

LIVER AND BILIARY

Nutritional factors in the aetiopathogenesis of amoebic liver abscess in man

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Abstract Thirty-seven patients with amoebic liver abscess and 20 controls were studied for their nutritional status. Their dietary history suggested deficient intake of total calories, protein, fat, Vitamin A and β carotene. No significant difference was observed in the levels of iron intake in patients and controls.

Biochemical parameters suggested a hypoproteinemic state associated with low levels of cholesterol, VLDL_c, HDL_c, Vitamin A, β carotene, iron and TIBC in the patients in comparison to controls. The protein electrophoresis pattern showed an increase in α_1 , α_2 , and γ fractions in patients compared with controls, whereas the albumin fraction was reduced.

On the basis of these findings and previously published experimental studies, it is suggested that amoebic liver abscess in human subjects is associated with undernutrition due to a poorly balanced diet. Thus, undernutrition may facilitate invasive amoebiasis in man.

INTRODUCTION

Amoebiasis is an endemic disease known to occur in almost every part of the world. Five to 30 per cent of the world's population has been found to carry *Entamoeba histolytica*

cysts in the colon.¹ Fortunately, prevalence of amoebic liver abscess is very much less amongst those who have protozoal parasites in the colon. Why do a few succumb and develop liver abscess? Alcoholism, malnutrition and decreased resistance of the host

have been suggested to favour the development of liver abscess, but none of these has been carefully investigated and proved responsible.

Wilmot and Singh *et al.* have stated that invasive amoebiasis is a disease of the lower socio-economic class where sanitation is poor and both poverty and malnutrition are common.^{2,3} Bran suggested that an insufficient or poor diet predisposed an individual to acute amoebic infection.⁴

The present study was undertaken to discover the association of common nutrient deficiencies, namely, protein, calories, Vitamin A and iron, with the amoebic liver abscess and to examine its possible pathophysiological significance.

METHODS

Subjects

A total of 37 patients (mean age, 37 ± 11 years) with amoebic liver abscess and 20 normal volunteer control subjects were studied. They were matched for age, sex and socio-economic status.

Diagnostic criteria for amoebic liver abscess

The diagnosis of amoebic liver abscess was established as per WHO recommendations which included: clinical features, aspiration of 'anchovy sauce' pus from the liver which was sterile on bacterial culture, demonstration of specific antibodies to *Entamoeba histolytica* and successful response to anti-amoebic therapy.¹ Normal healthy volunteers did not show *E. histolytica* cysts or trophozoites on stool examination and serological tests were negative.

Methods

Dietary history

The detailed dietary history of the patients and controls was obtained by questionnaire

and interview. This was used in conjunction with a 24 h recall of food intake.⁵ The dietary intake of each individual was determined and the nutrient intake — namely, calories, fat, carbohydrate, protein, Vitamin A, β carotene and iron — was calculated with the help of the Indian Council of Medical Research tables.⁶

Biochemical estimations

Plasma total proteins were estimated by the method of Kingsley,⁷ and albumin by the method of Doumas and Biggs.⁸ Paper electrophoretic fractionation of the serum proteins was carried out according to the method of Block *et al.*⁹ Lipoproteins were fractionated by the dual precipitation method of Wilson and Spiger.¹⁰ Cholesterol and triglycerides in plasma and its lipoprotein fractions were measured by chemical techniques.^{11,12} Serum iron and total iron-binding capacity (TIBC) were determined by the method of Mikac-Devic,¹³ while a micromethod was used for the estimation of serum Vitamin A and β carotene.¹⁴ The Student's *t*-test was used to assess the differences statistically.

RESULTS

Dietary intake

The dietary intake by patients and controls is shown in Table 1. The intake of calories, protein, carbohydrate, fat, Vitamin A and β carotene was significantly low in the patient group compared with the controls ($P < 0.001$). However, no significant difference was observed in the intake of iron between the two groups (Table 1).

Blood biochemistry

Blood biochemistry reflected a pattern of undernutrition for most of the essential nutrients amongst patients of amoebic liver abscess; levels of proteins and albumins in the

Table 1 Nutrient intakes of amoebic liver abscess patients and controls

	Controls		Patients		<i>P</i> *
	mean	s.d.	mean	s.d.	
Number of cases	20		37		
Calories	2502	123	1561	62	<0.001
Protein (g)	76	4	47	2	<0.001
Carbohydrates (g)	354	20	242	13	<0.001
Fat (g)	79	6	45	2	<0.001
Iron (mg)	48	6	37	2	NS
Vitamin A (iu)	2006	165	914	82	<0.001
β Carotene (μg)	3236	155	2237	142	<0.001

* Significant difference at the 99.9% level.

plasma of patients with amoebic liver abscess were found to be significantly reduced in comparison with the control group ($P < 0.001$). The A/G ratio was found to be altered in the patients (Table 2). The protein electrophoresis pattern in patients showed an increase in the α_1 , α_2 and γ fractions and a

decrease in the albumin fraction (Table 3). There was no significant difference in the plasma triglycerides and the lipoprotein fractions (Table 4). However, the levels of plasma cholesterol and lipoproteins were found to be significantly lower in patients compared with the controls ($P < 0.001$) (Table 5). Significant

Table 2 Plasma proteins in amoebic liver abscess patients and controls

	Controls		Patients		<i>P</i> *
	mean	s.d.	mean	s.d.	
Number of cases	20		37		
Protein					
Total	7.60	0.8	6.43	0.12	<0.001
Albumin	4.20	0.04	2.95	0.10	<0.001
Globulin	3.36	0.06	3.60	0.11	NS
A/G ratio	1.26		0.83		<0.01

* Significant difference at the 99.9% level.

Table 3 Protein electrophoresis pattern in amoebic liver abscess patients and controls

	Controls		Patients		<i>P</i> *
	mean	s.d.	mean	s.d.	
Number of cases	20		37		
Albumin (%)	57.4	1.0	29.8	1.4	<0.001
Alpha ₁ (%)	3.4	0.5	6.8	0.4	<0.001
Alpha ₂ (%)	5.7	0.5	12.0	0.9	<0.001
Beta (%)	8.3	0.6	8.5	0.7	NS
Gamma (%)	25.3	1.4	43.3	1.9	<0.001

* Significant difference at the 99.9% level.

Table 4 Mean values of plasma triglycerides and lipoproteins in amoebic liver abscess patients and controls

	Controls		Patients		P
	mean	s.d.	mean	s.d.	
Number of cases	20		37		
Triglycerides (mg%)					
Total	135	11	145	10	NS
VLDL	47	8	53	8	NS
LDL	34	4	43	4	NS
HDL	45	5	51	6	NS

NS = not significant.

Table 5 Values of plasma cholesterol and lipoproteins in amoebic liver abscess patients and controls

	Controls		Patients		P*
	mean	s.d.	mean	s.d.	
Number of cases	20		37		
Cholesterol (mg%)					
Total	163	7	84	5	<0.001
VLDL	42	4	21	2	<0.001
LDL	72	5	38	3	<0.001
HDL	39	4	19	2	<0.001

* Significant difference at the 99.9% level.

differences in the levels of Vitamin A and β carotene were noted between the patients and the controls ($P < 0.001$). Iron and TIBC levels were found to be low in patients compared with controls. The mean level of iron was 134 $\mu\text{g} \%$ in controls and 55 $\mu\text{g} \%$ in patients; TIBC levels were 349 $\mu\text{g} \%$ in controls and 264 $\mu\text{g} \%$ in patients.

DISCUSSION

The results of the present study clearly suggest an association of undernutrition with amoebic liver abscess in man. The dietary history of patients with amoebic liver abscess shows a deficient intake of calories, protein, fat and Vitamin A. A few earlier clinical studies have also suggested that acute amoebiasis in human subjects is related to poorly balanced diet.^{15,16} Undernutrition was further confirmed by serum biochemistry. Total protein and albumin were diminished in the patients compared with the controls. Hypo-

albuminaemia has been demonstrated in 100% of patients with hepatic amoebiasis by El Zayadi.¹⁷ Powell has also reported hypoalbuminaemia in patients with amoebic liver abscess.¹⁵ Hypoalbuminaemia has been presumed to be predominantly of dietary origin.¹⁸ Data from the present study support this possibility. Since the illness is of short duration, it is unlikely to be secondary to the liver abscess. Further, in a previous experimental study it was demonstrated that acute illness due to liver abscess did not result in a significant fall in serum protein and albumin levels.¹⁹ It is well known that in amoebic liver abscess the liver functions are well preserved with minimal alteration detected by liver function tests.^{1,17} Therefore, it is unlikely that hypoproteinaemia observed in patients of amoebic liver abscess is due to liver dysfunction.

Cholesterol and lipoprotein fractions (i.e. VLDL_c, LDL_c and HDL_c) are significantly reduced in patients when compared with controls. Segovia *et al.* have reported low

levels of cholesterol, pre- β , β and α -lipoproteins in amoebic abscess with extensive liver lesions.²⁰ Several factors may account for the low serum cholesterol levels in these patients. Exogenous sources of preformed cholesterol may be limited since the diet of the patients is primarily of vegetable origin. Synthesis of endogenous cholesterol might also be reduced due to calorie deficiency. Reduced synthesis of endogenous cholesterol has been reported in rats²¹ and chicks²² infected with trophozoites.

The average daily fat intake by the patients in the present study was 45 g, which is much less than the intake by the controls. Yet the levels of triglycerides were normal in the patients. This could be due to the regulatory mechanism, directing acetyl CoA to fatty acid synthesis and thereby to triglycerides.²³

Low levels of iron and TIBC were observed in patients in comparison with the controls, in spite of the fact that there was no significant difference in their iron intake. Diamond *et al.* studied iron and TIBC levels in 33 male patients of active hepatic amoebic disease and showed that their serum iron levels were approximately one-half that of healthy males, and TIBC one-third less than that of the controls.²⁴ They suggested that the host reacted by inducing a hypoferrimic state and as part of this process transferred iron to the liver, thereby providing the environment for colonization by the amoebae, since iron is utilized by the parasite for its growth and multiplication.

Low levels of Vitamin A and β carotene were observed in patients in the present study. This is probably due to inadequate intake of Vitamin A and B carotene, but it may also reflect poor intestinal absorption, as the diet had low fat content and absorption of both Vitamin A and β carotene is enhanced by dietary fat and vice versa.²⁵ Rodgar and associates have shown low serum β carotene and Vitamin A values in individuals with hookworm disease compared with healthy individuals in the same community.²⁶

An association of calorie, protein and Vitamin A undernutrition with amoebic liver

abscess seems to be established by the results of this study. These, together with iron, are the four major nutrient deficiencies apparent in India and in many other parts of the world. The findings raise the question of whether the undernutrition is the cause or the effect of amoebiasis. This question cannot be completely resolved by clinical studies, and experimental investigations have revealed some significant findings on this issue.¹⁹ Hamsters reared on deficient nutritional diets (low calorie, low protein, low Vitamin A) were more susceptible to amoebic liver abscess compared with hamsters reared on a balanced diet. The striking feature of the study was that although blood levels of protein, albumin, cholesterol and Vitamin A were significantly reduced at the end of 4 weeks of deficient diet intake, there was no further reduction of these biochemical markers in blood after the experimental abscess was reduced. This led to the conclusion that acute amoebic liver abscess does not lead to any significant malnutrition in experimental animals, whereas amoebic abscess is more common in undernourished animals. One must be careful in extrapolating from results in animals to human beings and with this caution in mind it can be suggested that in the human situation investigated in the present study, the nutrient deficiency is likely to be dietary in origin and malnutrition could favour the occurrence of liver abscess in persons with *Entamoeba histolytica* infection in the colon. Further absence of significant improvement in caloric and nutrient intake and serum lipid and lipoprotein levels after successful therapy in patients of amoebic liver abscess supports the suggestion that undernutrition is the cause rather than the effect of amoebic liver abscess.²⁷

Diamond, in his review article on the role of malnutrition predisposing amoebiasis, opined that nutritional deficiencies of the host possibly correlates with a higher incidence of infection and/or severity of the disease. He named this association 'synergism'. The present study also demonstrated a synergistic association between nutritional deficiencies and amoebic liver abscess.

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