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Anemia and hypoalbuminia as an adjunct to soil-transmitted helminthiasis among slum school children in Visakhapatnam, South India

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A longitudinal study was conducted over the period August 1993 to August 1994 on 217 children from a fishing community of Visakhapatnam, Andhra Pradesh. The subjects were aged between 7 and 13 years. Children were screened for *Ascaris lumbricoides, Trichuris trichiura* and hookworm. Intensity of infection was estimated by the formalin-ether sedimentation technique. Simultaneously, blood samples ware also collected for estimation of hemoglobin and serum proteins using standard techniques. Blood parameters and ova count were monitored both prior to and following treatment with albendazole, administered at a single oral dose of 400 mg/child in November 1993. Post-treatment recordings were done at the end of the second, fourth and fifth months while hemoglobin estimation was also monitored at the ninth month. Study showed a prevalence of 82% with intestinal helminths and a mean hemoglobin level of 9.7 g/dL + 1.7 (5–13 g/dL), with 88% of the children being anemic. Total serum protein level was normal (8.61 ± 1.03 g/dL), with an elevated serum globulin response (4.63 ± 0.88). Post-treatment observations showed the complete expulsion of worms with the significant lowering of globulin levels. However, moderate anemia persisted in the population with gradual improvement by the ninth month. Significant increase in weight was not registered at the end of the fifth month probably coinciding with the rapid establishment of infection. Sex-wise there was no significant deviation from the general trend.

Key words: slum school children, *Ascaris lumbricoides, Trichuris trichiura*, hookworm, albendazole, prevalence, hemoglobin, total serum protein, globulin, pre-treatment, post-treatment, anemia, Visakhapatnam, Andhra Pradesh, South India.

Introduction

Intestinal helminth infections affect over 1800 billion people particularly children in developing countries of Africa, Asia and Latin America.[1] Secondary disease manifestations due to the soil-transmitted helminths are varied ranging from malnutrition to respiratory complications. It is probable that protein energy malnutrition and iron-deficiency anemia cause severe morbidity and growth retardation among children.[2] However, the intensity of infection remains the key factor for the pathological changes (e.g. heavy infection of the *Ascaris lumbricoides* are often associated with kwashiorkar, stunting growth and avitaminoses;[3] *Ancylostoma duodenale* is known to drain nearly 50 mL of blood per day when the worm burden is about 250[4] thereby decreasing the blood cell count, hemoglobin and serum proteins). In the case of *Trichuris trichiura* which lacks direct contact with the digestive tract, host reaction is limited to excess mucus secretion, loss of blood, reduced albumin synthesis and increased plasma concentration of tumour necrosis factor (TNF) in systemic circulation.[5] These pathogenic effects are generally more pronounced among children than in adults, perhaps attributable to the age-dependent resistance.[6]

Nutritional disturbance caused by intestinal nematode infections can either be assessed by conventional anthropometry or by estimating the biochemical changes in blood. Hypoalbuminia and hyperglobulinemia associated with nematode infections among children were reported by several authors.[7–10] Nesheim attributed hypoalbuminia to protein malabsorption or maldigestion in the gut of the host.[11]

In India, although a number of epidemiological studies of intestinal helminths have been documented, investigations on the biochemical changes and effects of malabsorption on the host are few and fragmentary.[9,12]

In the present investigation, an attempt has been made to assess the impact of soil-transmitted helminths (*A. lumbricoides, T. trichiura* and hookworms) on hemoglobin and serum protein profile among primary school children of Relliveedhi in Visakhapatnam, South India.

Methods

Subjects and collection of data

Two hundred and seventeen children aged between 7 and 13 years (115 boys, 112 girls; sex ratio 1:1.03) from Relliveedhi, a slum in Visakhapatnam, Andhra Pradesh, India, were recruited for the study. Prior to the study, the consent of parents, school teachers and health authorities of the Municipal Corporation Visakhapatnam was obtained. Data on each child were obtained by a questionnaire covering anthropo-

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metric, clinical, occupational and dietary information, and living and housing conditions. An identification number was provided to each child at the beginning of the study and this maintained throughout.

Determination of egg per gram and worm burden

Single pre-treatment and post-treatment stool samples were obtained from the subjects for estimation of egg per gram (epg) count using formalin-ether sedimentation technique.[13] All infected children received a single oral dose of 400 mg/child of albendazole. Worm expulsion was monitored for a period of 48 h and the expelled worms stored in separate plastic containers**.**

Collection of blood sample

Pre-treatment blood samples were collected between August 1993 and November 1993 for the estimation of serum protein and hemoglobin. Following drug intervention blood samples were collected simultaneously with stool samples at the end of the second (January 1994), fourth (March 1994), fifth (April 1994) and ninth (August 1994) months. A 3 mL sample was drawn from the anti-cubital vein (except at the ninth month for hemoglobin estimation obtained by finger prick method). A total of 1 mL preserved in acetate-citrate-dextrose (ACD) for estimation of hemoglobin and 2 mL was allowed to clot and was stored at –20°C for quantification of total serum protein, albumin and globulin.

Estimation of hemoglobin and serum proteins

Hemoglobin was estimated using Sahli's method and serum protein quantifications were done with the aid of a diagnostic reagent kit (Span diagnostics, Code no. 25931, Mumbai, India) and the optical density measured on a photoelectric colorimeter.

Statistical tests

The population was divided into five groups: uninfected children (n = 40), group 1 (all infected children, n = 177), group 2 (with single infection of either *Ascaris* (n = 33) or *T. trichiura* (n = 17)), group 3 (double infection of *A. lumbricoides* and *T. trichiura* (n = 107)), group 4 (multiple infection of *A. lumbricoides, T. trichiura* and hookworm (n = 17)). Post-treatment observations (in pairs) were compared using t- and Z-tests. Variation in blood parameters were analysed using two-way analysis of variance (ANOVA). Bivariate and multiple variate regression analysis was employed with albumin and hemoglobin level as the dependent variable.

Results

The study showed an overall high prevalence of 82% with intestinal helminths. *Ascaris lumbricoides* was reported in 72% of the population while *Trichuris trichiura* and hookworm associations were noted in 66% and 9%, respectively. Intensity of infection ranged between low to moderate with no child harboring heavy infection (Table 1).

Blood samples collected for the estimation of hemoglobin and serum proteins (total serum protein and albumin) showed no significant difference between the uninfected and infected population, except for mean globulin level (Z = 2.32, P < 0.01, Table 1). In order to find out the impact of parasitic infections on hemoglobin and serum protein levels of the children, in different groups, tests of significance (t- and Z-tests) were employed. It was observed that single species association with *Ascaris* rather than *T. trichiura* seemed to affect the albumin level of the host more pronouncedly (t = 4.51, P < 0.05). Multiple species association further depressed the albumin level (t = 9.34, P < 0.05); no significance was found between children with double (group 3) and multiple infections (group 4). A significant difference in the hemoglobin level was noticed in relation to the level of infection in groups with double and multiple infections (Z = 2.52, P < 0.05). Anemia was highly prevalent in all the groups.

Post-treatment observations

Follow-up observations were carried out for a period of 5 months for estimation of serum protein and hemoglobin

Table 1. Prevalence, intensity and hematological pattern in children with different degrees of intestinal helminth associations

	Uninfected (n = 40)	Group 1 (n = 177)	Group 2 Single infection *Ascaris* (n = 33)	Group 2 Single infection *Trichuris trichiura* (n = 17)	Group 3 Double infection *Ascaris* and *Trichuris trichiura* (n = 107)	Group 4 Triple infection *Ascaris*, *Trichuris trichiura* and hookworm (n = 17)
Prevalence (%)	18	82	15	8	49	8
Intensity						
Ascaris	—	3046 (5797)*	1914 (3505)		4026 (6875)	2635 (3014)
Trichuris trichiura	—	742 (546)		755 (696)	1019 (1878)	541 (727)
Hookworm	—	165 (189)				184 (199)
Hemoglobin (g/dL)	10	9.65	9.65	8.38	9.91	8.85
Serum total protein (g/dL)	8.43	8.65	8.33	9.06	8.74	8.25
Serum albumin (g/dL)	3.99	3.98	3.99	4.23	4.00	3.61
Serum globulin (g/dL)	4.44	4.67	4.34	4.82	4.75	4.67
A/G ratio	0.94	0.87	0.92	0.80	0.90	0.84
Anemia (% Hb < 12 g/dL)	80	89	91	100	86	94

* Mean (SD).

response. Ninth month post-treatment data were collected only for hemoglobin levels. Second month post-treatment studies showed significant reduction in globulin ($Z = 3.90$, $P < 0.05$) and total serum protein ($Z = 3.43$, $P < 0.05$) values. However, A/G ratio increased significantly. Mean hemoglobin level was significantly depressed compared with the pre-treatment level ($Z = 8.28$, $P < 0.05$, Fig. 1). Sex-wise and among different groups of infection the trend was similar. At the end of the fourth month globulin level and A/G ratio showed significant differences. Mean hemoglobin response remained depressed compared with pre-treatment level. By the end of the fifth month reinfection had set in and the hematological profile remained more or less similar as the fourth month with a slight increase in albumin level (Table 2). Two-way ANOVA employed on A/G ratio data for children in different groups ($F1 = 58.60$, d.f. $v1 = 3$, $v2 = 528$, $P < 0.01$; $F2 = 15.48$, d.f.: $v1 = 176$, $v2 = 528$, $P < 0.01$) showed highly significant improvements indicating the efficacy of the drug. By the end of the ninth month hemoglobin level increased but not to the pre-intervention level (Fig. 1).

Correlation analysis

Since albumin is a nutritive index of an individual, linear correlation analysis between albumin and protein intake of children showed a significant positive association ($r = 0.395$, $t = 2.53$, $P < 0.05$) in the uninfected group and not among infected children, indicating a condition of hypoalbuminia and protein loss in the latter. Bivariate associations were not established between hemoglobin and other variables. Multiple correlation analysis was employed to determine the degree to which the dependent variable hemoglobin was influenced by various factors such as age, height, weight, calorie intake/day, protein input, *Ascaris* epg, *Ascaris* worm burden, *Trichuris* epg. Coefficient of determination (R) was found to be significant for children belonging to group 1 ($R = 0.313105$, $P < 0.05$) and group 2 with single infection of *Ascaricas* ($R = 0.613906$, $P < 0.05$).

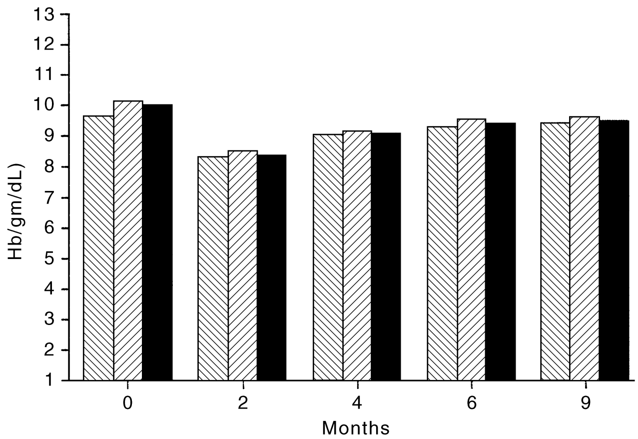

Figure 1. Pre- and post-treatment hemoglobin levels among infected children (group 1, $n = 177$). (▧), boys; (▨), girls; (■), total.

Table 2. Pre- and post-treatment serum protein profile of children in group 1 ($n = 177$)

		Post-treatment (months)		
	Pre-treatment	2	4	5
Total protein	8.65 (1.06)*	8.29 (0.91)	8.36 (0.86)	8.36 (1.06)
Serum albumin	3.98 (0.62)	3.96 (0.54)	4.07 (0.50)	4.14 (0.67)
Serum globulin	4.67 (0.85)	4.33 (0.79)	4.30 (0.70)	4.22 (0.76)

* Mean (SD).

Discussion

In the present investigation hemoglobin, total serum protein, albumin and globulin of uninfected and infected children were estimated. There was slight variation in the blood parameters between groups as they belonged to a similar socio-economic background with closely related dietary and occupational pattern. However, albumin level was found depressed in children with single species association of *Ascaris*. Blumenthal and Schultz reported ascariasis as the prime cause of hypoalbuminia.[8] Children harboring single infection of *T. trichiura* did not report low serum albumin level since they belonged to a low intensity group. Past studies have documented hypoalbuminia in patients only with severe trichiuriasis.[10,14] Intensity and prevalence of hookworm infection was very low and its direct impact on the hematological profile was negligible. Yet children with multiple species association had low albumin level which suggests a cumulative effect of the parasites on the host. A number of studies indicate that a measurable amount of protein loss occurs in hookworm infection and is related to worm burden.[15,16]

The occurrence of hypoglobulinemia is common in intestinal parasitic infections where tissue penetration exists. In the present investigation globulin level was elevated in the infected group compared with the uninfected children, in agreement with earlier workers.[7,17] The rise in serum globulin in ascariasis and other helminth infections has been attributed to the increased production of antibodies bound to gammaglobulin in response to parasitic infection.[18]

Post-treatment observations following albendazole intervention showed a lowering of serum globulin and a gradual rise in albumin level in accordance with similar studies from other parts of the globe.[10–14] Stephenson *et al.* reported significant improvement in growth rates of Kenyan children infected with schistosomes and hookworm following treatment.[19] However, in the present popuation no significant gain in weight was registered, which was probably attributable to differences in baseline nutritional status, food intake, presence and treatment of other associated diseases and socio-economic status.[19,20]

Results showed that the children belonged to an anemic group. Because *Ascaris* does not contribute significantly to anemia, marked differences were not observed between the uninfected children and those harboring only *Ascaris* infection. Among intestinal helminth infections hookworm anemia is the most serious pathological complication and the small group (group 4) of 17 individuals with triple species combination had reduced hemoglobin level; probably *T. trichiura* and hookworm acted synergistically. Previous reports document blood loss and anemia due to *T. trichiura* infection.[21] High incidence of anemia could be dietary in origin. Due to the limited scope of the project, an estimation of ferritin and iron content of blood were not possible, which may have provided additional information to the source of anemia. The overall population exhibited decreased hemoglobin level even after drug intervention. It may be assumed that parasitic infection was an additional contributor to an existing anemic condition.

In conclusion, it needs to be emphasized that the role of soil transmitted helminths in the etiology of childhood malnutrition is significant. Therefore, control measures through intervention strategies of intestinal helminths is a prerequisite for any epidemiological study in an endemic area. The source of the infection needs to be targeted because multiple factors contribute to depressed food intake, intestinal function, nutrient absorption and malnutrition. The public health importance of intestinal helminths not only encompasses prevalence and intensity estimates but also other problems in terms of morbidity and mortality afflicting one-quarter of the world's population, especially infants and children of school age.

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印度南部Visakhapatnam 貧民區學齡兒童感染以土壤爲傳播媒介的蠕蟲病和由此導致的貧血和低白蛋白血症

摘要

在印度南部 Andhra Pradesh 省的 Visakhapatnam 魚民區 217 名學齡兒童（7－13 歲〕進行了爲期一年（1993 年八月至1994 年八月〕的追踪調查。利用福爾馬林－乙醚沉澱法來普查兒童的蛔蟲，鞭蟲和鈎蟲病的感染以及嚴重程度。同時，用標準方法測定了血清白蛋白和血紅蛋白。于1993 年十一月用口服400 毫克的Albendazole 對蠕蟲感染兒童進行了一次性的治療。在治療前后對患者進行了血液檢測和蟲卵計數。同時分别在治療后的第二個月，四個月和五個月的月尾做了治療后的蟲卵檢測；在第九個月尾做了血紅蛋白的檢查。調查結果顯示有82％的兒童患有腸道蠕蟲病，血紅蛋白平均值在9.7 ± 1.7 克/dl (5-13 克/dl)。約有88％兒童處于貧血狀態. 血清球蛋白升高 (4.63 ± 0.88)，但總血清蛋白水平仍屬正常 (8.61 ± 1.03 克/dl). 治療后的觀察顯示了徹底的驅蟲效果并且明顯地降低了血清球蛋白水平。但是仍然保持着中等程度的貧血，盡管在治療后九個月貧血狀態逐漸有所改善。治療后第五個月尾時的體重并没有顯著的增加。總的調查結果没發現有性别的差异。

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अगस्त 1993 से अगस्त 1994 के दौरान विशाखापट्टनम, आंध्र प्रदेश, के मछुआरे वर्ग के 217 बच्चों पर एक वृहद अध्ययन किया गया । ये सारे बच्चे 7 - 13 वर्ष के आयुवर्ग के थे । उन पर पेट की विभिन्न कृमियों Ascaris lumbricoides Trichuris trichiura एवं hookworm के लिए परीक्षण किए गए ।

रोग की गहनता के अध्ययन के लिए फार्मलीन - ईथर सेडिमेन्टेशन तकनीक का प्रयोग किया गया । इसके साथ हीमोग्लोबीन एवं सीरम प्रोटीन के माप के लिए रक्त के नमूने लिए गए और प्रचलित पद्धतियों का प्रयोग किया गया । रक्त के विभिन्न मापदंडों एवं अण्डकोषों की मात्रा, ऐल्बेन्डाजोल के 400 mg / बच्चा एकक चिकित्सा मात्रा, के पूर्व एवं चिकित्साकालीन परिणमों के लिए लगातार नापी गई । यह नवम्बर 1993 में हुआ । चिकित्सा - उपरान्त अध्ययन और परिणाम दूसरे, चौथे तथा पाँचवे महीनों में भी लेखबद्ध किए गए तथा हीमोग्लोबीन की मात्रा नौवें महीने में भी नापी गई ।

अध्ययन द्वारा 82 % में आंत की कृमियों तथा औसतन 9·7 g/dl ± 1·7 5 - 13 g / dl) मात्रा में हीमोग्लोबीन का आधिक्य, तथा 88% बच्चों में अनीमिया पाया गया । कुल सीरम प्रोटीन औसत मात्रा 8·61 ± 1·03 g/dl) का मिला तथा बढ़ा हुआ सीरम ग्लोब्युलिन 4·63 ± 0·88) पाया गया ।

चिकित्सा - उपरान्त अध्ययनों द्वारा कृमियों का पूर्ण-निकास एवं औसत सीरम ग्लोब्युलिन का स्तर पाया गया । यद्यपि सारी आबादी में औसत अनीमिया पाया गया जिसमें नौवें महीने में औसत सुधार आया । वजन में पाँचवे महीने तक कोई विशेष सुधार नहीं दिखा, संभवत: कारण यह हो सकता है कि तभी संक्रमण का विशेष दौर भी होता है । लिंग - भेद के अनुसार साधारण दरें से विशेष कोई बदलाव नहीं दिखा ।

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