

ELECTROPHORETIC PATTERN OF HYPERPROTEINEMIC SERA IN A POPULATION GROUP OF RURAL PANAMA*

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Elevated serum protein levels of unknown etiology have been described in several specific population groups.^{3, 6, 11, 14, 15} In the Central American area, hyperproteinemia is particularly common among adults in rural Panama.¹¹ The present study was designed to determine whether the increase of a particular serum protein fraction or fractions could account for these high values or whether all of the fractions were elevated proportionately. The results are pertinent to the basic problem of the mechanisms involved in the production of these hyperproteinemias.

MATERIALS

The study was conducted during May in the village of La Arena, Chitré, Panama, located at sea level approximately 5 kilometers from the Pacific Coast. The mean temperature was approximately 28° C. The subjects were an ethnic mixture of white, Negro and Indian, whose cultural characteristics and dietary habits have been carefully investigated.¹³ The total consumption of protein was inadequate in at least 50% of the families studied, although calorie intakes closely approximated estimated requirements. About 33% of their dietary protein was of animal origin. Their average intake of riboflavin was 50% and that of calcium 34% of the recommended allowances for Central America and Panama.⁸ No other dietary deficiencies of minerals or vitamins were found. Total serum proteins were determined in 98 individuals, 58 males and 40 females ranging in age from 13 to 66 years. To study the distribution of the serum protein fractions and its possible relation to the level of total proteins, 9 subsamples were analyzed by electrophoresis from three groups selected as follows: Group I: Total protein contents below the median; Group II: values between the median and the third quartile; Group III: protein levels above the third quartile. The

latter represented unusually high serum total protein values. Previous serum protein data obtained from 98 healthy middle and upper income adults in Guatemala City were used for comparison.

METHODS

Venous blood samples were collected during both morning and afternoon from ambulatory individuals and allowed to stand for 30 minutes before centrifugation. In the Guatemalan subjects the majority were mid-morning specimens. Total proteins in the sera were determined immediately afterwards by the gradient method of Lowry and Hunter.⁹ Hemoglobin concentration was estimated in a sample of the fresh blood with a standardized Sahli hemoglobinometer. The remainder of the serum from each sample was packed in ice for air shipment to the central laboratories in Guatemala where analysis of the serum protein fractions was carried out by free flow electrophoresis in a Kern microelectrophoresis apparatus. A barbital buffer at pH 8.6 with an ionic strength of 0.1 was employed, and a current intensity of 200 milliwatts was applied for 35–45 minutes. Since with this method the separation of the α_1 globulin from the albumin is imperfect, these two fractions could not be estimated individually.

RESULTS

In Figure 1, the quartile values and limits of the total serum protein in 98 Panamanian subjects are compared with the control group of 98 adults from Guatemala City. The data show the relatively large number of high serum protein values among the Panamanians. Table 1 shows the average and range of total serum protein values for each of the three Panamanian groups selected for electrophoretic study together with the relative concentration of the protein fractions per 100 ml of serum. The average hemoglobin values for 79 of the Panamanian subjects was 13.8 ± 0.18 . No relation between the serum

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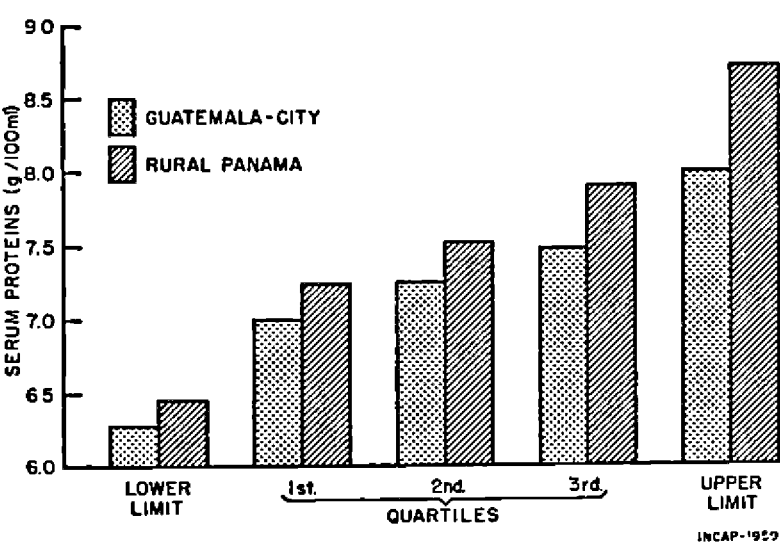


FIG. 1. Total serum proteins (grams per 100 ml) in adult subjects from "La Arena," Panama, and Guatemala City (98 individuals per group).

protein levels and the hemoglobin values was evident.

Analysis of the data suggests that the variation in protein within Group I (protein values below the median) was due mainly to differences in gamma globulin ($r = 0.846$, 7 *d.f.*). Although there were also small positive correlations with the albumin-alpha₁ and beta globulin fractions, these were not statistically significant. In contrast, the variation in total serum protein within Group II (values between second and third quartiles) seemed to be associated with differences in the albumin-alpha₁ globulin fraction, paralleled by a reciprocal change of approximately the same magnitude in the alpha₂ globulin. Nevertheless, both of these ($r = 0.655$ and -0.633 respectively, 7 *d.f.*) fell short of the 5% level of significance. Variations in the beta globulin seemed to have a very small effect on total protein, while those of the gamma fraction

had none. Although the study was designed because of special interest in the behavior of serum protein fractions within Group III made up of individuals with serum protein values above 8.21 g per 100 ml, none of the correlations between the serum protein fractions and total serum protein reached statistical significance. The correlations (7 *d.f.*) were, however, positive for the gamma globulin fraction ($r = 0.633$), essentially zero for the alpha₂ globulin ($r = 0.010$) and negative for the beta ($r = -0.517$) and the albumin-alpha₁ globulin fractions ($r = -0.229$). Because of the limitations imposed by the relatively small size of the groups, the relationships suggested by the within-group analysis were examined by analysis of the pooled data. The analysis of the combined data for all groups indicated that while the groups differed in absolute concentration of the various fractions, the latter increased proportionally with total protein content and remained unchanged in their relative concentrations.

DISCUSSION

It has been previously pointed out that relatively high serum proteins may be found in population groups with relatively poor quality or quantity of dietary protein.¹¹ Although the most striking examples come from tropical regions, the phenomenon is also seen to a lesser extent in temperate zones, as illustrated by reports from Rochester,¹¹ Detroit,¹⁰ and the Netherlands.¹ If it is due in any way to an inadequate intake of protein, it is not surprising that most reports come from the technically underdeveloped areas of the tropics where this type

TABLE 1
Electrophoretic fractions of serum proteins in adult subjects of La Arena, Panama (9 individuals per group)

| Group | Serum total protein (g/100 ml) | | Protein fractions in per cent of total proteins | | | | | | | |
|-------|--------------------------------|-----------|---|------|--------------------|------|-----------|------|-----------|------|
| | | | Albumin + alpha ₁ globulin | | Globulins | | | | | |
| | \bar{x} | Range | | | Alpha ₂ | | Beta | | Gamma | |
| | | | \bar{x} | S.D. | \bar{x} | S.D. | \bar{x} | S.D. | \bar{x} | S.D. |
| I | 7.24 | 6.54-7.39 | 59.0 | 3.51 | 9.6 | 1.93 | 13.7 | 2.16 | 17.7 | 1.98 |
| II | 7.72 | 7.63-7.90 | 61.6 | 2.15 | 7.7 | 2.52 | 14.6 | 3.06 | 16.1 | 2.61 |
| III | 8.34 | 8.21-8.55 | 60.4 | 4.18 | 8.5 | 2.33 | 14.4 | 3.06 | 16.7 | 5.99 |

of deficiency is exceedingly common and severe. Similarly, tropical areas suffer most from acute and chronic infections which may also be a factor in hyperproteinemia.

It has been recognized for some time that serum protein in the adults of at least certain populations in rural Panama were markedly higher than normal for well-nourished populations, despite their relatively poor diet.¹² This is strikingly shown by the comparison between the Panamanian subjects and the "control" Guatemalan group in the present study. The time of day at which samples are collected seems unimportant since Fawcett and Wynn⁵ have shown no definite diurnal variation of serum protein levels except for the elevation of protein concentration on rising from bed. The same tendency as in the rural Panamanian adults was observed in a less striking fashion in rural school populations studied in several of the Central American countries.¹¹ It was apparent from the separation of protein fractions in a sample of the school children that the elevations could not be fully accounted for by increased globulins but must also be associated with a rise in albumin. The present study establishes that this is also true for the much higher serum protein values of rural Panamanian adults. The electrophoretic pattern of the hyperproteinemic sera was similar to that of a group of clinically healthy subjects from Guatemala City with total serum protein within the range accepted as normal.⁴

The fact that the Panamanian subjects were ambulatory clinically healthy individuals, consuming food and readily available water *ad libitum*, as well as the lack of correlation between the levels of serum proteins and the hemoglobin concentrations, suggest that dehydration is not playing a significant role in this phenomenon. At least three different mechanisms appear, however, to be operating to produce high serum protein values. In some studies^{2, 3, 7, 15} they are explained by an elevation in the gamma-globulin fraction, while Holmes et al.⁶ attributed the increase in total serum protein to a rise in the beta globulin fraction, and in the present study a proportionate increase in all fractions was observed. These differences emphasize the need to investigate the nature of the hyperproteinemias occurring in each specific population. Certainly a single general explanation does not

seem to be applicable and the tendency to attribute all such increases to a specific increase in gamma globulin due to the prevalence of infection is unwarranted.

SUMMARY

A high prevalence of hyperproteinemias has been found among the inhabitants of La Arena in Panama in a random sample of 98 individuals. The values for the first, second and third quartiles were 7.24, 7.52 and 7.90 g of total protein per 100 ml of serum, with a range of 6.45 to 8.72. For electrophoretic studies, three subsamples of 9 subjects each were selected, with total serum protein values as follows: Group I, below the median; Group II, between the median and second quartile; and Group III, above the third quartile. Each of the electrophoretic fractions determined (albumin plus alpha₁ globulin, alpha₂, beta and gamma globulin) was proportionately responsible for the total serum protein elevation.

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