Impact of Liver Cirrhosis on Nutritional and Immunological Status

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Abstract

The aims of the study were to determine the prevalence of protein calorie malnutrition (PCM) in Thai cirrhotic patients and to evaluate nutritional and immunological status in various stages of cirrhosis. Subjective Global Assessment (SGA) and anthropometric measurement were used as nutritional assessment in sixty cirrhotic patients. Delayed-type hypersensitivity skin test, lymphocyte count, immunoglobulin and complement were assessed for immune status. Blood samples were sent for routine tests, prealbumin, thiamine and riboflavin level. There were 7/60 (11.7%) patients with percentage of ideal body weight (%IBW) less than 90 per cent. SGA, hemoglobin, protein indices and cholesterol level showed the deterioration of nutritional status in the late stage of the disease. Five (8.3%) patients with thiamine deficiency, and thirteen (21.7%) patients with riboflavine deficiency were detected. Lowest levels of complement and highest levels of immunoglobulin also occurred in the late stage of the disease. In conclusion, defining %IBW <90 per cent as malnutrition, the prevalence of malnutrition in Thai cirrhotic patients was 11.7 per cent. Nutritional and immunological status deteriorated according to the advanced stage of disease. If nutritional support is given in the early stage, it may improve nutritional status and reduce morbidity and mortality in cirrhotic patients.

Key word : Liver Cirrhosis, Nutritional Status, Immunological Status

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It is well accepted that protein calorie malnutrition (PCM) can occur in patients with chronic liver disease from many causes(1). Derangement in nutrients metabolism and decreased appetite are two of the important factors which potentiate this condition. The prevalence of PCM in chronic liver

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disease from previous studies has ranged between 10 per cent and 100 per cent[2,3]. Moreover, PCM is an independent risk factor predicting clinical outcomes and survival rate of these patients[2,4,5]. The prevalence of malnutrition correlated closely with the severity of liver disease[2,3]. However, the results from other studies did not support this finding[6]. Some studies suggested that nonalcoholic cirrhosis had less severe PCM than alcoholic cirrhosis[7,8]. Malnutrition status is aggravated by direct damage of alcohol on intestinal mucosa which leads to abnormality in nutrients absorption mechanisms. Nevertheless, one study revealed that PCM was common in both alcoholic and nonalcoholic cirrhosis, but was more pronounced in the latter[9]. Therefore, the aims of this study were to determine the prevalence of PCM in Thai cirrhotic patients, to evaluate nutritional and immunological status according to stages of cirrhosis, and to compare nutritional status of alcoholic and nonalcoholic cirrhotic patients.

MATERIAL AND METHOD

The research was conducted as an analytical and cross-sectional study between 1 June 1999 and 31 December 1999 at the outpatient clinic, Department of Medicine, Ramathibodi Hospital, Faculty of Medicine, Mahidol University. All patients provided written informed consent and fluid status was effectively controlled with diuretic drugs before enrollment. Sixty patients with underlying cirrhosis were diagnosed by the presence of cutaneous stigmata of chronic liver diseases, biochemical test suggestion and at least one of the following criteria: esophageal or gastric varices, sonographic diagnoses or liver histology confirmation. Patients with other underlying diseases, allergic diseases, renal insufficiency (Cr>2mg/ml), unstable condition and noncooperation were excluded from the study. The study began with the assessment of clinical, nutritional and immunological status. Nutritional assessment was performed by an experienced nutritionist. Patients were interviewed to recall 24 h dietary intake[10], and their nutritional status was evaluated for Subjective Global Assessment (SGA)[11] and was classified further into three classes : A (normal), B (suspected or moderate malnutrition), C (severe malnutrition). Mid-arm circumference (MAC) and skin fold thickness at triceps (TSF), biceps (BSF), subscapular and suprailiac were measured as anthropometric measurement[10]. Then, arm muscle area (AMA) was calculated[10]. Hand grip strength was evaluated by hand grip dynometry[12]. Immunological assessment comprised absolute lymphocye count and intradermal skin test with three antigens (: *Candida* spp, Tetanus and Diptheria toxoid) for cell-mediated immune response. If patients do not any skin reaction larger than 5 mm after antigen sensitization, their immune status will be interpreted as in anergy state[13]. Moreover, immunoglobulin and complement levels were evaluated for humoral immune response[13]. Blood was collected for routine tests, prealbumin and vitamin level. Thiamine level was assessed by using erythrocyte transketolase activity (ETKA) and thiamine pyrophosphate effect (TPPE). TPPE value higher than 15 per cent was considered as thiamine depletion. Riboflavin status was assessed by using erythrocyte glutathione reductase activity (EGRA) and activity coefficient (AC), AC value equal or greater than 1.2 indicated riboflavin depletion[14]. Twenty-four hour urine was collected and calculated for creatinine height index (CHI)[10].

Collected data were compared between the alcoholic and nonalcoholic cirrhotic groups, and among the three stages of cirrhosis according to Child-Pugh classification[15]. Unpaired *t* test, analysis of variance and non-parametric test were used to analyze data as appropiate. A p value of 0.05 or less was considered significant.

RESULT

Sixty cirrhotic patients were recruited into the study. Thirty-three patients were male and twenty-seven patients were female. A mean age of the patients was 56.3±11.0 (21-76 years). The characteristics of the alcoholic and nonalcoholic cirrhotic groups are shown in Table 1. Fat mass (mean TSF) of the alcoholic group was significantly lower than that of the nonalcoholic group. Nutritional changes according to varying stages of cirrhosis are demonstrated in Table 2. Muscle mass (CHI) between Child B and Child C groups was significantly different. In addition, hemoglobin and cholesterol levels were significantly lowest in the Child C group. Fig. 1 shows worsening of SGA status which appeared increasingly in the late stage of the diseases. (p= 0.007) Decreasing levels of albumin and prealbumin

Table 1. Data classified by causes of cirrhosis.

	Alcoholic cirrhosis (n=29)	Nonalcoholic cirrhosis (n=31)
Age (years)	54.8 ± 9.9	57.8 ± 11.9
Male, n (%)	18 (62.1)	15 (48.4)
BMI (kg/m^2)	22.8 ± 3.9	24.5 ± 3.4
Percentage of IBW (%)	107.9 ± 16.4	111.5 ± 17.4
Calorie intake (kcal/kg/day)	21.9 ± 6.5	21.8 ± 7.4
Protein intake (g/kg/day)	0.95 ± 0.5	0.91 ± 0.4
TSF (mm)[a]	13.0 ± 5.5	16.5 ± 7.2
AMA (cm^2)	42.4 ± 11.8	40.5 ± 10.2
Hemoglobin (g/dl)	12.1 ± 2.3	12.6 ± 1.8
Cholesterol (mg/dl)	171.8 ± 54.7	166.5 ± 51.3
Calcium (mg/dl)	9.5 ± 0.6	9.3 ± 0.6
Phosphate (mg/dl)[b]	3.6 ± 0.7	3.1 ± 0.7

Values are expressed as mean ± SD, [a] p=0.039, [b] p=0.011
BMI = Body mass index, IBW = Ideal body weight, TSF = Triceps skin fold,
AMA = Arm muscle area

Table 2. Comparison of nutritional status according to stages of liver cirrhosis.

	Child A (n=31)	Child B (n=21)	Child C (n=8)
Age (years)	58.2 ± 9.5	52.9 ± 14.4	52.5 ± 5.2
Percentage of IBW<90%, n (%)	4 (12.9)	2 (9.52)	1 (12.5)
TSF (mm)	15.5 ± 5.8	13.6 ± 5.5	12.9 ± 7.8
AMA (cm^2)	42.9 ± 10.9	41.3 ± 11.2	35.6 ± 9.3
CHI[a]	71.2 ± 14.6	80.4 ± 24.9	56.6 ± 17.3
Hemoglobin (g/dl)[b, c]	12.7 ± 1.9	12.8 ± 1.9	10.1 ± 1.7
Cholesterol (mg/dl)[d, e]	178.6 ± 48.6	173.1 ± 56.9	124.5 ± 29.8
Phosphate (mg/dl)	3.4 ± 0.8	3.4 ± 0.5	3.1 ± 1.0

Values are expressed as mean ± SD
[a] p=0.024 between Child B & C, [b] p=0.001 between Child A & C,
[c] p=0.001 between Child B & C, [d] p=0.008 between Child A & C,
[e] p=0.023 between Child B & C
IBW = Ideal body weight, TSF = Triceps skin fold, AMA = Arm muscle area,
CHI = Creatinine height index

according to stage of cirrhosis are shown in Fig. 2. Of sixty patients, there were five (8.3%) patients with thiamine deficiency, with two of them in the alcoholic group, and the remainder in the other group. Furthermore, there were thirteen (21.7%) patients with riboflavine deficiency. Six of them were in the first group, and the remainder were in the latter group. Lymphocyte count, number of anergy and complement level among various stages of cirrhosis are demonstrated in Table 3. Anergy tended to increase in the late stage of disease. Immunoglobulin G and A levels were significantly elevated in Child C group. (Fig. 3)

DISCUSSION

Nutritional status of the alcoholic cirrhotic group, in terms of fat mass, was more impaired than that of the other group but this can be influenced by the presence of more male patients in the first group. Some studies showed that sex could affect nutritional assessment[16]. Even though both alcoholic and nonalcoholic cirrhotic groups had a mean percentage of ideal body weight (%IBW) higher than 100 per cent, there were seven (11.7%) patients with %IBW less than 90 per cent. The disadvantage of using body weight index to study nutritional status in cirrhotic liver diseases which have a salt

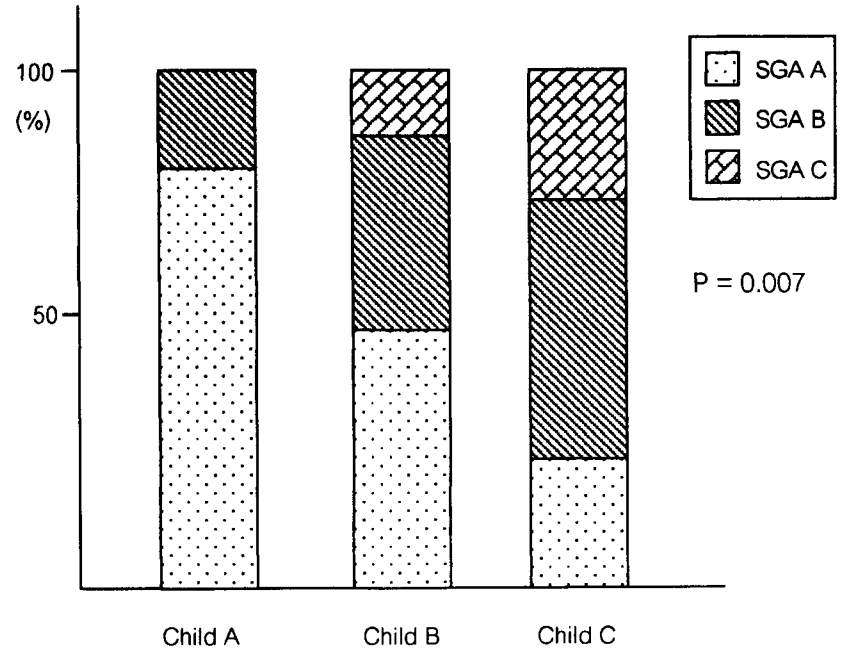

Fig. 1. Comparison of Subjective Global Assessment (SGA) according to stages of cirrhisis.

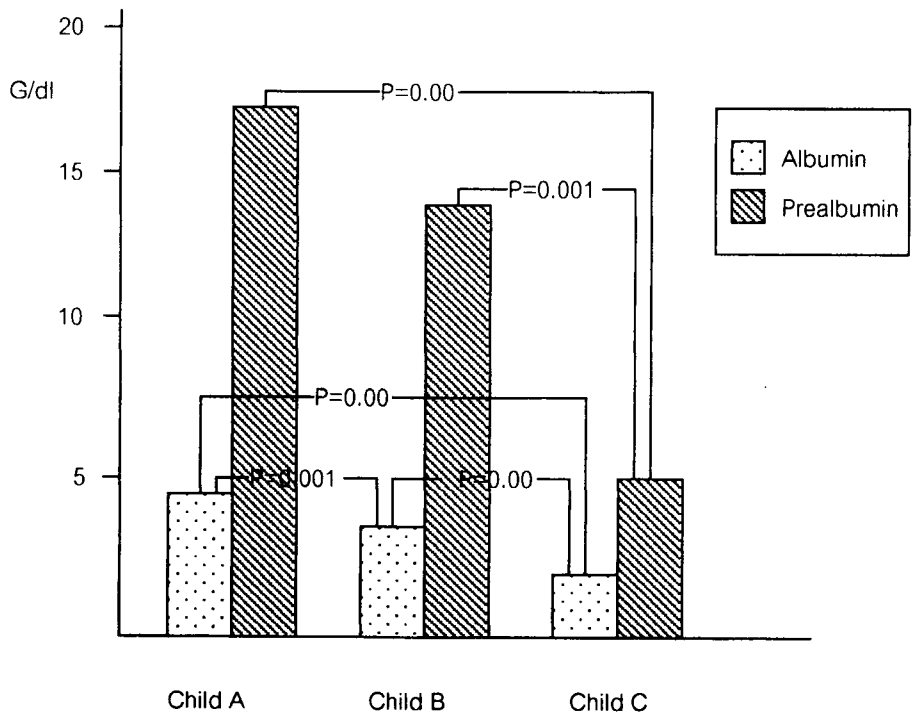

Fig. 2. Comparison of protein synthesis indices according to stages of cirrhosis.

Table 3. Comparison of immunological status according to stages of cirrhosis.

	Child A	Child B	Child C
Lymphocyte count (mm^3)	15,68.6 ± 758.1	1,580.3 ± 528	1,196 ± 309.4
Anergy, n (%)	5 (16.1)	4 (20)	4 (50)
C3 (mg/dl)[a, b]	1,091.7 ± 512.5	834.5 ± 360.4	700 ± 245.5
C4 (mg/dl)[c]	188.0 ± 66.1	160.6 ± 67.8	125.9 ± 49.3
CH50 (%)	78.2 ± 4.2	82.1 ± 25.2	65.6 ± 8.6

Values are expressed as mean ± SD, [a] p=0.04 between Child A & B, [b] p=0.03 between Child A &C, [c] p=0.02 between Child A & C

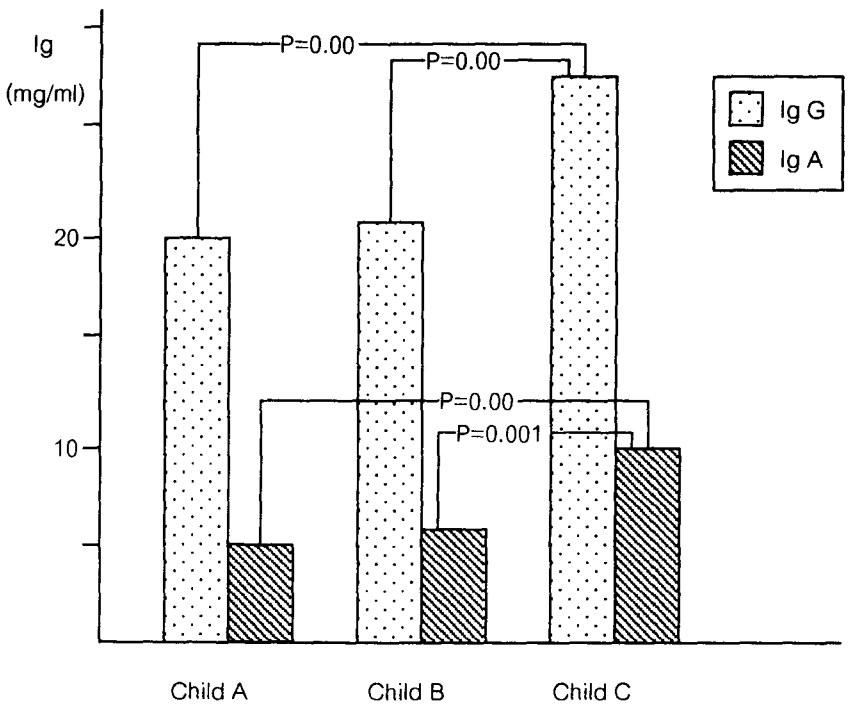

Fig. 3. Comparison of humoral immune response according to stage of cirrhosis.

and water retention state was the underestimation of both the prevalence and degree of malnutrition. SGA combined with CHI, the levels of hemoglobin, cholesterol, albumin and prealbumin demonstrated the deterioration of nutritional status in the advanced state of cirrhosis. However, albumin and prealbumin which are synthesized from the liver can be affected by the stage of liver disease. Furthermore, the changing pattern of amino acids observed in chronic liver disease consists of a rise in aromatic amino acids and a fall in branched chain amino acids[17,18]. From this study, calorie intake which was lower than recommendation (25-40 kcal/kg/day)[19] may be one of the factors that contributed to PCM in the patients. Deficiency of nutrients is often associated with liver disease and may be caused by decreased dietary intake from anorexia, decreased nutrients absorption and storage, abnormalities in metabolism or the increased requirement for nutrients[17,20,21]. A large number of patients with thiamine or riboflavine deficiency were detected in the study. Multiple vitamins deficiency

has been a common problem occurring in patients with chronic liver disease[17,22]. Impaired cell-mediated immune response and complement synthesis occurred in the advanced stage of the disease. This can be explained by poor nutritional status and impaired liver cell function, respectively. In contrast, there was increased immunoglobulin level in the advanced stage of cirrhosis. The major factors of elevated immunoglobulin seem to be the failure of the damaged liver to clear intestinal antigens. Such antigens bypass the liver through porto-systemic channels or through the internal shunt around the cirrhotic nodule[15].

In conclusion, defining %IBW less than 90 per cent as malnutrition, the prevalence of malnutrition in Thai cirrhotic patients was 11.7 per cent. Overall nutritional status, biochemical evaluation and immunological response were impaired in the late stage of cirrhosis. If nutrition supplementation is given in the early stage of cirrhosis, it may improve the nutritional and immunological status and reduce morbidity and mortality in these patients.

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ผลของโรคตับแข็งต่อภาวะโภชนาการและภูมิต้านทานของร่างกาย

อาภัสณี โสภณสฤษฏ์สุข, พ.บ., จุฬาภรณ์ รุ่งพิสุทธิพงษ์, พ.บ.*, กนกรัตน์ นันทิรุจ, พ.บ.*, ไสวรินทร์ กุลพงษ์, พ.บ.**, ศรีวัฒนา ทรงจิตสมบูรณ์, วท.ด.**, แขไข สุมาลย์นพ, วท.บ.*, นันทา บุษกร, วท.บ.**

การศึกษาภาวะโภชนาการและภูมิต้านทานร่างกายของผู้ป่วยโรคตับแข็ง 60 คน เพื่อหาความชุกของภาวะขาดสารอาหาร พลังงานและศึกษาความเปลี่ยนแปลงของภาวะทั้งสองในระยะต่าง ๆ ของโรคตับแข็ง ผู้ป่วยทุกคนได้รับการซักประวัติอาหาร ประเมินภาวะโภชนาการด้วยแบบประเมิน Subjective Global Assessment (SGA) วัด Anthropometry ร่วมกับประเมินภูมิต้านทานร่างกายด้วยการทดสอบภูมิต้านทานที่ผิวหนัง จำนวนเม็ดเลือดขาวและระดับของ Complement และ Immunoglobulin พบผู้ป่วย 7 ราย (11.7%) มี %IBW ต่ำกว่า 90% การประเมินภาวะโภชนาการด้วย SGA, ความเข้มข้นของเลือด, ระดับของโปรตีนและไขมันพบภาวะโภชนาการต่ำลงเมื่อระยะของโรคตับแข็งสูงขึ้น พบผู้ป่วย 5 ราย (8.3%) ขาดวิตามินบี 1 และผู้ป่วย 13 ราย (21.7%) ขาดวิตามินบี 2 ผู้ป่วยโรคตับแข็งระยะท้ายมี Complement ต่ำลง แต่ Immunoglobulin สูงขึ้นอย่างมีนัยสำคัญทางสถิติ การศึกษานี้สรุปได้ว่าพบภาวะขาดสารอาหารและพลังงานในผู้ป่วยโรคตับแข็ง 11.7% ภาวะโภชนาการและภูมิต้านทานโดยทั่วไปต่ำลงในระยะท้ายของโรคตับแข็ง จึงมีความจำเป็นที่ต้องคำนึงถึงภาวะนี้ในผู้ป่วยโรคตับแข็ง

คำสำคัญ : โรคตับแข็ง, ภาวะโภชนาการ, ภาวะภูมิต้านทาน

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