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A COMPARATIVE STUDY OF 15-ISOPROSTANE F2T IN BLOOD OF EXTRA HEPATIC CHOLESTASIS CHILDREN AND HEALTHY CHILDREN.

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ABSTRACT

Cholestasis is impairment of bile the digestive fluid secretion caused by dysfunction of hepatocytes or obstruction of bile flow through intra-or extra hepatic bile ducts. Cholestasis always indicates a pathological process that can result in chronic liver dysfunction, the necessity of liver transplantation and even death. Cholestasis can occur at any age. Oxidative stress occurs as a consequence of imbalance between the formation of oxygen free radicals and in activation of these species by antioxidant defense system.15-isoprostane F2t has been proposed as good indicator of oxidative stress, 15-isoprostane F2t have been found in the blood of patients with cholestasis. The purpose of this study is to investigate Comparison of oxidative stress between two group by determine 15-is prostate F2t. In the cholestasis patients, a significant increase was found in mean levels of 15-isoprostane F2t compared to control children.15 isoprostane F2 t In the cholestasis patients was 47.03±26.193 and in control children was 0.73±1.17, Oxidative stress may potentially be used as diagnostic markers of disease progression.

KEYWORDS: ***15-isoprostane F2t, extra hepatic cholestasis, total bilirubin, alkaline phosphatase, direct bilirubin.***

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INTRODUCTION

The liver is known for its capacity for compensatory regeneration after parenchymal injury or cell loss and has numerous mechanisms for adaptation and protection in cholestasis conditions. This may be an underlying reason for the prolonged natural history of cholestasis liver disease. Cholestasis is a process in which there is a decrease in biliary flow, histological evidence of deposition of bile pigments in hepatocytes and bile ducts, and an increase in the serum concentrations of products excreted in bile. Cholestasis can occur at any age.[1-7] (Between the liver cells which produce bile and the duodenum the first segment of the small intestine). Therefore, the clinical definition of cholestasis is any condition in which substances normally excreted into bile are retained. The classification of cholestasis are divided into intrahepatic and extra hepatic diseases .intrahepatic disease include acute hepatitis, alcoholic liver disease, primary biliary cirrhosis with.

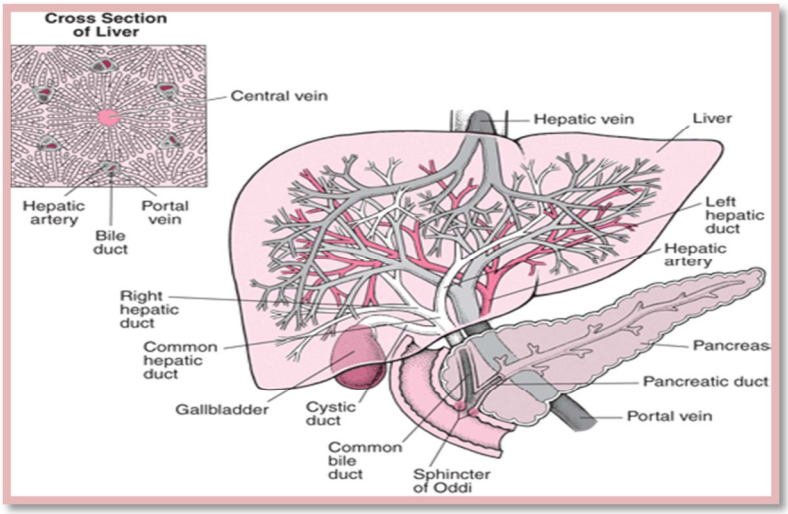

Figure 1
Cross section of liver

inflammation and scarring of the bile ducts, cirrhosis due to viral hepatitis B or C, drugs, and cancer that has spread to the liver. Extra hepatic diseases include a stone in a bile duct, stricture of a bile duct, cancer of a bile duct, cancer of the pancreas, and pancreatitis. Cholestasis is now regarded as a disorder of oxidant overload of the liver and it has systemic effects, increased oxidative stress has been proposed as the main mechanism underlying dysfunction, Oxidative stress can be defined as increased formation of reactive oxygen species or decreased antioxidant defense system.[2] High levels of reactive oxygen species can lead to cellular damage and death and extremely cytotoxic resulting from damage to bimolecular including lipid peroxidation, DNA and protein oxidation, which is collectively known as oxidative stress [3-10] 15-isoprostane F2tis a product of lipid peroxidation that can be used as a measure of free radical exposure or injury.15-isoprostane F2t has been proposed as good indicator of oxidative stress,15-isoprostane F2t have been found in the blood of patients with cholestasis.

MATERIALS AND METHODS

The study was conducted at the Department of Pediatrics at Al Imamain kadhimain Medical City (PBUH). And Gastroenterology and Liver Hospital City Medicine, Baghdad, Iraq. Patients studied were admitted between January 2017 to March 2018 on 400 children age range between (0 mon-12years), the subjects in this study were divided into two main groups: extra hepatic cholestasis and healthy children. Studied cases these children who met the inclusion and the exclusion criteria of this study gave informed consent in the Medical Clinic before being included in the study, and then they were interviewed and subjected to the same questionnaire

Inclusion Criteria

- Children age (0-12) year
- Extra hepatic cholestasis
- Chronic cholestasis
- Magnetic resonance cholangiopancreato graphy report

Exclusion Criteria

- Extreme of age (>12 years)
- Renal disease
- Heart disease
- Diabetes
- Anemia
- Chronic drug intake
- Acute cholestasis
- Urinary tract infection
- Metabolic disorder
- Passive smoking
- Congenitally information

Concentration of 15-isoprostane F2t in serum was determined by specific ELISA Kit for human (15-isoprostane F2t) of US Biological Chemical Company, United States. Concentration of total bilirubin, direct bilirubin and alkaline phosphatase by Chemistry Analyze -PZ CORMAY\ ACCENT 300, Poland

STATISTICAL ANALYSIS

The Data obtained were analyzed using statistical packages of SPSS 18 (statistical packages for social sciences-version 18). All data were presented as a mean ± Sd. Statistical differences among groups were carried out by one-way analysis of variance (ANOVA).probability value (p) of less than 0.05 was considered statistically significant.

RESULTS

During the period of the study a total sample of 400 children. Among this sample gave 221 extra hepatic cholestasis children and the remaining 179 are healthy children, as shown in figure (2).

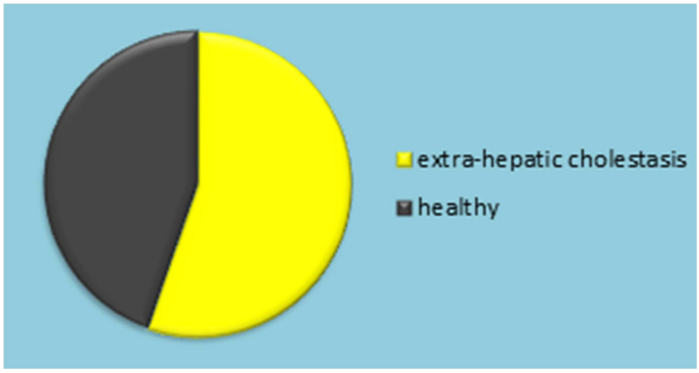

Figure 2
Distribution of study cases

Demographic characteristics
Table (1) (2) describes the demographic characteristics of studied; no Characteristic statistically significant difference among study groups was noted.

Table 1
Demographic characteristics of studied groups

Characteristic	Extra hepatic cholestasis	Healthy group	P value
Age	3.34±3.5	3.6±4.01	0.489

Mean ± SD

Table 2
Demographic data distribution of studied groups

Characteristic		Extra hepatic hole stasis N=221		Healthy N=179		P value
		No	%	No.	%	
Sex of child	Male	121	54.84	137	76.67	0.103
	Female	100	45.16	42	23.33	
Place of residence	Urban	128	58.06	95	53.33	0.579
	Rural	93	41.94	84	46.67	
Children education	Nursery education	99	45	100	55.86	0.17
	Pre- school	77	35	35	19.55	
	Elementary School	45	20	44	24.58	

(*significant using Pearson chi-squared test at 0.05 level of significance)

15-isoprostane F2t
Box and whisker plot showing relative median of 15-isoprostane F2t levels with 25th and 75th percentiles which there were increase in extra hepatic cholestasis children compared with healthy group as shown in figure (3).

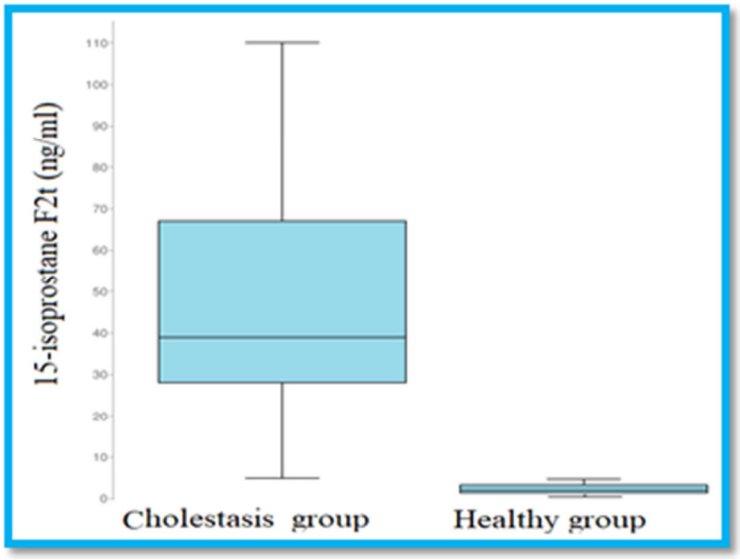

Figure 3
Box plot of 15-isoprostane F2t in the studied groups

Table (3) revealed that there significant differences mean of 15-isoprostane F2t in cholestasis and healthy children, p value <0.001 by doing one-way ANOVA test

Table 3
Comparison of 15-isoprostane F2t in studied groups.

Oxidative stress marker	Extra hepatic cholestasis (n=221) Mean±SD	Healthy (n=179) Mean±SD	P value
15-isoprostane F2t (ng/ml)	47.03±26.193	0.73±1.17	<0.001*

(*significant using one-way ANOVA test)

As shown in table (4) compare the effect of age on 15-isoprostane F2t, the result showed that mean of 15-isoprostane F2t in were significant decrease in newborn compared with other subgroups of extra hepatic cholestasis.

Table 4
Comparison of mean 15-isoprostane F2t in extra hepatic cholestasis subgroups.

Parameters	New born N=43	Infants N=45	toddler N=35	Pre-school N=42	School age N=52	P value
15-isoprostane F2t (ng/ml) Mean±SD	27.28± 8.86	46.4± 11.56	56.62± 25.53	47.4± 21.57	54.23± 37.56	0.002*

(*significant using one-way ANOVA test)

Biochemistry marker

Table (5) Shown highly significant difference concentration of Liver function marker in extra hepatic cholestasis than healthy children (p value 0.001).

Table 5
Comparison of studied parameters between extra hepatic cholestasis and healthy

Parameters	Extra hepatic cholestasis (n=221) Mean±SD	Healthy (n=179) Mean±SD	P value
Total bilirubin (g\dl)	3.88±0.99	0.6±0.278	0.001
Direct bilirubin (ng\ml)	3.39±1.04	0.258±0.59	0.001
ALP (ng\ml)	705.195±271.17	83.7±34.9	0.001

DISCUSSION

Diseases that manifest as cholestasis in children often result from pathologic processes that begin early in postnatal life 8 when the liver has not reached functional maturity and also Obstructive cholestasis is usually the result of physical obstruction of the biliary system at the level of the extra hepatic bile ducts. Retention of bile salts results in injury to biological membranes throughout the body. The liver is most affected[4] Chronic cholestasis conditions are characterized by metabolic alterations in bile salts, lipids, and nutrients, and are associated to membrane lipid destruction and mitochondrial dysfunction.[5] The major liver function

marker which were going to be studied are total bilirubin, direct bilirubin and alkaline phosphatase and oxidative stress marker of lipid peroxidation 15-isoprostane F2t, This study describes and evaluates the association of lipid peroxidation with extra hepatic cholestasis children, it was found that levels of 15-isoprostane F2t were significant higher in extra hepatic cholestasis children as compared with healthy children (table 4). The clinical extra hepatic cholestasis children is closely related to the degree of lipid peroxidation, and the natural antioxidant system might fail to work effectively in the presence of lipid peroxidation damage in extra hepatic cholestasis children. The implication of oxidative stress in the progression of the liver diseases with higher prevalence worldwide[6] Oxidative stress is a major pathogenetic event occurring in several liver disorders ranging from metabolic to proliferate ones[9] Many studies have shown that oxidative stress takes part in the pathogenesis of cholestasis by way of cytokines[12] and lipid peroxidation is responsible for the tissue injury in cholestasis[13] In present study the Liver function marker (bilirubin, direct bilirubin and alkaline phosphatase) level was found to be higher in extra hepatic cholestasis children to healthy children (P<0.001). Show in table (6) Increased serum bilirubin level is a widely used diagnostic marker for hepatic illnesses.[4]

CONCLUSION

Oxidative stress could play a role in the pathogenesis of cholestatic chronic liver diseases. These preliminary results are encouraging to conduct more extensive clinical studies using adjuvant antioxidant therapy. OS may potentially be used as diagnostic markers of disease progression.

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CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES

1. Hisham, N. Medscape.2017, medical news. Available from: https://www.medscape.com/features/year-in-Medicine/public/2017
2. Gulbayzar S, Arica V, Hatipoglu S, Kaya A, Arica S, Karatekin G. Malonaldehyde Levels in the Cord Blood of New Born Infants. Iran J Pediatr. 2011;21(3):313-19. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3446175/
3. Niki E. Biomarkers of lipid peroxidation in clinical material. Biochim Biophys Acta - Gen Subj. 2014;1840(2):809–17. DOI:http://dx.doi.org/10.1016/j.bbagen.2013.03.020
4. *Fidelis E Ejezie, Edwin A Onwusi, Uchenna I Nwagha*. Some biochemical markers of oxidative stress in pregnant Nigerian women. Trop J.Obstet.Gynaecol. 2004;21(2):122-124. Available from: https://www.ajol.info/index.php/tjog/article/viewFile/14484/16064
5. Gazzin S, Masutti F, Vitek L, Tiribelli C. The molecular basis of jaundice: An old symptom revisited. Liver Int. 2017;37(8):1094–102. DOI: http://dx.doi.org/10.1111/liv.13351
6. Grattagliano I, Oliveira PJ, Vergani L, Portincasa P. Oxidative and Nitrosative Stress in Chronic Cholestasis. Liver Pathophysiology. Elsevier. 2017:p.225–37. Available from: https://www.researchgate.net/publication/314666170_Oxidative_and_Nitrosative_Stress_in_Chronic_Cholestasis
7. Fernández-Iglesias A, Hide D, Gracia-Sancho J. Oxidative Stress in Liver Diseases. Gastrointestinal Tissue. Elsevier.2017.p.125–40. DOI:http://dx.doi.org/10.1016/b978-0-12-805377-5.00009-6
8. Fawaz R, Baumann U, Ekong U, Fischler B, Hadzic N, Mack CL, et al. Guideline for the Evaluation of Cholestatic Jaundice in Infants. J Pediatr Gastroenterol Nutr. 2017;64(1):154–68. DOI: http://dx.doi.org/10.1097/mpg.0000000000001334
9. Catzola A, Vajro P. Management options for cholestatic liver disease in children. Expert Rev Gastroenterol Hepatol. 2017;11(11):1019–30. DOI: http://dx.doi.org/10.1080/17474124.2017.1359538
10. George Notas, Ioannis E, Koutroubakis, Elias A. Kouroumalis, Oxidants and Antioxidants in Liver Disease, Antioxidants: New Research. 2006:2-48. Available from: https://books.google.co.in/books?hl=en&lr=&id=RjtableXBIIC&oi=fnd&pg=PA1&dq=10.%09George+Notas,+Ioannis+E,+Koutroubakis,+Elias+A.+Kouroumalis,+Oxidants+and+Antioxidants+in+Liver+Disease,+Antioxidants:+New+Research.2006:2-48.&ots=TlMobLUz2V&sig=3FivndEEinbDN0wDoy32emcLTYs
11. Ergul Belge Kurutas, The importance of antioxidants which play the role in cellular response against oxidative- nitrosative stress current state. Nutrition Journal .2016 July 25;15(1):71. Available from: https://nutritionj.biomedcentral.com/articles/10.1186/s12937-016-0186-5
12. Nagwa A. Ismail, Sawsan H. Okasha, A. Dhawan, Azza O. Abdel-Rahman, Olfat G. Shaker, and Nehal A. Sadik. Antioxidant Enzyme Activities in Hepatic Tissue from Children with Chronic Cholestatic Liver Disease. Saudi J Gastroenterol. 2010 Apr;16(2):90–94. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3016512/
13. Sha Li, Hor-Yue Tan, Ning Wang, Zhang-Jin Zhang, Lixing Lao, Chi-Woon Wong, and Yibin Feng. The Role of Oxidative Stress and Antioxidants in Liver Diseases. Int J Mol Sci. 2015 Nov;16(11):26087–124. Available from: https://www.mdpi.com/1422-0067/16/11/25942/pdf