SERUM THYROID STIMULATING HORMONE (TSH) IN MALNUTRITION: PRELIMINARY RESULTS

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ABSTRACT

This is a report of a cross sectional study involving 3 groups of children, moderately malnourished (BMI<15), mildly malnourished (BMI 15 - 18) and well nourished (BMI>18) to determine the differences in hormonal and biochemical parameters between the groups. The children were of age range from 7 - 17 years old. The children were from the same area with exposure to the same food, drinking water and environment. There were significant differences in the nutritional indices between the three groups. No differences were observed in levels of triiodothyronine (T3), thyroxine (T4) and T3:T4 ratio. Significant difference however was found in the TSH levels using highly sensitive IRMA TSH assays. Moderately malnourished children had higher TSH levels ($p<0.05$) compared to mildly malnourished and well-nourished children. No difference was found between the mildly malnourished and well-nourished groups. There were no significant differences in serum cortisols done at similar times, fasting growth hormone and calcium. Serum alanine transaminase (ALT) however was higher in moderately malnourished than in well-nourished children. Thus using highly sensitive IRMA TSH assays, we were able to detect differences in TSH levels even though T3, T4 and T3:T4 ratio, cortisol, growth hormone and calcium were normal, implying in moderately malnourished children, a higher TSH drive to maintain euthyroid state.

Keywords: *Serum thyroid stimulating hormone (TSH), thyroxine, triiodothyronine, growth hormone, cortisol, malnutrition*

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INTRODUCTION

Malnutrition is a widespread problem around the world especially in developing countries. It was estimated that about 500 million people in developing countries suffer from malnutrition and starvation especially among children[1]. Malnutrition not only causes high mortality but also morbidity especially due to deficiency of various essential elements and minerals. Malnutrition has been known to have short and long term effects on disease response, cognitive function, reproductive competence, work output, social behaviour of the individuals[2]. Protein Energy Malnutrition (PEM) is known to induce a variety of metabolic disturbances, some of which may be mediated through dysfunction of the endocrine glands. Chronic starvation and calorie restriction has been found to alter the function of the thyroid gland, pancreas, pituitary and gonads. The alterations represent adaptation of the organism to the altered nutritional status[3]. The aim of this study is to look at the hormonal and biochemical abnormalities associated with malnutrition of various degrees among the children living in the same environment.

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MATERIALS AND METHODS

Subjects

This study is part of a large project to determine the relationship between malnutrition and endocrine disorders in Peninsular Malaysia. Twenty-six children aged 7 to 17 years old (10 male and 16 female) from Kuala Pangsoon area, 40 km from Kuala Lumpur, were selected according to their nutritional status by using anthropometric assessments. They were divided into 3 groups, moderately malnourished, mildly malnourished and well nourished according to their body mass index (BMI) and nutritional assessment. Ten children with BMI of less than 15 were classified as moderately malnourished, 7 children with BMI of 15 to 18 as mildly malnourished and 9 children with BMI above 18 as well nourished[4,5]. Apart from weight and height, other indices of nutritional status were utilised to examine the criteria of classification. As shown in Table I, there were significant differences in the mid-arm circumference (MAC), supra iliac skinfold thickness (SIST) between the groups. None of the children were severely malnourished (Kwashiorkor or marasmus).

Weight was measured using Seca bathroom scale, read to the nearest 0.5 kg, whilst height was measured by Microtoise, read to the nearest 0.1 cm following standard procedures. Mid-arm circumference was measured on the left upper arm by using flexible tape and SIST by using calibrated Harpenden's caliper.

Hormonal and biochemical evaluations

Following overnight fast, 20 ml of blood were obtained by venepuncture for various biochemical and hormonal assessments. Fasting blood glucose were measured using glucose analyser (Reflotron, Boehringer Mannheim). Serum total thy-

roxine (T4) and triiodothyronine (T3) levels were measured by using radioimmunoassay (RIA), Thyrotropin (TSH) by immunoradiometric assay (IRMA) from North East Thames Region Radioimmunoassay Unit, St. Bartholomew's Hospital, London (NETRIA)[6]. The sensitivity for T3 assay was 3.2nM, T4 0.29 nM and TSH<0.1 mU/L. Serum growth hormone and cortisols were measured using in-house radioimmunoassays[7]. Calcium and serum alanine transaminase (ALT) were analysed by using Technicon SMA II autoanalyser.

Table I - Nutritional indices among moderately malnourished, mildly malnourished and well-nourished children (age range from 7 - 17 years)

		Moderately malnourished children (n=10)	Mildly malnourished children (n=7)	Well nourished children (n=9)
age+ (years)	7 - 12	7	4	3
	13 - 17	3	3	6
BMI (kg/m)	median	14.6	16.6	21.4
	range	13.0-14.9	15.7-17.4	18.0-36.1
	mean [sd]	14.3 [0.7]	16.5 [0.8]	21.4 [6.2]
MAC (cm)	median	18.2*a,b	20.8	23.3
	range	15.5-19.0	19.0-22.5	16.9-30.0
	mean [sd]	17.4 [1.5]	20.9 [1.3]	23.3 [3.8]
SIST (cm)	median	5.9*b	6.9	9.8
	range	4.1-8.1	5.3-16.0	5.4-22.2
	mean [sd]	5.9 [1.1]	8.7 [3.8]	10.9 [4.9]

* : Mann-Whitney signed rank test
a : p<0.05 moderately malnourished vs mildly malnourished
b : p<0.05 moderately malnourished vs well-nourished
+ : number of subjects in a particular age group

Statistical analysis

The results were analysed using Mann-Whitney signed rank test (non-parametric statistical procedures). A statistically significant difference was considered to be present at $p<0.05$.

RESULTS

Thyroid hormones (T3, T4) and TSH

No significant differences were observed between the groups for serum T3, T4 levels and T3:T4 ratio. There was a significant difference in the serum TSH levels between moderately malnourished and mildly malnourished (Mann Whitney z=2.1, p=0.04) or well-nourished children (z=2.2, p=0.03). Moderately malnourished children had higher TSH compared to the other two groups. No differences were observed between mildly malnourished and well-nourished children (Fig 1a, 1b, 1c and 1d).

Growth hormone

Single morning fasting serum specimen for growth hormone did not show any differences between the groups (Fig 2). Three of moderately malnourished children (30%), three of mildly malnourished (43%) and five of well-nourished (55.5%) had growth hormone levels higher than 15.0 mIU/L which is equivalent to the value of 10 mIU/L using reference standard IRP 66/217[8]. Using the test between the two proportions, the difference in proportion between moderately malnourished children or mildly malnourished children with well-nourished children was not statistically significant (p>0.05).

Cortisol

Even though the median value for moderately malnourished children tended to be lower compared to the other two groups there was no significant difference (p>0.05) between the groups (Fig 3) (normal values 93-315 nmol/l).

Other metabolic indices

There were no significant differences (p>0.05) in the median of fasting blood glucose (FBS) and serum calcium between the groups. None of the children had abnormal level of calcium and ALT. However ALT was significantly higher (p<0.05) in malnourished childred compared to well-nourished children (Table II).

Fig 1a - Serum triiodothyronine among moderately malnourished, mildly malnourished and well-nourished children

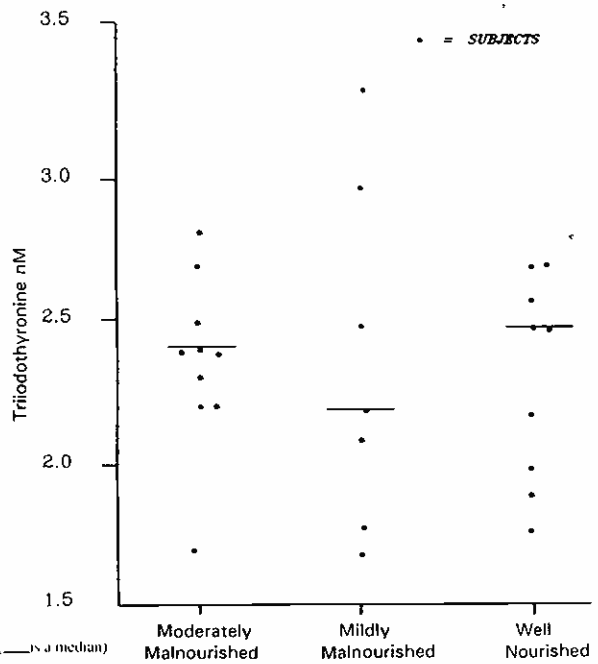


Fig 1b - Serum thyroxine among moderately malnourished, mildly malnourished and well nourished children

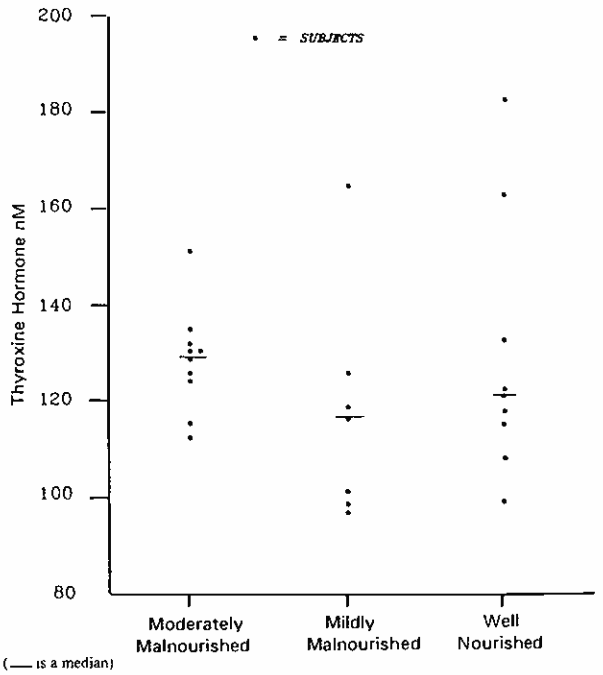
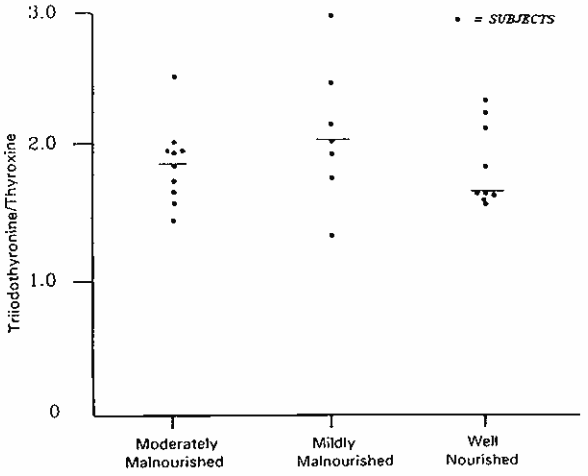
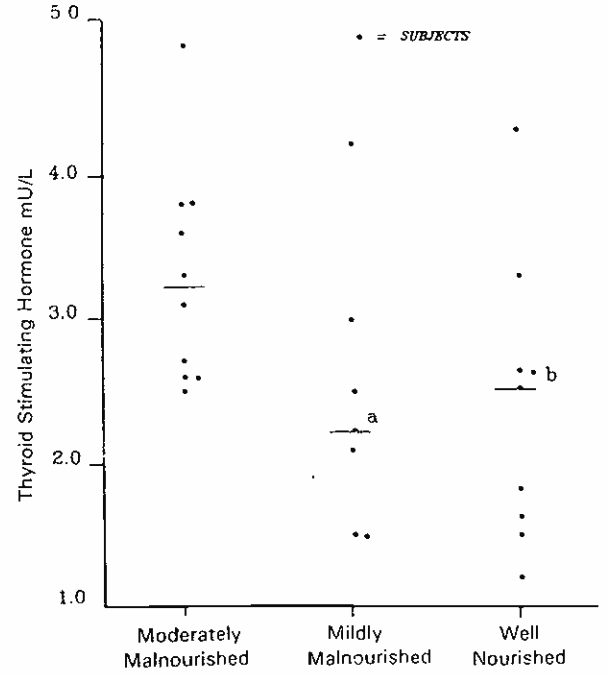


Fig 1c - The ratio of triiodothyronine : thyroxine among moderately malnourished, mildly malnourished and well-nourished children



(— is a median)

Fig 1d - Serum thyroid stimulating hormone among moderately malnourished, mildly malnourished and well-nourished children

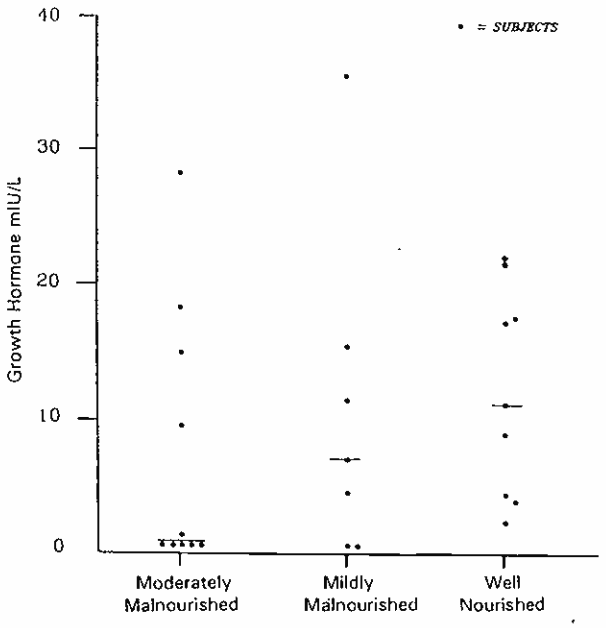


(— is a median)

Mann-Whitney signed rank test on TSH level
a : p=0.04 (moderately malnourished vs mildly malnourished)
b : p.0.03 (moderately malnourished vs well-nourished)

No significant difference for the other hormones.

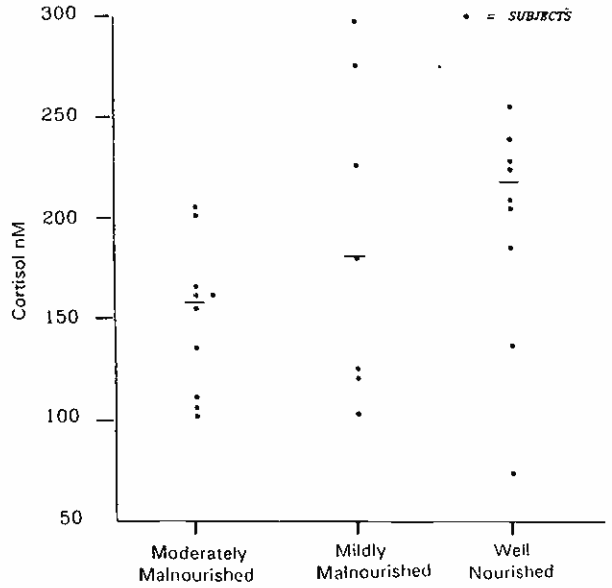
Fig 2 - Serum growth hormones level among moderately malnourished, mildly malnourished and well-nourished children



(— is a median)

No significant difference between groups (p>0.05)

Fig 3 - Serum cortisol levels among moderately malnourished, mildly malnourished and well-nourished children



(— is a median)

No significant difference between groups (p>0.05)

DISCUSSION

Hormones play important roles in the adaptive processes of energy and protein metabolism in PEM[3]. In this study, serum total T4 and T3 levels were normal in the children with or without malnutrition. In other studies, the level of T4 were either normal or decreased, and level of T3 usually decreased in PEM[9-11]. The serum level of T3 was not decreased in this study, in contrast to other studies where the level of T3 were low in PEM[12]. In that study, the lower T3 levels were found among hospitalised severely malnourished children with marasmus and kwashiorkor[12]. The T3:T4 ratio was not significantly different between the 3 groups. This ratio is usually reduced in malnourished children and increased during recovery with protein-rich diet[11]. The difference in our study compared to others thus is likely to be due to the severity of malnutrition in the children we assessed compared to those reported previously[9-12]. Even though the BMI, MAC and SIST were significantly different, no differences could be detected

Table II - ALT and calcium level among moderately malnourished, mildly malnourished children and well-nourished children

		Moderately malnourished children	Mildly malnourished children	Well nourished children
ALT (IU/L)	median	22**	20	7
	range	14-28	14-26	4-28
	mean [sd]	22.7 [4.4]	19.8 [4.5]	10.9 [8.4]
Calcium (mmol/L)	median	2.3	2.3	2.4
	range	2.1-2.5	1.1-2.4	2.1-2.8
	mean [sd]	2.3 [0.1]	2.1 [0.5]	2.4 [0.2]

* : Mann-Whitney signed rank test for median

a : p<0.05 moderately malnourished vs well-nourished

in T4, T3 or T3:T4 ratio, implying that only in severe malnutrition would there be changes in these parameters. Serum TSH were elevated in malnourished children. This finding is comparable to other studies reported elsewhere[5,12]. Thus even though T4, T3 and T3:T4 ratio were not significantly different in moderately malnourished children, using highly sensitive IRMA TSH assays, we were able to demonstrate significant differences in serum TSH. TSH would also be elevated in endemic goitre but in this study only one malnourished child had a goitre. Elevated serum TSH in PEM was associated with exaggerated response to stimulation by thyrotropin releasing hormone (TRH)[13]. However, impaired catabolism of TSH rather than increased secretion would also be responsible for the increase in TSH[12].

Growth hormone (GH) levels have been reported to be high in severe malnutrition such as in kwashiorkor[12]. This was postulated to be due to the low albumin level that stimulates the secretion of growth hormone and the absence of feedback inhibition by somatomedins[13,14]. Differences in GH were not found in this study. Even though some of the children had high levels of GH, there was no significant difference between malnourished and well-nourished groups. Similarly, the lack of difference could be due to the fact that none of the children were severely malnourished, and also because growth hormone levels vary with age and pubertal stages[15].

Serum cortisol levels were lower among malnourishcd children compared to well-nourished children but the difference was not statistically significant. Cortisol levels were reported to be high in PEM due to stress induced by low food intake, hypoglycemia, fever and infections[16-19]. The lack of differences in serum cortisol levels are probably due to less severe cases chosen in this study, and none of the malnourished children had hypoglycemia, fever or infections.

Calcium levels normally get affected only in severe malnutrition. The level will be decreased (hypocalcemia) partly because of acidosis, and partly because of hypoproteinemia which causes less protein available to bind calcium ion[20]. In this study the serum calcium level was normal at various levels of nutritional status.

The serum level of ALT was significantly higher among malnourished compared to well-nourished children. The level of ALT among moderately malnourished children was two times higher than the mildly malnourished and three times that of well-nourished. ALT is necessary for tissue energy production and it is a relatively specific indicator of acute hepatocellular damage. The increase does not correlate with the extent of hepatocellular necrosis[21]. Even though the level of ALT was higher among malnourished children, it does not necessarily indicate liver abnormalities. The higher level of ALT may be associated with high intake of cassava because higher percentage of malnourished population (52%) took cassava at least once a week in their diet as reported earlier[22].

In conclusion, this study revealed that moderately malnourished children had significantly higher TSH level than mildly malnourished or well-nourished children, even though serum T4 and T3, cortisol, growth hormone, blood glucose and calcium levels were not signicantly different.

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