days of diarrhoea, respiratory tract infection or fever between the groups of mothers at delivery or at any time during the follow up (Table 4). Among other types of illnesses, a significant number of women in the control group developed pedal oedema compared to none in the vitamin A supplemented group (6 *vs* 0, $P < 0.04$). A high proportion of infants were breastfed in both groups during the study period (92% *vs* 96% in supplemented and unsupplemented group respectively).

The infants of supplemented mothers had significantly shorter episodes of respiratory tract infection (3.1 *vs* 3.7 d, $P = 0.03$) compared to those of the control group (Table 5). The infants of supplemented mothers also had a lower mean number of episodes of fever (0.1 *vs* 0.3, $P < 0.002$). However, there was no significant impact of maternal retinol supplementation on infant growth rate during the nine month follow up period.

Discussion

Our study shows certain clear benefits of postpartum high dose vitamin A supplementation to mothers and to their breastfed infants. Yet there are some limitations of this study which deserves consideration. Infant's serum retinol levels were not determined as it was not considered suitable in our field condition. Secondly, the sample size might not have been large enough to detect differences in incidence and prevalence of infectious diseases in mothers or infants. Lastly, the design of the study was randomized but not placebo-controlled or masked. There was no bias in morbidity data collection as the health workers were not aware of the objective of the study. Further the retinol status of blood or breastmilk were also unknown to the health workers.

Potential health and nutrition benefits of Vitamin A supplementation of adult women has not been thoroughly evaluated. Vitamin A supplementation in adult populations especially in lactating women of developing countries highly endemic for infectious diseases combined with dietary deprivation are difficult to evaluate. Moreover, there is no available information on retinol metabolism in malnourished women and the response to the demands of lactation, stress and infection. Variable dietary intake of provitamin A is likely to cause fluctuations in both blood and breastmilk levels of retinol (Lesher *et al*, 1947) although it was not apparent in the present study. In addition, infectious diseases affect vitamin A metabolism, and our study subjects were found to suffer from such illness frequently.

This observation is similar to that of a study in Indonesian women who received a large dose of vitamin A postpartum which resulted in an increased serum retinol for six months and that was maintained for eight months (Stoltfuz *et al*, 1993). The longer duration of improved serum retinol in the Indonesian women compared to our study population is most likely because the former received a dose of vitamin A nearly 1.5 times greater than the Bangladeshi mothers (312 µmol *vs* 209 µmol) and the dose was given later (1–3 weeks) after delivery. Further, the Indonesian women were not as vitamin A deficient as our subjects as indicated by baseline blood retinol concentrations.

Brown *et al* (1982) noted that Bangladesh infants receive approximately 70% of their vitamin A requirements from breastmilk. A sustained retinol concentration in breastmilk for up to six months after maternal supplementation as in our subjects would therefore be expected to

Table 5 Comparison of episodes of illnesses in children during the follow-up mean episodes/duration per child-week of observation (95% confidence interval)

Illness observation	*Supplemented child-weeks n = 515*	*Unsupplemented child-weeks n = 522*	*Statistical significance (P-value)*
Diarrhoea episodes	0.12 (0.09, 0.15)	0.11 (0.08, 0.14)	0.59
Diarrhoea duration (days)	0.74 (0.53, 0.95)	0.71 (0.50, 0.92)	0.78
ARI episodes	0.42 (0.38 0.46)	0.45 (0.41, 0.49)	0.51
ARI duration	3.1 (2.7, 3.5)	3.7 (3.25, 4.15)	0.03
Febrile illness episodes	0.1 (0.09, 0.11)	0.3 (0.27, 0.30)	< 0.002
Episodes of measles	0.004 (0, 0.01)	0.002 (0, 0.01)	0.55
Epsiode of vitamin A deficiency	0.01 (0, 0.02)	0.02 (0, 0.04)	0.64
Episodes of ear infection	0.01 (0, 0.01)	0.01 (0, 0.02)	0.70

provide substantial benefits to the infants since more than 85% of Bangladeshi infants continue to be breastfed through the first year of life (Baqui *et al*, 1993). Breastmilk retinol declined during the first month of lactation in both the supplemented and unsupplemented groups and most likely reflects the increased concentration of this as well as many other nutrients known to exist in colostrum compared to more mature breastmilk. Of interest, while the absolute blood retinol concentrations were higher in the supplemented women, there was a pattern of decreasing serum retinol concentration beginning at 24 h after the megadose that continued through the third postpartum month in the supplemented but not unsupplemented women. It is possible that this decline reflected an increased maternal utilization of greater available vitamin A stores as the result of the supplementation. Alternatively, it might be due to increased mobilization and maternal loss of vitamin A stores through breastmilk or perhaps to a reduction in RBP. The fall of serum RBP concentrations in both groups of women might also be ascribed to a diversion of protein synthesis toward breastmilk proteins or perhaps to a relative state of protein deficiency due to the low intake of dietary protein in this population (Hassan *et al*, 1990).

Vitamin A supplementation of older children is known to reduce infectious disease mortality (Sommer *et al*, 1986; Rahmatullah *et al*, 1990). While our sample size is too small to thoroughly define changes in morbidity due to our intervention, we utilized a uniquely intensive alternate-day surveillance to increase the sensitivity of the morbidity assessment. The effect of the maternal vitamin A supplementation on infant morbidity was mixed. The incidence of ARI was comparable between the groups, but duration of ARI was shorter in the infants of the supplemented mothers suggesting improved recovery from ARI due to the supplementation. Similarly, the incidence of unspecified febrile illness was less in infants of supplemented compared to unsupplemented mothers. Adequate vitamin A nutriture is known to be necessary for a variety of physiologic functions that might explain the improved recovery, including the maintenance of epithelium and normal immune function. While our study showed certain effects of supplementation on morbidity, no effect on mortality was apparent given our study design. However, a recent study from this Centre (ICDDR,B) documented significant reduction in mortality among exclusively and predominantly breasted infants of mothers supplemented with high-dose vitamin A after delivery (de Fransisco *et al*, 1994). This latter study did not detect a reduction in morbidity in these infants most likely because the collection of morbidity data was infrequent at monthly intervals. The observed reduction in certain morbidity characteristics in our study is even more striking given our small sample size, and implies a strong effect of the maternal supplementation.

Concerns have been registered about employing high dose vitamin A supplementation of young infants primarily because of the potential for toxic symptoms (Gopalon C, 1994). In this regard, supplementation of mothers with a large dose of vitamin A immediately after delivery as in our study has shown a safer alternative public health strategy to improve the vitamin A status of young infants. The promotion of exclusive breastfeeding of infants, particularly within the first several months of life, would be additionally important to realize maximum benefits of this strategy.

Acknowledgement—This study was funded by the United States Agency for International Development (USAID) with the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). The ICDDR,B is supported by the aid agencies of the Governments of Australia, Bangladesh, Belgium, Canada, Denmark, Germany, Japan, the Netherlands, Norway, Saudi Arabia, Sri Lanka, Sweden, Switzerland, Thailand, the United Kingdom and the United States; international organizations including Arab Gulf Fund, Asian Development Bank, European Union, the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA) and the World Health Organization (WHO); private foundations including Aga Khan Foundation, Child Health Foundation (CHF), Ford Foundation, Population Council, Rockefeller Foundation and the Sasakawa Foundation; and private organizations including American Express Bank, Bayer A.G., CARE, Family Health International, Helen Keller International, the Johns Hopkins University, Macro International, New England Medical Centre, Procter Gamble, RAND Corporation, SANDOZ, Swiss Red Cross and the University of Alabama at Birmingham, the University of Iowa, and others. We thank Ms. Rekha Chanda and Mr. Dipak Barua for field work, Drs. Iqbal Kabir and Rafiqul Islam for reviewing the manuscript and Mr. K.M. Rafiq for preparation of this manuscript.

References

Baqui AH, Palyor N, Nahar Q & Slimperi DR (1993): Infant and child feeding practices in Dhaka Urban Slums. Urban RP/MCH Working Paper No. 6, ICDDR,B, 10–15.

Brown KH, Black RE, Becker S, Nahar S & Sawyer J (1982): Consumption of foods and nutrients by weanling in rural Bangladesh. *Am. J. Clin. Nutr*. **36**, 878–889.

Brown KH, Akhter NA, Robertson AD & Ahmed MG (1986): Lactational capacity in marginally nourished mothers: relationship between maternal nutritional status and quantity and proximate composition of milk. *Pediatr*. **78**, 909–919.

Francisco A de, Chakrobarty J, Chowdhury HR, Yunus M, Baqui AH, Siddique AK & Sack RB (1993): Acute toxicity of vitamin A given with vaccines in infancy. *Lancet*. **342**, 526–527.

Gopalon C, Rama Sastriva BV & Bala Subramanium SC (1982): Nutrition value of Indian foods. NIN: Hyderabad, India.

Gopalon C (1994): Acute toxicity of vitamin A in infancy. *Bull. Nutr. Found. India*. **15**, 1.

Greene HL (1991): Vitamin intakes during rapid growth. In: Heird WC (ed). *Nutritional Needs of the Six to Twelve Month Old Infant*. Raven Press, Ltd: New York, pp 251–267.

Hassan KZ, Sack RB, Siddique AK, Roy E, Rahman MN & Ali M (1995): Factors influencing birth weight in a rural community in Bangladesh (abstract). *Diarrhoeal Dis. Res*. **13 (1)**, 71–72.

Hassan N & Ahmad K (1990): Regional variation in the intake of food and nutrients in rural Bangladesh: its impact on nutritional status. *Bangladesh J Nutr*. **3**, 9–20.

HKI, Nutritional Surveillance Project (NSP) (1996): The impact of rice prices on the nutritional status of children in rural Bangladesh pp 8–13.

Lesher M, Brody JK, Williams HH & Macy IG (1947): Metabolism of women during reproductive cycle: utilization of vitamin A during lactation. *J. Am. Dietet. A*. **23**, 211–217.

Neeld JB Jr. & Pearson WN (1963): Macro and micromethods for the determination of serum vitamin A using trifluoroacetic acid. *J. Nutr*. **41**, 369–387.

Newman V (1993): Vitamin A and breastfeeding: comparison of data from developed and developing countries. Wellstart International: San Diego.

Rahmatullah L, Underwood BA, Thulasiraj RD & Milton RC (1991): Diarrhoea, respiratory infections and growth are not affected by a weekly low-dose Vit-A supplement: a masked, controlled field trial in children in southern India. *Am. J. Clin. Nutr*. **54**, 568–577.

Robinson CH & Lawer MR (1977): Normal and therapeutic nutrition, 15th edn. Macmillan: New York.

Shirali GS, Oelberg DG & Mehta KP (1989): Maternal-neonatal serum vitamin A concentrations. *J. Pediatr. Gastroenterol. Nutr*. **9**, 62–66.

Sommer A, Tarwotjo I, Hussain G & Susanto D (1983): Increased mortality in children with mild vitamin A deficiency. *Lancet*. **11**, 585–588.

Sommer A, Tarwotjo I & Katz J (1987): Increased risk of xerophthalmia following diarrhoea and respiratory disease. *Am. J. Clin. Nutr*. **45**, 977–980.

Stoltfuz RJ, Hakimi M, Miller KW, Rasmussen KM, Dawiesah S, Habict JP & Dibley MJ (1993): High dose vitamin A supplementation of breastfeeding Indonesian mothers: effects on the vitamin A status of mother and infant. *J. Nutr*. **123**, 666–675.

UNICEF, Bangladesh Bureau of Statistics (1996): Progatir Pathe; progress towards the achievement of the goals for the 1990's. Results of multiple indicator cluster survey 1995. pp. 8–13.

Wahed MA, Alvarez JO, Rahman MM, Hossain M, Jahan F & Habte D (1996): Subclinical vitamin A deficiency in young infants from Bangladesh. *Nutr. Res*. (In Press).