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Plasma Lipoproteins and Apolipoproteins in Protein Energy Malnutrition

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Abstract

Twenty-nine Kwashiorkor (KWO) cases, 13 marasmic cases, 19 marsmic - KWO cases and 20 healthy controls were chosen from the New Children Hospital, Cairo University to study the aetiology of the anomalies of lipid parameter and to explore the effect of malnutrition in hepatic function. All were subjected to full clinical examination, estimation of trigylcerides, total cholesterol, high and low density lipoproteins (HDL and LDL), apolipoproteins A and B, albumin, SGOT, SGPT activities and cholyglycine levels. The results showed that cholyglycine bile acids were 144.90 ± µg/dl - 113.22 ± 53.92 µg/dl - 82.23 ± 53 - 37.45 ± 21.01 in KWO, marasmaico KWO, marasmus and normal 21.01 in KWO, marasmaico KWO, marasmus and normal controls. Triglycerides were 95.70 ± 23.79 mg/dl-78.85 ± 12.21 - 70.84 ± 18.32 - 67.43 ± 22.33 in normal controls, marsmus, marsmico KWO and KWO respectively. Serum total cholesterol HDL and LDL in marasmic infants was significantly lower than normal controls ($p < 0.005$, <0.001 and < 0.005 respectively). The mean value of triglycerides total cholesterol, HDL and LDL in maramico KWO were significantly lower than controls ($p < 0.001$, $p < 0.001$, $p < 0.001$ $p < 0.005$ respectively). The serum Apo A and Apo B was lower in KWO and maramico KWO compared to normal control ($p < 0.001$ and $p < 0.05$) if compared with marsmus ($p < 0.001$) for each if compared with normal controls. Sepsis, defective intake and defective metabolism result in reduced level of Apo A and B in PEM. Children with PEM showed, in addition to reduced weight, imparied heaptic function with alteration of serum albumin and lipoprotein profile.

Introduction

PROTEIN energy malnutrition (PEM) is a serious problem in developing countries. It accounts for more than half of the deaths in children under 5 years of age [1]. Patients with PEM show reduced weight, plasma total protein and disturbed lipid concentration [2]. Moreover, fatty infiltration of the liver of variable degree is a common finding in Kwashiorkor (KWO).

The major plasma lipids are chylomicrons cholesterol, triglycerides, phospholipids and fatty acids. They are hydrophobic and transported in the form of lipoprotein complex [3].

Each lipoprotein particle contains specific proteins. Apoproteins that are partly exposed at the surface [4]. Lipoproteins are classified into five classes based on ultra centrifugal floatation density: Chylomicrons, very low density lipoproteins VLDL, intermediate density lipoprotein IDL, low density lipoprotein LDL and high density lipoprotein HDLP [5].

The function of lipoprotein is to transport dietary endogenously synthesized lipids to tissue utilize exogenous lipids for oxidative metabolism (liver and muscles), storage, steroid hormone biosynthesis and cell membrane integrity [6].

Apolipoproteins have three main functions they help to solubilize cholesterol and triglycerides by interacting with the other major classes of lipids mainly phospholipids, they regulate the reactions of these lipids with enzymes such as lecithin cholesterol acyl transferase and lipoprotein lipase and they bind to cell surface receptors and thus determine the site of uptake and rate of degradation of other lipoprotein constituents notably cholesterol [7].

Serum lipoproteins are important risk factors in coronary heart disease with LDLP cholesterol and HDLP cholesterol showing positive and negative risk association respectively [8]. Plasma apolipoproteins are even better indicators of risk factor for the development of coronary heart disease than plasma lipids. Consequently there has been a surge of interest in studying lipoprotein in children.

The aim of this work is to estimate the serum levels of proteins, lipoproteins and apolipoproteins in a group of PEM and to compare them with control healthy group in a trial to clarify serum lipoprotein profile in PEM and the etiology of the anomalies in lipid parameters and to explore the effect of malnutrition in hepatic function.

Material and Methods

Sixty-one infants and children were chosen from the New Children Hospital, Cairo University classified into KWO (29 cases) marasmus (13 cases), and marasmic-KWO (19 cases) according to Mclaren

Score [9]. Malnourished children were subjected to full clinical examination and thorough history taking. They were classified as 1st, 2nd, and 3rd degree malnutrition by criteria of Gomez of al [10]. They are matched against 20 normal control of the same age group.

All patients and controls were subjected to the following laboratory tests:

- Serum albumin
- Serum bile acids.
- SGOT and SGPT
- Serum triglycerides
- Serum cholesterol.
- HDL cholesterol
- LDL cholesterol
- Apolipoprotein A
- Apolipoprotein B

Results

Results are illustrated in tables 1,2 and in Figs. 1-6.

Discussion

It is well known that no single liver function test can be used alone to fully evaluate liver function. Any single test may be normal despite other abnormal liver function tests. The choice of suitable tests is according to clinical situation and combinaton of two or more tests is better than any single one. The serum bile acids seem to be highly sensitive indicator of hepatobiliary disease especially in monitoring patients at high risk [11].

In this work the mean value of fasting serum cholyglycine bile acids was very high in KWO (144.90 ± 19 μ /dl) and marasmic - KWO (113.22 ± 53.92 μg/dl) compared with the normal controls 37.45 ± 21.01). In this study remarkable finding was a significant rise in serum bile acids in marasmic cases with normal serum albumin and transaminases as compared to normal controls (mean in marasmus = 82.23 ± 53.94 μ/dl ($p < 0.01$). There was no significant difference between KWO and marasmic - KWO while significant rise ($p < 0.01$) was detected in KWO group as compared to marasmic group. So, fatty liver in malnutrition is not followed by cirrhosis but is associated with impaired liver function [12].

As regards the mean value of ALT SGPT was high 35.67 ± 9.39 in KWO and 37.45 ± 16.68 in marasmic - KWO if compared to normal controls (27.62 ± 6.09 μg/ml). Also the mean values of AST SGOT was high in KWO (46.97 ± 17.75) and in marasmic- KWO (44.61 ± 15.88) as compared to normal controls (33.75 ± 0.14 μ/ml). These results are comparable to those of Said et al [13].

Serum transaminases are increased in hepatic disease with destructive release or leaking. The main liver pathology in PEM is fatty infiltration without cell damage [14].

The mean value of serum albumin in this study was low in KWO (2.84 ± 0.52

Table (1): Cumulative Table Showing the Range, Mean, S.D., S.E., and the Statistical Comparison of Serum Albumin, Cholylglycine Levels as well as Serum Activities of ALT and AST in the Four Investigated Groups.

		Albumin g/dl	Cholylglycine µg/dl	ALT U/ml	AST U/ml
I.	**Controls:**				
	Number	20	20	20	20
	Range	3.14-4.45	12-74	15-41	21-41
	Mean	3.959	37.45	27.67	33.75
	S.D. ±	0.401	21.01	6.20	6.01
	S.E. ±	0.090	4.70	1.39	1.35
II.	**Marasmus:**				
	Number	13	13	13	13
	Range	3.00-4.59	28-200	11-49	17-60
	Mean	3.727	82.23	28.12	36.54
	S.D. ±	0.536	53.94	13.81	13.72
	S.E. ±	0.149	14.96	3.83	3.80
	p_1	> 0.1	< 0.001	> 0.9	> 0.4
	Significance	N.S.	*	N.S.	N.S.
III.	**Kwashiorkor:**				
	Number	29	22	29	29
	Range	1.23-3.61	24-260	26-70.5	24-92
	Mean	2.184	144-90	35.67	46.97
	S.D. ±	0.522	55.19	9.39	17.75
	S.E. ±	0.097	10.27	1.74	3.30
	p_1	< 0.001	< 0.001	< 0.001	< 0.001
	Significance	*	*	*	*
	p_2	< 0.001	< 0.005	> 0.05	< 0.05
	Significance	*	*	N.S.	*

Table (2): Cumlative Table Showing the Number of Cases Range, Mean, S.D., S.E. and the Statistical Comparison of Serum Triglycerides, Total Cholylglycine HDL and LDL Cholesterol, Atherogenic Index, Apo A and Apo B in the Four Investigated Groups.

	T.C. mg/dl	Total cholesterol mg/dl	HDL-cholesterol mg/dl	Atherogenic index	LDL-cholesterol mg/dl	Apo A mg/dl	Apo B mg/dl
I. Controls:							
Number	20	20	20	20	20	20	20
Range	66-151	129-236	32-55.7	3.18-4.75	68.5-153.2	160-300	63-147
Mean	95.70	168.65	41.26	4.115	104.62	242.90	96.50
S.D. ±	23.79	27.89	7.14	0.412	22.97	49.75	25.70
S.E. ±	5.32	6.24	1.60	0.092	5.74	11.12	5.70
II. Marasmus:							
Number	13	13	13	13	13	13	13
Range	66-100	116-176	21.38.5	4.00-6.47	65.125	160-245	65.106
Mean	78-85	139.23	29.08	4.916	88.69	194.85	80.36
S.D. ±	12.21	20.22	6.63	0.822	18.97	21.38	13.76
S.E. ±	3.39	5.61	1.84	0.228	5.26	5.93	3.80
p_1	< 0.02	< 0.005	< 0.001	< 0.005	< 0.05	< 0.001	< 0.05
Significance	*	*	*	*	*	*	*
III. Kwashiorkor:							
Number	28	28	28	28	28	28	28
Range	38-127	52-221	7.9-45.5	2.72-9.07	36-130	98.210	31-116
Mean	67.43	111.68	20.71	5.658	72.75	138.89	59.96
S.D. ±	22.33	36.62	8.05	1.499	24.42	27.35	22.70
S.E. ±	4.22	9.62	1.52	0.283	4.61	5.71	4.30
p_1	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Significance	*	*	*	*	*	*	*
p_2	< 0.05	< 0.005	< 0.005	< 0.05	< 0.05	< 0.001	< 0.001
Significance	*	*	*	*	*	*	*
IV. Marasmic Kwashiorkor:							
Number	19	19	19	19	19	19	19
Range	45-110	75-160	14.90-36.5	4.16-7.92	50-115	100.240	40-90
Mean	70.68	119.05	24.18	5.054	79.84	170.26	68.63
S.D. ±	17.28	25.15	6.84	0.830	18.32	42.21	16.00
S.E. ±	3.96	5.77	1.57	0.190	4.28	9.68	3.68
p_1	< 0.001	< 0.001	< 0.001	< 0.001	< 0.005	< 0.001	< 0.001
Significance	*	*	*	*	*	*	*
p_2	> 0.100	< 0.02	> 0.050	> 0.600	> 0.200	< 0.050	< 0.05
Significance	N.S.	*	N.S.	N.S.	N.S.	*	*
p_3	> 0.500	> 0.40	> 0.100	> 0.05	> 0.200	< 0.01	> 0.10
Significance	N.S.	N.S.	N.S	N.S.	N.S.	*	N.S.

p_1 = Compared to controls.
p_2 = Compared to marasmus.
p_3 = Compared to kwashiorkor.
N.S. = Nonsignificant
* = Significant.

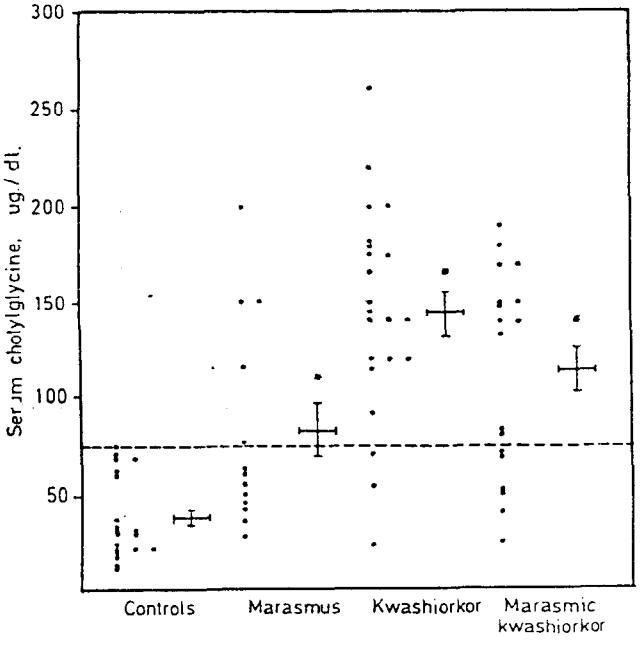

Fig. (1): Serum cholylgycine levels in control, marasmic, kwashiorkor and marasmic kwashiorkor infants.

------- = Upper range in controls.

= Mean ± S. E.

* = Significant.

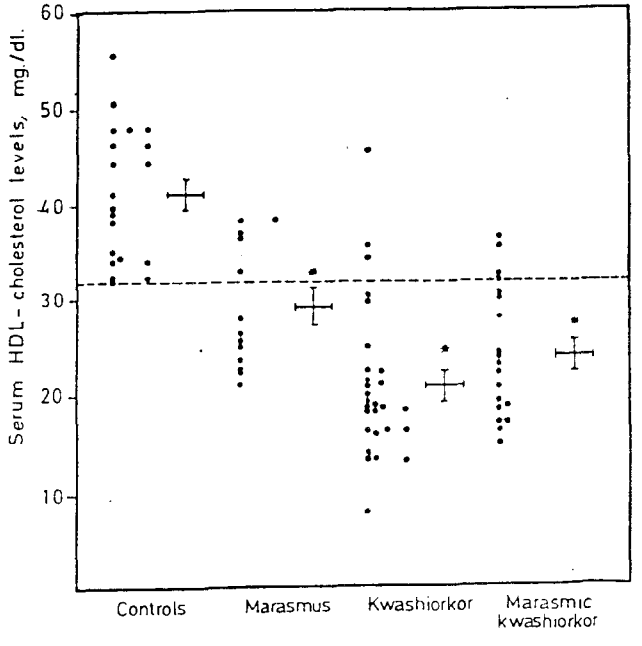

Fig. (2): Serum HDL-cholesterol levels in control, marasmic,kwashiorkor and marasmic kwashiorkor infants.

------- = Lower range in controls.

= Mean ± S. E.

* = Significant.

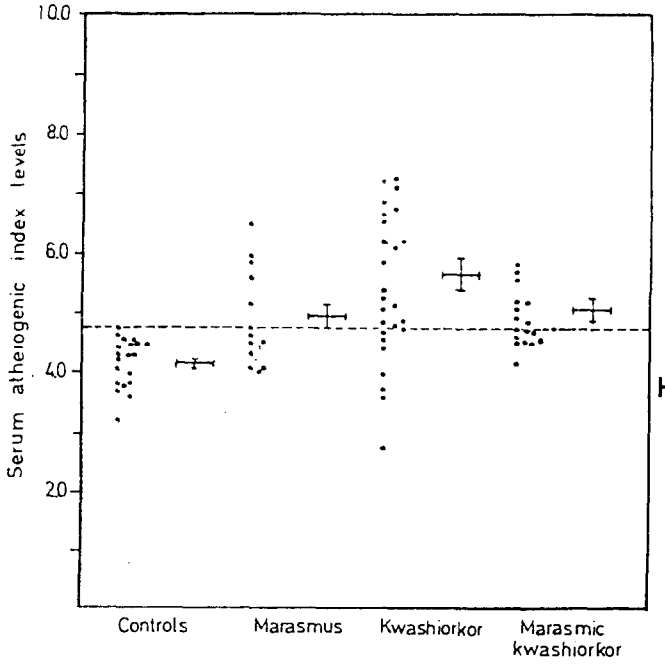

Fig. (3): Serum atherogenie index levels in ontrol, marasmic, kwashiorkor and marasmi kwashiorkor infants.

------- = Upper range in controls.

= Mean ± S. E.

* = Significant.

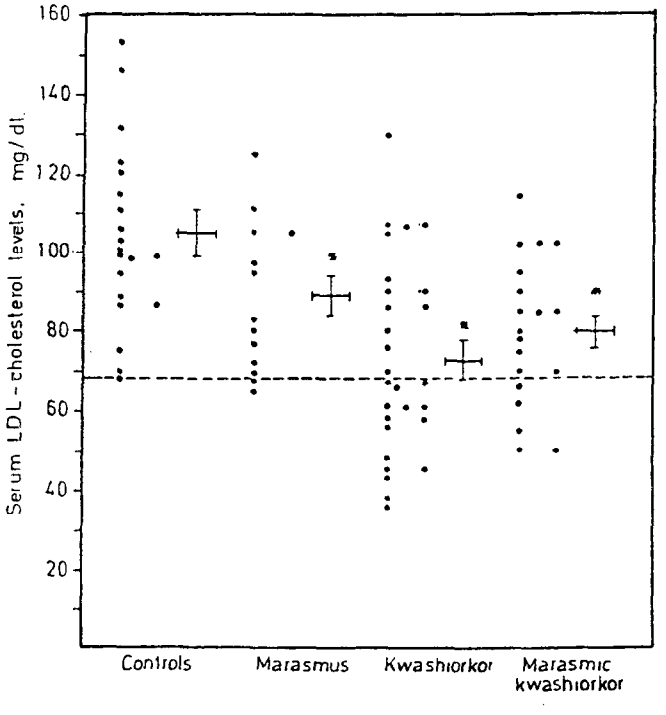

Fig. (4): Serum LDL-cholesterol levels in control, marasmic, kwashiorkor and marasmic kwashiorkor infants.

------- = Lower range in controls.

= Mean ± S.E.

* = Significant.

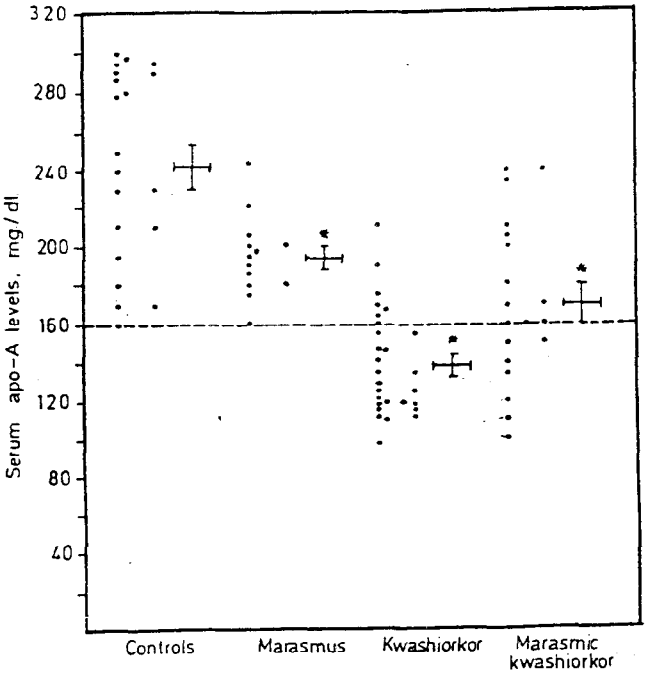

Fig. (5): Serum apo-A levels in control, marasmic, kwashiorkor and marasmic kwashiorkor infants.

------- = Lower range in controls.

= Mean ± S. E.

* = Significant.

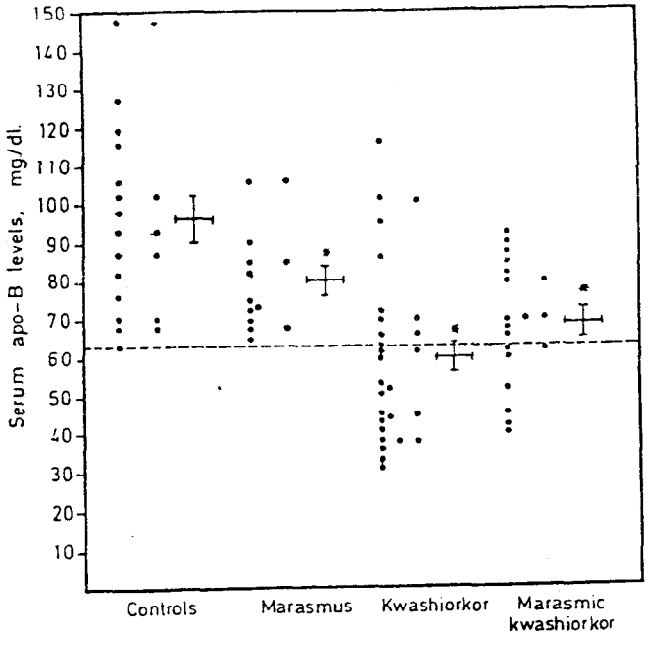

Fig. (6): Serum apo-B levels in control, marasmic, kwashiorkor and marasmic kwashiorkor infants.

------- = Lower range in controls.

= Mean ± S. E.

* = Significant.

gm/dl) and marasmic-KWO (2.8 ± 0.9 gm/dl) compared with normal controls (3.96 ± 0.399 gm/dl) or the marasmic cases (3.71 ± 0.576 g/dl). A significant decrease was detected in the marasmic - KWO group compared to the marasmic group ($p < 0.001$). Serum albumin fall due to prolonged dietary or protein restriction, reduced hepatic synthesis and when there is gastrointestinal or renal loss.

Serum albumin is a sensitive indicator of the severity of chronic liver diseases and is used for follow up of PEM cases but it is less sensitive than other proteins as prealbumin and transferrin as changes in serum level of these proteins occur earlier than albumin [15].

In this study the serum level of all lipoproteins were reduced in all types of PEM compared to normal controls being more marked in KWO than in marasmic-KWO and in marasmic KWO and in marasmic KWO are more marked than in marasmic patients. The mean value of triglycerides was 95.70 ± 23.79 mg/dl 78.85 ± 12.21 mg/dl 70.84 ± 18.32 - 67.43 ± 22.33 in normal controls, marasmus, marasmic - KWO and KWO respectively. $p < 0.02$, $p < 0.01$ and $p < 0.01$ in the three groups compared to the normal controls respectively marasmus, marasmic- KWO and KWO.

The mean value of serum total cholesterol, its HDL and LDL fractions in marasmic infants were 139.23 ± 20.22. 29.08 ± 6.63 and 88.69 ± 18.97 mg/dl each was significantly lower compared to controls $p < 0.005$, $p < 0.001$ and $p < 0.05$ respectively.

The mean values of serum triglycerides, total cholesterol, its HDL and LDL fractions in marasmic-KWO patients were significantly lower compared to normal controls ($p < 0.001$, $p < 0.001$. $p < 0.001$ and $p < 0.005$ respectively). These results coincide with others [16,2]. Ladijan and Reeds had emphasized the importance of inadequate diet together with infection in the etiology of PEM, it is thererfore difficult to separate the effects of these two factors on the observed low levels of lipoproteins in PEM.

It has been shown that fat absorption is not impaired in PEM and that early introduction of vegetable fat to diet of KWO not suffering from diarrhea seems to be well tolerated and absorbed. Being the richest source of calories quicker restoration of body weight can be expected if fat is introduced early into the diet of malnourished infants in absence of diarrhea.

The serum level of apo A and apo B was lower in infants of PEM compared to controls with mean serum level of 242.90 mg/dl, 194.85, 170.26 and 138.89 in normal controls, marasmus, marasmic KWO and KWO respectively.

In marasmus, KWO and marasmic KWO values were all significantly lower compared to normal controls ($p < 0.001$) for each compared to the level in marasmus. The mean in KWO and in marasmico KWO was significantly lower $p < 0.001$ and $p < 0.05$ respectively). But in marasmico KWO serum APO A was significantly higher than in KWO ($p < 0.01$) compared to marasmus. The mean apo B serum level in KWO and in marasmico KWO were significantly lower $p < 0.001$ and $p < 0.005$ respectively and the difference between the mean apo B serum in KWO and marasmico KWO was insignificant ($p < 0.1$).

Serum level of Apo A and Apo B are decreased in cases of sepsis, extra hepatic biliary obstruction, early phase of acute hepatitis, liver fibrosis and liver cirrhosis, sickle cell anemia and in patients receiving long term parenteral nutrition [17, 18]. This coincides with our results as sepsis, defective intake and defective metabolism are prominent features in most cases of PEM showing reduced levels of serum apo A and apo B levels. Children with protein energy malnutrition showed in addition to reduced weight impaired hepatic function with consequent alteration of serum albumin and lipoprotein profile. These changes were associated with decreased apo A and B serum levels which constitute the major protein outermost coat of HDL - particles.

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