

Another Look at Cord Blood Proteins

CHANGES WITH BIRTHWEIGHT AND AS A PREDICTOR OF HYALINE MEMBRANE DISEASE IN NEONATES

B. SINGER, J. WOLFSDORF

SUMMARY

The total cord protein (TCP) and albumin levels of 287 Black babies (155 term and 132 low birthweight) were measured, related to birthweight, and compared with international figures, in order to clarify previously published inconclusive data.

An assessment was also made as to whether a previously published level of 4.6 g/100 ml TCP or less, proved of good predictive value to the development of hyaline membrane disease (HMD) in Black babies.

TCP levels, as measured by a chemical and meter method, were noted, and the accuracy of the methods compared and statistically evaluated.

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Virtually no data exist for TCP or cord albumin levels in Black infants. While it has previously been shown that the Black neonate and infant is more mature at birth and during the first 6 years of life in terms of motor development,¹⁻⁴ others⁵ have found no differences in somatic and neurological development at birth, as compared with matched White infants. It is thus possible that, at a metabolic level, Black babies may be in advance of other racial groups during the later weeks of gestation, this effect possibly being demonstrated by an increased TCP and/or cord albumin level. Furthermore, as some authors⁶⁻¹⁰ have, while others¹¹⁻¹⁴ have not, been able to find any statistical correlation between TCP levels and birthweight or gestational age in other racial groups, it was elected to investigate TCP and albumin levels once again—this time in Black babies. Two different methods (chemical and TS meter) were utilised, the results were related to birthweight, and compared with levels previously published for other communities. Further, since Bland¹⁰ has postulated that TCP can accurately predict the development of HMD in infants so tested, and since prevention of this disease seems, at present, to be

possible only by enzyme induction in immature fetuses,¹⁵ early and vigorous treatment remains the pillar of the therapeutic approach to this problem. It was thus further decided to reassess whether Bland's level of 4.6 g/100 ml TCP could distinguish, in this population, the 'at-risk' group early. Such a simple bedside test would contribute a great deal to the achievement of a significant reduction in neonatal mortality, since HMD not infrequently accounts for 30-50% of all deaths in the neonatal nursery of this unit.¹⁶

PATIENTS AND METHODS

Two hundred and eighty-seven (155 term—38 to 40 weeks, and 132 low birthweight (LBW)—28 to 37 weeks) consecutive, apparently healthy, Black babies born by spontaneous vaginal delivery, were utilised in this study. After birth, the placental cord was 'milked' and 2 ml of blood removed. This was immediately centrifuged and the serum frozen at -20°C until required for analysis, which was always within 18 hours. All haemolysed specimens (visual inspection) were discarded. TCP and albumin levels were then estimated on well-mixed, thawed specimens by a standard chemical method,¹⁷ in addition to which the TCP was measured by a TS meter. Levels were noted and a correlation between the two methods was sought. All data were related to birthweight, and a scattergram and regression equation, where indicated, were calculated.

The clinical status of the babies was assessed during the first three days of life for evidence of HMD, using accepted clinical criteria.¹⁸ When HMD was present, further confirmation was obtained by X-ray film of the chest and blood gas studies. Autopsy confirmation was sought in those infants who died. TCP levels were examined in relationship to the incidence of HMD.

RESULTS

The mean birthweights, TCP (chemical and TS meter) and serum albumin levels for term and LBW infants are recorded in Tables I and II. These infants were overwhelmingly appropriate for their gestational ages.⁵ Their TCP and serum albumin values compare favourably with levels obtained from infants matched for weight, born in developed communities. No differences between male and female levels were detected. Total protein and albumin levels were statistically different ($P < 0.001$) when the preterm group, as a whole, was compared with the term group.

Department of Paediatrics and Child Health, Godfrey Huggins School of Medicine, University of Rhodesia, Salisbury, Rhodesia

B. SINGER, M.B. CH.B., M.R.C.P., D.C.H.

J. WOLFSDORF, B.SC., M.B. B.CH., DIP. PAED., F.R.C.P., *Professor*

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Reprint requests to: Professor J. Wolfsdorf, Harare Central Hospital, Box ST 494, Southerton, Salisbury, Rhodesia.

TABLE I. TERM INFANTS—NEWBORN WEIGHTS AND TCP/ALBUMIN LEVELS WITH METER AND CHEMICAL METHOD

Sex	No.	Mean weight ± 2 SD g	Total cord protein			
			Meter ± SD g	Chemical method		Albumin g
				Total g ± SD	Albumin g	
Males	92	3 240 ± 357	6,39 ± 0,83	6,37 ± 0,82	3,42 ± 0,66	
Female	63	3 142 ± 340	6,37 ± 0,80	6,45 ± 0,79	3,54 ± 0,56	

TABLE II. LBW INFANTS—NEWBORN WEIGHTS AND TCP/ALBUMIN LEVELS WITH METER AND CHEMICAL METHOD

Sex	No.	Mean weight ± 2 SD g	Total cord protein			
			Meter ± SD g	Chemical method		Albumin g
				Total g ± SD	Albumin g	
Males	58	2 028,86 ± 400,31	5,29 ± 0,86	5,32 ± 0,87	2,89 ± 0,43	
Female	74	2 001,5 ± 453,45	5,46 ± 0,94	5,43 ± 0,92	2,94 ± 0,51	

Fig. 1 compares birthweight in term and LBW male babies with TCP (TS meter). Statistical correlation exists in the LBW babies at the 1% level ($P < 0,01$), no correlation existing for the full-term babies. Since information on the male and female groups was statistically similar, only the data on the males are shown. When a comparison was made of albumin levels with birthweight, a correlation was found for male LBW infants and term female infants ($P < 0,05$), and no statistical relationship was detected for the LBW female group or the male term infants.

Table III gives the incidence of HMD in term and preterm, male and female infants, in relation to TCP values. Two out of 155 term infants (2,3%) and 29 of 133 preterm infants (21,8%) had TCP levels of 4,6 g/100 ml or less. Of these, no term infant, and only 5 of 29 (17%) preterm infants, developed HMD. Further, 7 of 103 (6,8%) preterm infants with TCP levels greater than 4,6 g/100 ml, developed HMD. Chi-square analysis of the LBW group indicates no relationship between TCP and HMD, either when the sexes are taken separately or combined as a group.

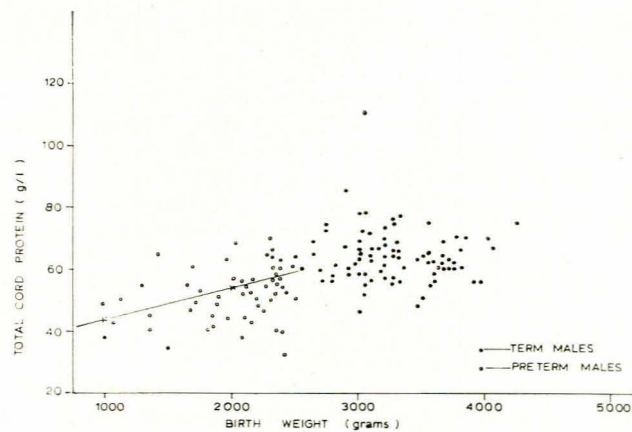


Fig. 1. Total cord protein (TS meter) v. birthweight.

TABLE IV. CORRELATION COEFFICIENTS FOR TOTAL CORD PROTEIN CHEMICAL VERSUS METER METHOD

Group	Sex	Correlation Coefficient
Term infants	Male	0,891
	Female	0,871
	Combined	0,884
Preterm infants	Male	0,969
	Female	0,979
	Combined	0,974

Table IV outlines the correlation coefficients for TCP chemical method versus TS meter in male and female term and LBW infants. No significant differences are apparent between the two methods in any of the groups, singly or combined.

Mean total cord protein for term infants (mean weight 3 200 g ± 0,351) was 6,37 g/100 ml ± 0,82 (males) and 6,45 g/100 ml ± 0,79 (females), while their cord albumin levels were 3,42 g/100 ml ± 0,66 (males) and 3,54 g/100 ml ± 0,56 (females) respectively. For the low birthweight infants (mean weight 2,01 kg ± 0,580) these levels were 5,32 g/100 ml ± 0,87 and 5,43 g/100 ml ± 0,92 (TCP) and 2,89 g/100 ml ± 0,43 and 2,94 g/100 ml ± 0,51 (albumin) for the male and female babies respectively. These values are similar to those previously published for term and LBW White infants, and further indicate no significant differences in the TCP and albumin

TABLE III. INCIDENCE OF HMD IN TERM AND LBW INFANTS RELATED TO TCP LEVELS

Total protein (meter) g	Term infants		No. with HMD	LBW infants		No. with HMD		%	
	M	F		M	F	M	F	M	F
	>4,6	90		63	Nil	44	59	4	3
4,6 or less	1	1	Nil	14	15	2	3	14	20

χ^2 male 0,003 NS.
 χ^2 female 1,849 NS.
 χ^2 (M + F) 1,85 NS.

levels between males and females matched for birthweight (TCP term $t:0,038$, df 153) (LBW $t:1,123$, df 130) (albumin: term $t:1,185$, df 153) (LBW $t:0,05916$, df 130). A significant difference was found, however, when TCP and albumin levels for term infants were compared with those of the LBW group ($P<0,001$).

A strong positive correlation was found between TCP and birthweight in the LBW babies as a group ($r = 0,378$, $P<0,001$), while no correlation could be detected for the full-term infants. Comparing albumin levels with birthweight, a correlation was found for male LBW infants and term female infants ($P<0,05$), no statistical relationship being detected for the LBW female group or the male term infants.

TCP levels of 4,6 g/100 ml or less proved a poor guide to the development of hyaline membrane disease (HMD) (analysed by either sex or birthweight), since only 17,2% (5 of 29) of preterm infants fulfilling the above criterion subsequently developed HMD, while 6,7% (7 of 103) with levels greater than 4,6 g/100 ml were similarly affected. Neither of the two term infants with TCP levels of less than 4,6 g/100 ml developed HMD.

The use of the meter (TS meter; American Optics, Buffalo, NY, USA) provided a rapid and accurate way of estimating TCP, as compared with the standard chemical method, independent of sex or birthweight of the baby ($P<0,001$).

DISCUSSION

It is of interest that although the data concerning the relationship of serum proteins to gestational age have been accumulating over many years, some doubt still exists as to whether a positive correlation is really present. Some of the studies which have tended to confuse the issue may, however, be disregarded on the grounds that either the numbers involved are too small to give statistical meaning to the information,^{11,13,14} or that no statistical evaluations were carried out at all.¹² Further, serum proteins were, on occasion, collected from capillary blood,¹⁹ a method which, in itself, alters values, or postpartum at different ages (0 - 68 days),²⁰ when different regimens of feeding were presumably being undertaken. If one then excludes the above information, a significant body of data⁶⁻¹⁰ supports the contention that there is a strong correlation between increasing birthweight and TCP levels. The present study is in accord with this view. It is not surprising that within the term group, no relationship to weight could be detected since, normally, levels appear to vary very little from the time of full gestation to adulthood.¹⁷ The anomalous situation found in this study with regard to the albumin levels could possibly be explained by the fact that the female term and LBW babies were

of slightly lower weights than their male counterparts, though this was not statistically evident. Albumin levels at the extremes of intra-uterine life may thus vary very little with birthweight. Further, the range of TCP/albumin levels found in this study was similar to those previously published for other racial groups, while no significant differences were observed in the levels found in the male and female babies, matched for weight.

The association between TCP levels and HMD appears, in general, to be well documented,^{8,10-12,21} though only Bland has been able to establish an exact level which separates the highly 'at-risk' group. Markarian *et al.*⁸ and Domville-Cooke¹² suggested that a TCP level of <5 g/100 ml appeared to increase the risk of HMD in the infant. However, neither author felt that any level could be used as a specific guide in the individual patient. The data from this investigation support the latter view. Only 17,2% of preterm babies having a TCP level of <4,6 g/100 ml subsequently developed HMD, while 6,8% of those with levels greater than this were similarly affected. With such large percentages of falsely negative and positive results, this test is obviously only of limited value as a screening procedure.

Finally, the results reported here concerning the use of the TS meter as a rapid, early, and relatively cheap means of assessing TCP levels, as compared with a standard chemical method, agree with previously published information.¹⁰

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