



## Evaluation of Lipid Profile changes in children with urinary tract infections

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### Abstract

**Background:** many researches about urinary tract infection has been conducted on adults but very little has been done on children. Therefore, this research is novel in Salahaddin city-Iraq.

Urinary tract infection is a bacterial infection that affects part of the urinary tract. It affects the lower urinary tract as well as upper urinary tract. It is characterized by painful urination, urge to urinate or sometimes frequent urination. Other symptoms include fever in addition to flank pains.

Bacteria infections cause a variety of changes in lipid profile concentrations by generating free radicals. Free radicals are reactive species generated by biochemical redox interactions that occur as a part of normal cell metabolism. These free radicals may cause lipid peroxidation and damage cellular structures of organism particularly erythrocytes and endothelium. Lipid peroxidation are free radicals mediated chain of reaction that, once initiated, results in oxidative deterioration of polyunsaturated lipids. The most common goal are components of biological membrane. When propagated in biological membranes, these reaction can be initiated or enhanced by a number of toxic products, including endoperoxides and aldehydes.

**Aim:** The aims of this study were to evaluate the lipid profile of the children in acute phase of urinary tract infections.

**Methodology:** Case-control study was designed to evaluate the lipid profile change in children with lower UTI. The study was performed on 130 children with ages between (4 – 12) years, 90 children with lower UTI (34.4% male) and (65.6% female,) and 40 control (45.0% male) and (55.0% female) in pediatric department of Salahaddin Teaching hospital from May 2017 till October 2017. The data were analyzed through the SPSS V.23 application, descriptive data analysis was done through frequency, percentage, mean, standard deviation in addition to T-test to compare results.

**Results:** The results showed there was a significant decreased in the levels of Cholesterol, LDL, and HDL when compared to control group ( $144.02 \pm 17.69$ ,  $75.76 \pm 12.695$ , and  $44.66 \pm 8.742$  vs  $167.65 \pm 13.13$ ,  $89.73 \pm 13.45$ , and  $60.95 \pm 6.26$  respectively), while there were a significant increase in triglycerides and VLDL in study group when compared to control group ( $118.03 \pm 18.66$ , and  $23.56 \pm 3.76$  vs  $85.95 \pm 10.25$ , and  $17.28 \pm 2.063$  respectively).

**Conclusion:** These observation shows that low levels of lipid, particularly total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and increased triglycerides (TG) probably be associated with urinary tract infections. Hence, the change in lipid profile could probably serve as indicators of urinary tract infection.

**Recommendations:** we recommend that the children with UTI probably need measurement the levels of lipid peroxidation as a reflect of infection.

## Introduction

Urinary tract infection are a bacterial infections that affects part of the urinary tract. It affects the upper urinary tract as well as lower urinary tract. It is characterized by painful urination, urge to urinate or sometimes frequent urination. Other symptoms include fever in addition to flank pains[1]. Bacteria infections cause a variety of changes in lipid profile concentrations by generating free radicals. These free radicals may cause lipid peroxidation and damage cellular structures of organism particularly erythrocytes and endothelium[1]. Lipid peroxidation is a free radical mediated chain of reaction that, once initiated, results in oxidative deterioration of polyunsaturated lipids[1].

Patients with a variety of different infections (gram positive bacterial, gram negative bacterial, viral, tuberculosis) have similar alterations in plasma lipid levels. Specifically, total cholesterol, LDL cholesterol, and HDL cholesterol levels are decreased while plasma triglyceride levels are elevated or inappropriately normal for the poor nutritional status [2,3]. As expected apolipoprotein A-I, A-II, and B levels are reduced [3,4]. While LDL-c levels were decreased, the concentration of small dense LDL-c has been found to be increased during infections [5]. That plasma cholesterol levels decrease during infection has been known for many years as it was described by Denis in 1919 in the Journal of Biological Chemistry (JBC 29: 93, 1919). The alterations in lipids correlate with the severity of the underlying infection i.e. the more severe the infection the more severe the alterations in lipid and lipoprotein levels [6,7]. Of note studies have demonstrated that the degree of reduction in total cholesterol, HDL-c cholesterol, and apolipoprotein A-I are predictive of mortality in patients with severe sepsis [8,9]. Moreover, epidemiologic studies have suggested that low cholesterol and HDL-c levels increase the chance of developing an infection [10]. During recovery from the infection plasma lipid and lipoprotein abnormalities return towards normal. The changes in lipid and lipoproteins that occur during infection can be experimentally reproduced in humans and animals by the administration of endotoxin and lipoteichoic acid [11].

Thus, in these different inflammatory disorders and infectious diseases, the alterations in plasma lipid and lipoprotein levels are very similar with decreases in plasma HDL-c being consistently observed. Also of note is the consistent increase in lipoprotein (a) levels and small dense LDL-c [12]. There is also a tendency for plasma triglyceride levels to be elevated. The greater the severity of the underlying disease the more consistently these abnormalities in lipids are observed. Additionally, treatment of the underlying disease leading to a reduction in inflammation results

in a return of the lipid profile towards normal. This is best illustrated in periodontal disease where intensive dental hygiene can reverse the abnormalities in the lipid profile [13,14].

Inflammation and infections increase the production of a variety of cytokines, including TNF, IL-1, and IL-6, which have been shown to alter lipid metabolism [2]. Many of the changes in plasma lipids and lipoproteins that are seen during chronic inflammation and infections are also observed following the acute administration of cytokines [2]. Multiple cytokines increase serum triglyceride and VLDL levels (TNF, IL-1, IL-2, IL-6, etc.) [2]. Following a single administration of a cytokine or LPS (a model of gram negative infections), which stimulates cytokine production, an increase in serum triglyceride and VLDL levels can be seen within 2 hours and this effect is sustained for at least 24 hours. The increase in serum triglycerides is due to both an increase in hepatic VLDL synthesis and secretion and a decrease in the clearance of triglyceride rich lipoproteins [2]. The increase in VLDL production and secretion is a result of increased hepatic fatty acid synthesis, an increase in adipose tissue lipolysis with the increased transport of fatty acids to the liver, and a decrease in fatty acid oxidation in the liver. Together these changes provide an increased supply of fatty acids in the liver that stimulate an increase in hepatic triglyceride synthesis [2]. The increased availability of triglycerides leads to the increased formation and secretion of VLDL. The decrease in the clearance of triglyceride rich lipoproteins is due to a decrease in lipoprotein lipase, the key enzyme that metabolizes triglycerides in the circulation [2]. A variety of cytokines have been shown to decrease the synthesis of lipoprotein lipase in adipose and muscle tissue [2].

In systemic lupus erythematosus, antibodies to lipoprotein lipase have been reported and are associated with increased triglyceride levels [15,16].

## Objective

The objective of this study was to evaluation of lipid profile changes in pediatric patients with urinary tract infections.

## Methodology

This case-control study was achieved in pediatric department, of Salahaddin teaching hospital from May 2017 till October 2017. It included 90 children with symptoms suggesting lower urinary tract infection, aged from (4 - 14) years, and 40 clinically healthy control with same age. Inclusion criteria were dysuria, frequency, urgency, and abdominal flank pain with or without fever. Children with, underlying liver and renal diseases, malignancy, hypo- or hyperthyroidism and patients treated with drugs affecting the serum lipid profile, were excluded from

this study. Their consent was obtained as ethical approval from the ethical committee of the hospital. Total serum cholesterol was measured by using cholesterol enzymatic Biolabo kit (Maizy, France). Determination serum triglycerides was done by enzymatic colorimetric method using Biolabo kit (Maizy, France). Serum HDL-C concentration was determined by the precipitation method, using HDL-C Biolabo kit (Maizy, France). Serum LDL-c was calculated by using Friedewald equation [17]. VLDL was calculated as TG/5.

The age, gender and clinical manifestations of each children with lower urinary tract infection, were recorded in a checklist for each patient.

According to the guidelines of United States National Cholesterol Education Program (NCEP), total cholesterol level less than 170 mg/dL, between 170- 199 mg/dL and more than 200 mg/dL were considered as desirable, at moderate risk, and high risk, respectively [18]. Also, LDL cholesterol levels less than 110 mg/dL, between 110-130 mg/dL, and more than 130 mg/dL were considered as desirable,

moderate and high risk, respectively. Regarding to the patients' age and gender, a serum triglyceride level less than the 90th percentile was considered in normal range. Thus, in boys and girls aging 1-4 years the triglyceride levels less than 85 mg/dL and 95 mg/dL and in 5 - 10 years, less than 70 mg/dL and 103 mg/dL were considered as normal, respectively [19].

**Blood samples**

Blood samples (2 ml) were drawn from each child by means of vein puncture and transferred to a plain vacutainer tubes for serum cholesterol, serum HDL, serum Triglycerides.

**Statistical study**

Data analysis was performed using statistical package of social science (SPSS) version 23.0 of windows. Numerical variables were reported in terms of mean and (T-Test) for comparison between categorical variables. The (p <0.05) was considered statistically significant for interpretation of result.

**Results**

**Table (1): Gender frequency and percentage of patients group.**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	59	65.6	65.6	65.6
	Male	31	34.4	34.4	100.0
	Total	90	100.0	100.0	

Table 1 shows that 90 children aged between (4 – 14) years were enrolled in the study. Ninety patients were admitted to the pediatric department in

Salahaddin general hospital with lower urinary tract infection, (31 male, 34.4%) and (59 female,65.6%).

**Table (2): Gender frequency and percentage of control group.**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	22	24.4	55.0	55.0
	Male	18	20.0	45.0	100.0
	Total	40	44.4	100.0	
Total		90	100.0		

Table 2 shows Another 40 healthy controls with same age, were studied in the outpatient department, 45%

were males and 55% females as in table 2.

**Table (3): frequency ages of patients group.**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	4	4	4.4	4.4	4.4
	5	11	12.2	12.2	16.7
	6	19	21.1	21.1	37.8
	7	13	14.4	14.4	52.2
	8	8	8.9	8.9	61.1
	9	7	7.8	7.8	68.9
	10	8	8.9	8.9	77.8
	11	5	5.6	5.6	83.3
	12	6	6.7	6.7	90.0
	13	5	5.6	5.6	95.6
	14	4	4.4	4.4	100.0
	Total	90	100.0	100.0	

Table 3 show that 90 children investigated in the study, urinary tract infection was more prevalence in

age 6 years (19 children, 21.1%).

**Table (4): frequency ages of control group.**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	4	1	2.5	2.5	2.5
	5	5	12.5	12.5	15.0
	6	3	7.5	7.5	22.5
	7	5	12.5	12.5	35.0
	8	2	5.0	5.0	40.0
	9	1	2.5	2.5	42.5
	10	4	10.0	10.0	52.5
	11	5	12.5	12.5	65.0
	12	5	12.5	12.5	77.5
	13	4	10.0	10.0	87.5
	14	5	12.5	12.5	100.0
	Total	40	100.0	100.0	

Table 4 show the frequency and percent of healthy control group were the same age of patients group. The table 4 shows that the age of

**Table (5): Mean serum cholesterol mg/dl of patients children and control.**

Group		N	Mean	Std. Deviation	Std. Error Mean	P-Value
Cholesterol	Patients	90	144.02	17.687	1.864	P<0.05
	control	40	167.65	13.134	2.077	

Table 5 show that the mean of serum cholesterol of children with UTI were  $144.02 \pm 17.687$ , while the mean of serum cholesterol of healthy children were  $167.65 \pm 13.134$ . Table 5 also show that the cholesterol of children with UTI were significantly decrease  $P < 0.05$  compared with control.

**Table (6): Mean serum LDL- chol mg/dl of patients children and control.**

Group		N	Mean	Std. Deviation	Std. Error Mean	P-Value
Patients LDL	Patients	90	75.76	12.695	1.338	P<0.05
	Control	40	89.73	13.453	2.127	

Table 6 show that the mean of serum LDL-c of children with UTI were  $75.76 \pm 12.695$ , while the mean of serum LDL-c of healthy children were  $89.73 \pm 13.453$ . LDL of children with UTI significantly decrease when compared with control  $P < 0.05$ .

**Table (7): Mean serum HDL- chol mg/dl of patients children and control.**

Group		N	Mean	Std. Deviation	Std. Error Mean	P-Value
Patients HDL	Patients	90	44.66	8.742	.922	P<0.05
	Control	40	60.95	6.255	.989	

Table 7 show that the levels of HDL-c in children with UTI ( $44.66 \pm 8.742$ ) were significantly decrease  $P < 0.05$  when compared with control ( $60.95 \pm 6.255$ ).

**Table (8): Mean serum TG mg/dl of patients children and control.**

Group		N	Mean	Std. Deviation	Std. Error Mean	P-Value
Patients TG	Patients	90	118.03	18.660	1.967	P<0.05
	Control	40	85.95	10.251	1.621	

Table 8 show that levels of TG were significantly increase ( $P < 0.05$ ) in children with UTI ( $118.03 \pm 18.66$ ) when compared with control ( $85.95 \pm 10.251$ ).

**Table (9): Mean VLDL mg/dl of patients and control**

Control		N	Mean	Std. Deviation	Std. Error Mean	P-Value
Patients VLDL	Patients	90	23.56	3.760	.396	P<0.05
	Control	40	17.28	2.063	.326	

Table 9 also show that VLDL were significantly increase ( $P < 0.05$ ) in children with UTI (23.56) compared with control (17.28).

### Discussion

The result of our study revealed that the female (59 female, 65.6%) was more susceptible for urinary tract infection than male (31 male, 34.4%) as showed in

table 1. These observation go with Mohammed A. Younis et al, that he was reported that the prevalence of UTI was common in females (64%) than males (36%) with 2:1 ratio<sup>(20)</sup>.

Table 2 shows that the UTI were more prevalence in children with age 6 (19 children, 21.1%). In girls, the first UTI usually occurs by the age of 5 years old. In

boys, most UTIs occur during the 1st year of life; UTIs are much more common in uncircumcised boys, especially in the 1st year of life [21].

The current study shows that there was a decrease in serum cholesterol level in children with UTI compared with control as showed in table 5. This could probably be associated with synthesis and utilization of plasma lipids as well as the interactions of cytokines which are produced during urinary tract inflammation. This is in line with the work of Vanleeuwen et al., 2003 which stated that increased cytokines caused decreased level of cholesterol in acute illness [22]. The changes in lipids and lipoproteins that occur during inflammation and infection are part of the innate immune response and therefore are likely to play an important role in protecting from the detrimental effects of infection and inflammatory stimuli [23,24].

Also the result of current study shows that levels of LDL were significantly ( $P < 0.05$ ) lower in children with UTI ( $75.76 \pm 12.695$ ) compared with control ( $89.73 \pm 13.453$ ) as showed in table 6. This could be associated with the host response to urinary tract infection which could induce LDL oxidation leading to reduced LDL-c [24].

The result of current study shows that levels of HDL were significantly decrease ( $P < 0.05$ ) in children with UTI ( $44.66 \pm 8.742$ ) compared with control ( $60.95 \pm 6.255$ ) as showed in table 7. Vermont et al., 2005 also reported the decreased levels of HDL in children with severe meningococcal disease [25]. During inflammation HDL particles tend to be larger with a decrease in cholesterol ester and an increase in free cholesterol, triglycerides, and free fatty acids.

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Furthermore, there are marked changes in HDL-c associated proteins and the enzymes and transfer proteins involved in HDL-c metabolism and function. The precise mechanism by which inflammation and infection decrease HDL-c levels is uncertain and is likely to involve multiple mechanisms [2].

Also current study shows that levels of TG were significantly ( $P < 0.05$ ) increase in children with UTI ( $118.03 \pm 18.66$ ) compared with control ( $85.95 \pm 10.251$ ). Multiple cytokines increase serum triglyceride and VLDL levels (TNF, IL-1, IL-2, IL-6, etc.). Following a single administration of a cytokine or lipoproteins lipase (a model of gram negative infections), which stimulates cytokine production, an increase in serum triglyceride and VLDL levels can be seen within 2 hours and this effect is sustained for at least 24 hours. The increase in serum triglycerides is due to both an increase in hepatic VLDL production and secretion and a decrease in the clearance of triglyceride rich lipoproteins [2]. This is in line with the work of Gordon et al., 2001. Urinary tract infections produce alterations in the functions and compositions of lipoproteins [26].

**Conclusion:** These observation shows that low levels of lipid, particularly total cholesterol, low density lipoprotein (LDL-c), high density lipoprotein (HDL-c) and increased triglycerides (TG) probably be associated with urinary tract infections. Hence, the change in lipid profile could probably serve as indicators of urinary tract infection.

**Recommendations:** we recommend that the children with UTI probably need measurement the levels of lipid peroxidation as a reflect of infection.

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## تقييم التغيرات الحاصلة في مرتسم الدهون للأطفال المصابين بالتهاب السبيل البولي

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## الملخص

## خلفية البحث:

العديد من البحوث العلمية حول موضوع التهاب المجاري البولية قد اجريت على المرضى البالغين ولكن القليل جدا من هذه البحوث اجريت على الاطفال. لذلك، يعد هذا البحث من البحوث الجديدة في محافظة صلاح الدين-العراق. التهاب المجاري البولية هو من الالتهابات البكتيرية والتي تصيب القناة البولية. قد تؤثر على الجزء السفلي من القناة البولية كما تؤثر على الجزء العلوي للقناة البولية. تتمثل الاصابة بألم أثناء التبول، الاستعجال على التبول، واحيانا تكرار عملية التبول. الاعراض المرضية الاخرى تتضمن ارتفاع درجات الحرارة إضافة الم الخاصة.

الالتهابات البكتيرية تسبب تغيرات مختلفة في تراكيز دهون الدم عن طريق توليد الجذور الحرة. الجذور الحرة هي مركبات ذات فعالية عالية جدا تتولد عن طريق تفاعلات الاكسدة الكيميائية والتي قد تحدث كنتيجة الايض الخلوي الطبيعي. هذه الجذور الحرة ربما تسبب اكسدة للدهون وكذلك تلف في الغشاء الخلوي وخصوصا كريات دم الحمر والخلايا الطلائية. الدهون المؤكسدة تعد نوع من انواع الجذور الحرة التي تكون بداية تفاعلاتها أكسدة الدهون غير المشبعة. والتي يكون اهدافها الرئيسية هي المكونات البيولوجية للاغشية. وعندما تزداد تراكيز هذه الجذور في الاغشية الخلوية فإنها قد تعد بداية تكوين مواد سامة اخرى والتي تتضمن الاندوبيروكسيدات والالديهيدات.

**الهدف:** تهدف هذه الدراسة الى تقييم مستوى الدهون في الاطفال المصابين بالتهاب المجاري البولية.

**المنهجية:** صممت هذه الدراسة كدراسة مقارنة بين مجموعتي المرضى والسيطرة حيث انها اجريت على 130 طفل تراوحت اعمارهم بين (4 - 14) سنة، 90 طفل مصاب بالتهاب المجاري البولية (34.4% ذكور) و (65,6% أنثى) و 40 طفل كمجموعة سيطرة (45.0% ذكور) و (55.0% أنثى) في قسم الاطفال التابع لمستشفى صلاح الدين التعليمي للفترة من حزيران 2017 ولغاية تشرين الاول 2017. تم تحليل النتائج بيانيا باستخدام البرنامج الاحصائي (SSPS V.23) حيث تم استعمال الاحصاء الوصفي والذي تضمن التكرارات، النسب المئوية، الوسط الحسابي إضافة الى اختبار (T-test) لمقارنة النتائج.

**النتائج:** النتائج التي حصلنا عليها بينت ان هناك نقصا معنويا في كل من مستوى الكوليسترول و الدهون ذات الكثافة الواطئة والدهون عالية الكثافة عندما قورنت بمستوى الدهون لمجموعة السيطرة (17.69±144.02، 12.695±75.76، 8.742±44.66 مقابل 13.13±167.65، 13.45±89.73، 6.26±60.95 على التعاقب)، في حين كان هناك زيادة معنوية في كل من مستوى الدهون الثلاثية ومستوى الدهون الواطئة الكثافة جدا (18.66±118.03، 3.67±23.56 مقابل 10.25±85.95، و 2.063±17.28 على التعاقب).

**الاستنتاج:** خلصت نتائج هذه الدراسة ان نقص مستوى الدهون في الدم وخصوصا مستوى الكوليسترول، الدهون واطئة الكثافة، والدهون عالية الكثافة، وزيادة مستوى الدهون الثلاثية في الدم وكذلك مستوى الدهون واطئة الكثافة جدا ربما له علاقة بالتهاب المجاري البولية في الاطفال. هنا يمكن استعمال التغيرات في مستوى الدهون كعلامات لالتهاب المجاري البولية لدى الاطفال.

**الاستنتاج:** نحن نوصي بان الاطفال المصابين بالتهاب المجاري البولية لربما يحتاجون لقياس مستوى الدهون المؤكسدة والتي لربما تزداد نتيجة التهاب المجاري البولية).