Lipid Profile and Essential Fatty Acid Concentration in Typhoid Fever Patients

Amal H.A. & Eman S.S.

Department of Clinical Laboratory Biochemistry,
College of Pharmacy, Baghdad University, Baghdad, Iraq.

الخلاصة

ان تحفيز الخلايا الملتهبة، إفراز محفزاتها وزيادة انتاج الجذور الحرة لها تأثير على دهون الدم، لكن لايوجد اثبات يدعم قانون عملية الاكسدة البيروكسيدية في علم الامراض لمرضى التايفوئيد.

تم قياس مكونات دهون الدم والاحماض الدهنية المهمة لـ 44 مريض من مرضى الحمى التايفوئيدية مقارنة بـ 25 شخص من الاصحاء.

وجد ان نسبة الاحماض الدهنية المشبعة وغير المشبعة الاحادية عالية في مصل مرضى حمى التايفود بالمقارنة مع الاحماض الدهنية المتعددة غير المشبعة حيث وجد انها اقل عند نفس المرضى اذا ما قورنت بالاشخاص الاصحاء، هذه ادت الى زيادة في نسبة حامض البالموتوليك الى حامض اللينوليك ($P<0.04$). وكذلك زيادة في نسبة حامض الايكوساترنويك الى حامض الاراجيدونيك ($P<0.03$) جدول رقم (2).

كما اظهر مرضى حمى التايفوئيد قلة في تركيز الكوليستيرول مع زيادة في تركيز LDL كوليستيرول ($P<0.001, P<0.003$) بالتعاقب جدول رقم (1) وشكل رقم (1).

بالعودة الى دهن الترايكلسيرايد والـHDL كوليستيرول لم يظهر اي تغيير لهما عند مرضى حمى التايفوئيد.

لمناقشة هذا الموضوع اظهر مرضى حمى التايفوئيد بعض التغييرات في مستوى دهون الدم والاحماض الدهنية المهمة لديهم والتي تعتبر ذو فائدة عملية.

الغاية من الدراسة:

لتبيان تأثير حمى التايفوئيد على مكونات دهون الدم وتركيز الاحماض الدهنية المهمة.

Abstract

The activation of inflammatory cells, the release of their mediators, and the excessive production of free radicals may affect circulating lipids, while no evidence supports a role for peroxidation in the pathogenesis of typhoid fever disease.

Lipid profile and essential fatty acids concentration were measured in 44 typhoid fever patients and 25 healthy controls.

The proportion of saturated and monounsaturated fatty acids were found to be higher in serum of typhoid fever patients, in contrast with polyunsaturated fatty acids which were found to be lower in those patients when compared with healthy controls, this results in a higher ratio of palmitoleic acid to linoleic acid ($P<0.04$) and of eicosatrienoic acid to arachidonic acid ($P<0.03$) (Table-2).

Typhoid fever patients showed also hypocholesterolemia and hyper LDL-cholesterolemia ($P<0.001$ and $P<0.003$ respectively) (Table-1, Fig.-1).

Regarding triglycerides and HDL–cholesterol, they demonstrated a non significant change in typhoid fever.

In conclusion, typhoid fever patients showed some disturbances in their lipid profile and essential fatty acid concentration which may be of clinical significance.

Objective

To show the effect of typhoid fever on lipid profile and essential fatty acids concentration.

Introduction

The genus Salmonella was named for the pathologist Salmon, who is firstly isolated the organism from animal intestine [1]. The bacterial genus Salmonella was divided into two species, Salmonella bogori and S.enterica. Salmonella enterica itself was composed of six subspeicies, they are S.enterica subspecies enterica, S.enterica subsp.salamae, S.enterica subsp arizonae, S.enterica subsp diarizonae, and S.enterica subsp houtenae. These six subspecies only subspecies enterica is associated with disease in worm blooded animals[2].

Subspecies enterica of Salmonella enterica was responsible for almost all salmonella infections of worm blooded animals, through subspecies enterica there are over 2,300 known serovars that differ in their prevalence and the diseases which is cause in different hosts. A few of these serovars are responsible for most salmonella infections in human and domestic animals [3].

Subgroup enterica accounts for most human diseases and contains the serotype typhi[4].

Salmonella was divided into distinct serologic groups (A through E) on the bases of their somatic O–antigens. Salmonella enterica serovars are defined by antigenic variation at lipopolysaccharides (O–antigens), flagellar antigens (H–antigen), and capsular polysaccharides (vi antigen)[5].

Salmonella enterica serovar typhi is a number of genus salmonella in the family Enterobacteriaceas. The agents that cause enteric fever are therefore salmonella enterica subspecies enterica serovar typhi and serovar paratyphi (A,Band C). Typhoid and paratyphoid fever are collectively referred to as

enteric fever. In almost endemic areas approximately 90% of enteric fever is typhoid [6].

Serovar paratyphi A is the second most prevalent cause of typhoid, responsible for one third of causes or more in southern and eastern Asia.

Paratyhi A and typhi cause a similar illness, with relapsing fever, paratyphi A generally causes a milder disease[7].

Lipid profile includes serum cholesterol, serum triglycerides, and the break up of various cholesterol fractions like low density lipoprotein cholesterol (LDL–cholesterol), high density lipoproteins cholesterol (HDL–cholesterol) and LDL/HDL ratio, which is of significance.

A serum cholesterol level greater than 5.2 mmol/l (200 mg/dl) is greater than the desired level.

The HDL–cholesterol level can also be measured and should be ≥1.55 mmol/l (>60 mg/dl). The LDL–cholesterol level should be < 3.36 mmol/l (<130 mg/dl) [8, 9].

Total cholesterol has been found to correlate with total and cardiovascular mortality in 30-50 years age group. Cardiovascular mortality increases 9% for each 10 mg/dl increase in total cholesterol over the baseline value of 180 mg/dl. Approximately 80% of the adult male population has values greater than this.

HDL–cholesterol is “good” cholesterol in that risk of cardiovascular disease decreases with increase of HDL[10]. Triglyceride level is a risk factor independent of the cholesterol level. Triglycerides are important as risk factors only if they are not part of the chylomicron fraction [11].

Lipid profile is known to alter in patients with severe sepsis, but few studies regarding the status of lipid levels in enteric fever are available, the analysis of the lipid profile is essential in making a diagnosis[12].

Materials and Methods

Subjects:

Forty four patients with typhoid fever were recruited from the inflammatory bowel disease clinic of Kadhimiya Teaching Hospital. The diagnosis of disease was based on standard clinical, histological features and chemical tests (widal test) [13]. The severity of the disease was evaluated by the severity of abdominal pain, general well being extra intestinal manifestations of the disease and high fever. Twenty five healthy persons served as control groups.

Blood samples:

Blood samples were collected after subjects had fasted for 12 hours overnight; serum was separated immediately by low speed centrifugation and stored pending analysis.

Lipid profile analysis:

Serum concentration of total cholesterol, and triglycerides were measured enzymatically with a commercial kit (Boehringer, Mannheir Montreal)[14].

High density lipoprotein cholesterol (HDL–cholesterol) was measured after precipitation of very low density lipoprotein cholesterol (VLDL) and low density lipoprotein cholesterol (LDL–cholesterol) with phosphotungstic acid, while LDL–cholesterol measured by Fried Weld equation as the following:

LDL = cholesterol – (HDL + triglycerides / 5)

When triglycerides concentration is less than 400 mg/dl [14].

Fatty acid analysis:

Fatty acids in serum were assayed by an improved method. Briefly, each sample to be analyzed was subjected to direct transesterification and then injected into a gas chromatograph (model Hp 5880; HewleH Packard, Rockville, MD) by using a 60-m fused silica capillary column coated with sp 2331[15].

Statistical analysis:

All values are expressed as means, standard deviation (SD), and ± standard error (±SE). Statistical differences were assessed by student's t–test, probability (P) values ≤0.05 were considered significant.

Results

There are several differences between the serum lipids of patients with typhoid fever and control subjects were shown in Fig.-1, Tab-1. Mean total cholesterol concentration were lower in typhoid patients than in control subjects, where as the LDL–cholesterol concentration were higher. Concentration levels of total cholesterol were characterized by increasing LDL–cholesterol with no significant variation of HDL–cholesterol and triglycerides. The proportion of linoleic acid (18 2n-6) is essential fatty acids were lower in patients. In contrast, the proportion of mono unsaturated fatty acid was higher in typhoid patients. (Tab-2). The overall percentages of various species and the ratios of fatty acids relevant for the assessment of essential fatty acids deficiency are summarized in table 2. Proportions of both total n–3 and n–6 polyunsaturated fatty acids (PUFAS) were lower in typhoid patients than in control subjects, where as proportions of saturated and monounsaturated (n–7 and n–9) fatty acids were higher. The ratios of eicosatrienoic acid (20–3n–9) to arachidonic acid (20–4n–6)and of palmitoleic acid (16,1n–7) to18,2n–6, established indexes of essential fatty acids status, were higher in typhoid patients than in control subjects, confirming essential fatty acid deficiency in typhoid patients.

variable	Control no=25		Patients no.=44			
mg/dl	mean	± SE	mean	SD	± SE	P
Total cholesterol	190.45	1.36	172.3	35.7	5.4	≤0.001
Triglyceride	135	7.3	137.4	47.5	7.55	N.S
HDL–cholesterol	36.6	2.7	34.75	14.7	2.3	N.S
LDL–cholesterol	102.3	3.5	120.5	35	5.4	≤0.003
LDL/HDL	2.79	0.5	3.46		2.3	≤0.01

Table-1: Mean, SD, ± SE of serum lipid profile levels and LDL/HDL ratio in typhoid fever patients and controls

Fatty acid	Control subjects n=25	Typhoid patients n=44	P
SFA(%)	30.4 ± 0.32	33.6 ± 0.35	0.03
MUFA(%)	25.77 ± 0.5	27.7 ± 0.78	0.002
PUFA(%)	43.6 ± 60.6	36.75 ± 0.77	0.001
PUFA/SFA	1.3 ± 0.03	1.1 ± 0.02	0.001
Total n=3(%)	3.27 ± 1.3	2.7 ± 0.11	0.02
Total n=6(%)	37 ± 0.97	33.35 ± 0.73	0.001
Total n=7(%)	3.17 ± 0.14	3.92 ± 0.17	0.03
Total n=9(%)	19.64 ± 0.5	22.65 ± 0.65	0.002
Ratio of 16:1n–7 to 18:2n–6	0.057 ± 0.006	0.075 ± 0.01	0.04
Ratio of 20:3n–9 to 20:4n–6	0.015 ± 0.001	0.023 ± 0.012	0.03

Table-2: Proportions of fatty acids families and indexes of essential fatty acid deficiency in serum of typhoid patients and control subjects.
SFA: saturated fatty acid
MUFA: monounsaturated fatty acid
PUFA: poly unsaturated fatty acids

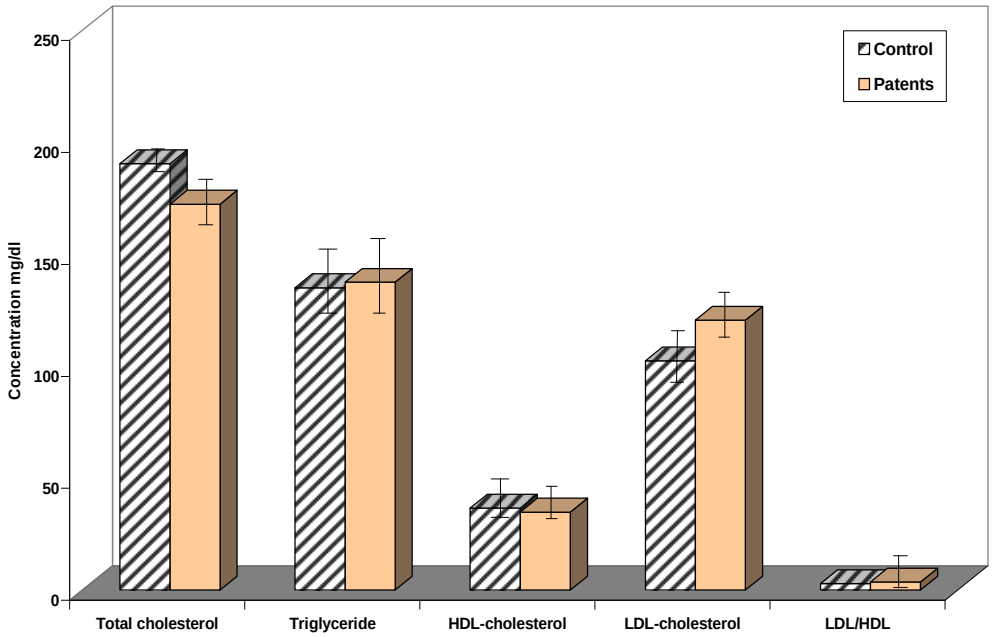

Fig-1: Mean ± SE serum lipid profile concentration in fasting typhoid patients (n=44) and control subjects (n=25) (total cholesterol, triglyceride, HDL–cholesterol, LDL–cholesterol and the ratio LDL/ HDL).

Discussion

To date a little information is available on the lipid profile, lipoprotein composition and essential fatty acids of patients with typhoid fever.

Our findings disclose various changes in this biochemical and selected clinical aspects of the patients, such as disease activity, site of disease, surgical history, or current medications.

Our clinical and experimental studies carried out previously suggest that essential fatty acids deficiency and malnutrition can negatively affect both the intestinal absorption, fat and lipoprotein metabolism [16, 17, 18, and 19].
At this time, it is uncertain whether the hypocholesterolemia presented in our results from intestinal malabsorption or malnutrition [20].

Typhoid fever characterized by increased chronic inflammatory cells infiltrates in the mucosal lesions. The excessive local production of soluble mediators from activated monocytes and polymorphonuclear leukocytes has been implicated in mediating the tissue injury [21]. Important among these mediators are oxygen free radicals. The chronic gut inflammation promotes an imbalance between oxidant and antioxidant mechanism at the tissue level [22].

Disturbances in lipoproteins resulting from peroxidative attack may affect their normal metabolism and the subsequent distribution of both lipid and vitamin moieties to peripheral organs [23].

The present study identified important alteration in the lipid profile concentration of patients with typhoid fever compared with healthy control subjects (fig-1, tab-1).

The patients had abnormal lipoprotein status characterized by lower concentration of total cholesterol with high concentration of LDL–cholesterol ($P \geq 0.001$, $P \geq 0.003$ respectively). While triglyceride and HDL–cholesterol had no significant value in typhoid fever patients.

Our data shows that typhoid fever patients are vulnerable to essential fatty acids deficiency contributing risk factors may include fat malabsorption, hypermetabolism and inadequate nutritional intake [13].

Further more (Esieve Comas et al) found that patients with active inflammatory bowel disease had elevated plasma concentration of α–linolenic acid and decreased proportion of di homo γ–linolenic acid compared with healthy subjects[24].

The inconsistent results of various studies reported to date may be due to methodologic differences, the activity or extent of disease in the patients studied, or the patient's variable nutrient intake. In addition, as hypothesized by some investigations, increased biosynthesis might be the causes of the high proportion of lipid profile [23].

The conclusion of our results indicate that the substantial abnormalities in the concentration of serum lipids of patients with typhoid fever. Although these abnormalities are not unique to typhoid fever, the occurrences of essential fatty acids deficiency is of concern, especially in the context of our current understanding of essential fatty acids in human biology. Our study serves to show the complexity of lipid variation during salmonella typhi infection.

References

1 - Crum, N.F. (2003). Current trends in Typhoid Fever. Current gastroenterology reports; 5, (4); 279-286, (Pub; Med-12864957).

2 - Kimbrough, T.G., and S.I.Miller, (2000). Contribution of Salmonella Typhi type III secretion components to needle complex formation. Proc. Natl. Acad.Sci. USA, 97; 11008-11013.

3 - Porwollik, S.; Boyd, E.F.; Choy, C.; Cheny, O.; Florea, L.; Proctor, E. and McClelland, M. (2004). Characterization of Salmonella enterica subspecies I genovars by use of micro arrays. J Bacteriol, 186 (17); 5883-5895-Pub.Med. 15317799.

4 - Rodenburg, W.; Boree- Oudenhoven, I.M.J.; Kreamer E.; Vand dermeer, R. and Kejer, J.(2007): Gene expression response of the rat small intestine

following oral salmonella infection, Physiol. Genomics, 30; 123-133 (Abstract Full Text).

5 - Pang, T.Z.A.; Bhatta, B.B. and Finlag M. Altwegy. (1998). Typhoid Fever and other Salmonellosis, continuing challenge. Trends microbial, 3; 253, [midline].

6 - Parry, C.M.; Kraunanayake, L.; Coulter, J.B. and Beeching, N.J. (2006). Test for quinolone resistance in Typhoid Fever: BMJ, 333(7561); 260-261 Pub. Med. (16878371).

7 - McClelland, M.; Sanderson, K.E. and Clifton, SW, Letreillep (2004). Comparison of genome degradation in paratyphi A and typhi, human restricted serovars of Salmonella enteica that cause Typhoid Nature genetics; 36(12) 1268-1274, Pub. Med (15531882).

8 - Mertens, A.; Vethamme, P, and Bielicki, J.K. et al: (2003). Increased low density lipoprotein oxidation and impaired high density lipoprotein antioxidant defense are associated with increased macrophage homing and atherosclerosis in dislipidemic obese mice. 107(12); 1640-6 [medline].

9 - Herano, K.; Kachi, S.; Ushida, C. and Naito, M. (2004). Corneal and macular manifestations in a case of deficient lecithin cholesterol acyltransferase Jpn J. ophthalmol. 48(1); 82-4 [midline].

10 - Framingham, (1998). Primary Prevention of Coronary Heart Disease: Guidance from Framingham; circulation. 97; 1876-1887, American Heart Association.

11 - Anderson, K.M. et al, (1987). Cholesterol and mortality, JAMA, 257; 2176-2180.

12 - Emile Levy; Yasmine Rizwan; Louise Thibault and Guy Lepage. (2000). Altered lipid profile, lipoprotein composition, and oxidant and anti oxidant status in pediatric crohn's disease. Am J Clin. Nutr. 71; 807-15.

13 - Olopoenia, L.A. and King, A.L. (2004). Widal agglutination test.100 years later, St, Plauged by controversy, Post graduate Medical J. 760-80-84, Pub Med (10644383).

14 - John Bernard Henry, M.D. (2001). Clinical Diagnosis and management of by laboratory methods. vol.(1); 230, Twentieth Ed.

15 - Chirico, S. (1994). High performance gas chromatography Method Enzymol. 223; 3114-8.

16 - Levy, E; Thbault, L. and Garofalo, C. et al. (1990). Combined (n-3 and n-6) essential fatty acid deficiency is a potent modular of plasma lipids, lipoprotein composition, and lipolytic enzymes, J. Lipid Res. 31; 2009-17.

17 - Levy, E.; Lepage, G. and Bendayan. M. et al: (1989). Relationship of decreased hepatic lipase activity and lipoprotein abnormalities to essential fatty acid deficiency in cystic fibrosis patients. J Lipid Res. 30; 1197-209.

18 - Levy, E.; Garofalo, C.; Daoust, L.; Dionne, S. and Roy, C.C. (1992). Intraluminal and intracellular phases of fat absorption are impaired in essential fatty acid deficiency. Am J Physiol. 262-G319-26.
19 - Levy, E.; Garofalo, C.; Roleau, T.; Gavino, V. and Bendayan, M. (1996). Impact of essential fatty acid deficiency on hepatic sterol metabolism in rats. Hepatology. 23; 848-57.
20 - Thomas, A.G.; Talyor, F. and Miller, V. (1993). Dietary intake and nutritional treatment in childhood crohn's disease. J. Pediatri Gastroenterol Nutr. 17; 75-81.
21 - Weiss, S.J. (1989). Tissue destruction by neutrophils, N Engl. J Med. 320; 365-76.
22 - Buffinton, G.D. and Doe, W.F. (1995). Depleted mucosal antioxidant defenses in inflammatory bowel disease. Free Radic. Biol. Med. 19; 911-8.
23 - Lepage, G.; Paradis, K. and Lacaille, F. et al. (1997). Ursodeoxycholic acid improves the hepatic metabolism of essential fatty acids and retinol in children with cystic fibrosis. J Pediatr. 130; 52-8.
24 - Esieve-Comas, M.; Ramirae, Z.M. and Fernandez-Banares, F. et al. (1992). Plasma poly unsaturated fatty acid pattern in active inflammatory bowel disease. Gut 33; 1365-9.