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Acute Phase Proteins in Small-for-Dates Babies

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Summary

Salimonu LS, Osinusi K, Dawodu AH, Damole OI, Oyelami OA, Adeniran SO and Odunuga SO. Acute Phase Proteins in Small-for-Dates Babies. *Nigerian Journal of Paediatrics* **1986; 13: 109.** Alpha 1 antitrypsin, alpha 2 macroglobulin and C-reactive protein (CRP) levels were measured in 18 small-for-dates (SFD) and 43 appropriate-for-dates (AFD) babies using the single radial immunodiffusion method. Mean concentration of alpha 1 antitrypsin was significantly higher (625±218mg/dl) in SFD babies than in AFD babies (450±246mg/dl) ($p<0.01$). However, no differences were observed in the mean levels of alpha 2 macroglobulins between the SFD (234±46mg/dl) and AFD (232±49mg/dl) babies. None of the SFD babies showed any detectable level of CRP whereas ,6 of the 43 AFD babies had detectable circulating CRP levels. Our findings on the 3 acute phase proteins in SFD babies in this study were different from those previously reported in post-natal malnutrition.

Introduction

THE similarities between post-natal malnutrition and foetal growth retardation include loss of subcutaneous fat, dry skin, hypoglycaemia and sub-optimal physical development.[1-3] Furthermore, frequent and severe infections are common to both groups of infants.[4 6] Defective immune mechanism has been consistently implicated as the major factor for the high susceptibility of these infants to frequent infections and death.[7-8] Such defects include diminished T-lymphocyte numbers[6 9 10] and functions,[6 11] impaired antibody responses to certain antigens[6 10] and impaired bactericidal activity by their leucocytes.[12 13] In addition, some acute phase proteins are known to be elevated in post-natal nutritional depletion,[14 15] probably as a result of concomitant infections that are usually prevalent in these children. In foetally growth retarded infants however, not much study on serum acute phase protein concentrations have been carried out apart from alpha fetoprotein levels which have been found to be elevated.[16]

In the present study, alpha 1 antitrypsin, alpha 2 macroglobulin and C-reactive protein levels were measured to assess the pattern and

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importance of these proteins in intrauterine growth retardation. We have also compared these findings with those previously reported in post-natal undernutrition.

Materials and Methods

The study was performed on cord sera obtained at birth, from 18 consecutive small-for-dates (SFD) and 43 appropriate-for-dates(AFD) babies, who served as controls. The infants were delivered at the University College Hospital, Ibadan, Catholic Hospital, Oluyoro, Ibadan and the Wesley Guild Hospital, Ilesa. Infants with congenital malformations, septicaemia or those who were delivered following prolonged labour and/or prolonged rupture of the foetal membranes, were excluded from the study. An intrauterine growth chart for Nigeria[17] was used to assess intrauterine growth among infants in this study. An infant was considered to be SFD if the birth weight was lower than two standard deviations (2SD) of the mean birth weight, and AFD if the birth weight fell within 2SD of the mean birth weight for his or her gestation.

The concentrations of each of the three acute phase proteins were measured using commercially prepared plates (*Behring Institute, West Germany*) by the single radial immunodiffusion method previously described.[18 19] The plastic plate containing agar/antiserum mixture was removed from the aluminium container. The agar plate was opened and allowed to stand at room temperature for 5 minutes to remove condensed water that might have entered the wells. Each of the wells was filled with 20 microlitres of test or standard serum. Each of the plates was incubated at room temperature for 3 days. The diameters of the precipitin rings were measured in two directions at right angles to the nearest 0.1mm, using a Hyland viewer with a micrometer eye piece (*Fisher Scientific Co*). Squares of the diameters of the precipitin rings of standards were plotted against concentration on linear graph papers which gave straight lines from which concentrations of the proteins were determined.

Results

The mean ($\pm$1SD) alpha 1 antitrypsin level in the SFD babies was 625 ($\pm$218)mg/dl: this was significantly higher than a corresponding level of 450 ($\pm$246)mg/dl in the AFD (control) babies (Fig 1) ($t = 2.75$; $p < 0.01$). The alpha 1 antitrypsin concentrations in the SFD babies clustered in the high range whereas the levels in most of the AFD babies were in the low range (Fig 1).

With regard to the alpha 2 macroglobulin levels however, there was no significant difference ($t = 0.15$; $p > 0.5$) in the mean levels between the test patients (234 ± 46mg/dl) and controls (232 ± 49mg/dl) (Fig 2).

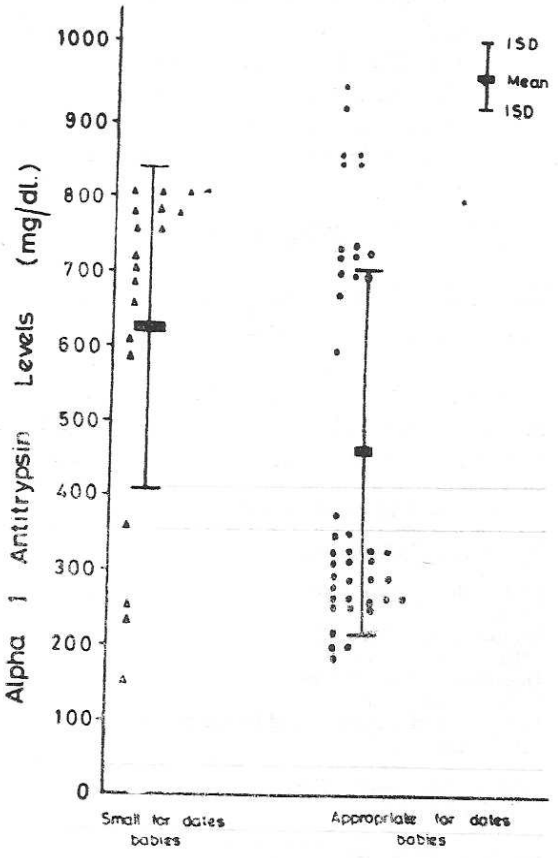

Fig 1. Mean ($\pm$1SD) concentrations of alpha 1 antitrypsin in small for dates (SFD) and appropriate for dates (AFD) babies.

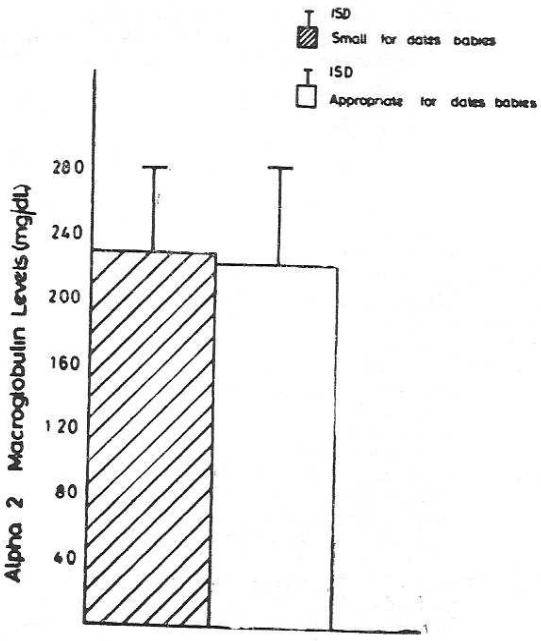

Fig 2. Mean (+ISD) levels of alpha 2 macroglobulin in small for dates (SFD) and appropriate for dates (AFD) babies.

None of the SFD babies had any detectable levels of C-reactive protein in their blood. However, 6 of the 43 AFD babies had detectable blood C-creative protein concentrations which were however, insignificant in most of them. The mean (±1SD) level was 0.2±0.7mg/dl (range 0.5 - 4.5mg/d1).

Discussion

The present study has revealed elevated mean alpha 1 antitrypsin concentration in SFD babies compared to the controls. The reason for this finding is not clearly understood. The role of alpha 1 antitrypsin in serum is poorly understood. It has previously been observed that cord blood alpha 1 antitrypsin level was lowest in infants of less than 25 weeks gestation and that this acute phase protein reaches maximum concentration sometime between 25 weeks and term[20]. increased levels of this protein have been reported in individuals of normal pi phenotype in various diseases of the liver.[21] In addition, it is also known that rupture of membranes for over 18 hours before delivery, is usually associated with elevated cord serum alpha 1 antitrypsin[20]. However, in the present series, there was no clinical evidence of liver dysfunction in any of the SFD babies neither was there delay in the delivery of the babies to account for the observed elevation. Presence of high levels of alpha 1 antitrypsin is known to adversely affect immunological responses (immunosuppression) *in vitro*[22] and *in vivo*[23]. Its elevation in SFD babies may therefore, be partly or wholly responsible for the impaired immunological responses that have been demonstrated in such babies[6].

Reports on alpha 1 antitrypsin levels in post-natal undernutrition have not been consistent. Razban *et al*[14] have observed a significant reduction whilst we[15] have demonstrated a slightly higher level in healthy age- and sex-matched well-fed infants than in malnourished ones.

The present study has shown that the SFD babies had a mean alpha 2 macroglobulin concentration that was similar to that of the AFD babies. This observation is different from the findings in post-natal undernutrition where diminished levels of alpha 2 macroglobulin have been consistently reported[14 15]. The mechanism responsible for the low serum concentration of this macroglobulin in the latter, is not known but could be due to a reduced synthesis of the protein or increased catabolism resulting from alpha 2 macroglobulin forming complexes with endopeptidases of lysosomal or bacterial origin.[24]

Whilst some authors have reported higher blood alpha 2 macroglobulin levels in adult males [25 26] than females, others have demonstrated significantly lower levels in males[27 28]. In the present study, we did not observe any sex related differences in the levels of alpha 2 macroglobulin in the babies.

None of the SFD babies in this study had any detectable concentration of C-reactive protein in

their blood. This is in contrast to our recent findings in post-natal undernutrition, where a greater proportion of the children had detectable C-reactive protein levels when compared with the well-fed children;[15] the mean C-reactive protein level was also significantly higher in malnourished than in control children[15]. Similar findings have also been reported by Razban *et al*[14]. Since the presence of C-reactive protein in the blood is an indication of recent or ongoing infection,[29] our findings would suggest that intrauterine infection probably did not play a major role in the causation of intrauterine growth retardation in this study.

It is concluded from the present study that alpha 1 antitrypsin levels are elevated in foetal growth retardation but to a lesser degree in post-natal undernutrition. Normal levels of alpha 2 macroglobulin are present in the blood of SFD babies whilst diminished levels were reported in protein-calorie malnutrition. The SFD babies did not show any evidence of the presence of circulating C-reactive protein whereas, higher levels than normal were observed in post-natal undernutrition. These observations suggest that although the SFD babies and malnourished children have some physical and immunological similarities, they have different concentrations of these three acute phase proteins.

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