

DETECTION THE ROLE OF CYTOKINES IN CHRONIC CALCULOUS AND ACALCULOUS CHOLECYSTITIS FORMATION

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ABSTRACT : Gallstones are a worldwide medical problem. TNF- α are vital cytokines, it can make the gallbladder inflammation is more by it directly affected gallbladder epithelial cell absorptive function contribute to hastening gallstone formation. However, IL-4 protects gallstone production. A recent study was performed on patients with chronic cholecystitis (acalculous and calculus type) ten tissue samples of chronic acalculous cholecystitis and ninety-five tissue sample from calculus patient can be referred to the surgical clinic of Al-Husain General Hospital. Gallbladder tissue sample put in formalin then transport to the laboratory for examination the expression status of these cytokines in gallbladder tissue by IHC technique and modern spatial visualization technique. There is a significant statistical difference between calculus and a calculous cholecystitis with TNF- α and IL-4 expression. Expression of IL4 and TNF- α have a role in the cholelithiasis pathogenesis and gallstone pathogenesis.

Key words : Cholelithiasis, cholecystectomy, cytokines, immunohistochemistry.

INTRODUCTION

Gallstones are hard accumulative of the bile fluid inside the gallbladder (Tanaja *et al*, 2017). It has many sizes, it ranged from sand grain to a golf ball. The gallstones are composed of calcium salts, bilirubin and cholesterol with protein at small amounts and some other materials (Njeze, 2013). Cholecystitis is the abrupt inflammation of the gallbladder. Gallstone occurrence is a complicated development mediated by genetic and environmental factors. The role of the immune system in the pathogenesis of gallstones was not considered a valid topic of research interest (Sarachik, 2016). Chronic cholecystitis is an inflammation of the gallbladder wall and leading to biliary system dysfunctions, associated with the gallstones results in biliary pain. A calculous cholecystitis is a life-threatening illness but it rare and pathogenesis is not fully showed yet. Cytokines are small, low molecular weights non-structural proteins that have a complex regulatory influence on inflammation and immunity (It is produced by the immune cells and from other cells have directly related to cellular damage). Cytokines are commonly classified in one or the other category like tumor necrosis factor-alpha (TNF- α) as pro-inflammatory cytokines whereas interleukin-4 (IL4), recognized as anti-inflammatory cytokines (Bastidas-

Coral *et al*, 2016). IL-4 is produced by TH2 cells, eosinophils, mast cells and basophils. IL-4 is the stimuli of TH2 cells and induces immunoglobulin E class-switching in B cells (Akdis *et al*, 2016).

MATERIALS AND METHODS

Ten tissue samples of chronic acalculous cholecystitis and ninety-five patients with chronic calculous cholecystitis referred to the surgical clinic of Al-Husain General Hospital. Gallbladder tissue sample put in formalin then transport to the laboratory for immunohistochemically (IHC) examination the expression status of TNF- α and IL4 in gallbladder tissue of the patients with cholelithiasis as related to CCC and CAC. Expression status of IL-4 and TNF- α in a gallbladder tissue sample of the patients with cholelithiasis and without cholelithiasis.

Ethical approval

Given by the Medical Research at AL Nasiriya, Health Directorate ethical committee before the collection of the samples. A special form of a questionnaire constructed to gather data reviewed & revised by subject matter expert for testing the validity & enrichment

Statistical analysis

Statistical analysis was done using Graph Pad Prism

and SPSS software. The results were expressed as mean ± standard deviations (mean ± SD). p-value <0.05 was represented significantly. One-way ANOVA, One-way ANOVA-Tukey' and a T-test was applied for comparison among the parameters in many groups.

The person correlation coefficient (r) was used to test the correlation among the different parameters in each patient group.

RESULTS

There is a significant statistical difference between calculus and acalculous cholecystitis for both TNF-á and IL-4 expression, P-value = 0.0005 and 0.05 respectively (high significant association for TNF-á) as demonstrated in Table 1.

TNF-á and IL-4 correlation

A significant correlation between TNF-á and IL-4 among CCC and CAC patients are none, as seen in Figs. 1 and 2.

Another classification of inflammation in gall bladder depends on the severity and divides it to 3 categories (mild, moderate and severe), but there are no significant differences between the CCC and CAC group in the distribution among these categories as revealed by Fig. 3.

DISCUSSION

There is a significant statistical difference between calculus and acalculous cholecystitis for both TNF-á and IL-4 expression. Previous study showed that TNF-á was detected in all patients of CCC and play a role in gallstone pathogenesis (Issa and Muthena, 2014). Another study revealed that TNF was highly expressed in calculus but not within acalculous, IL4 was low in both (Ebadi *et al*, 2013).

TNF-á is cytokines results increasing of the gallbladder inflammation and results in acceleration of the gallstone production. However, IL-4 protects gallstone formation. TNF-á has an important great in the host

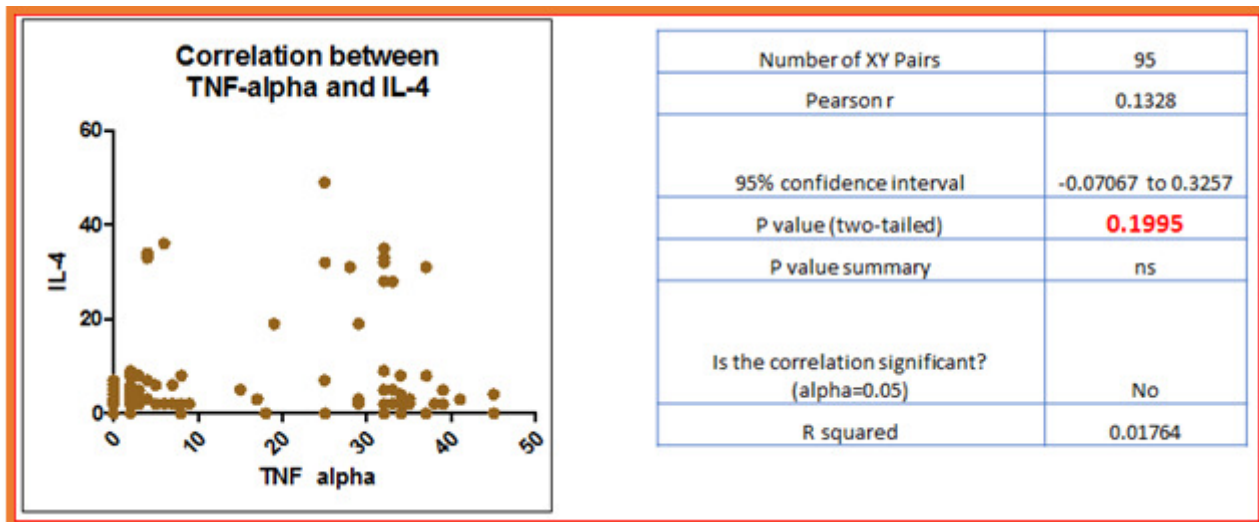


Fig. 1 : TNF-á and IL-4 Correlation among CCC, non-significant.

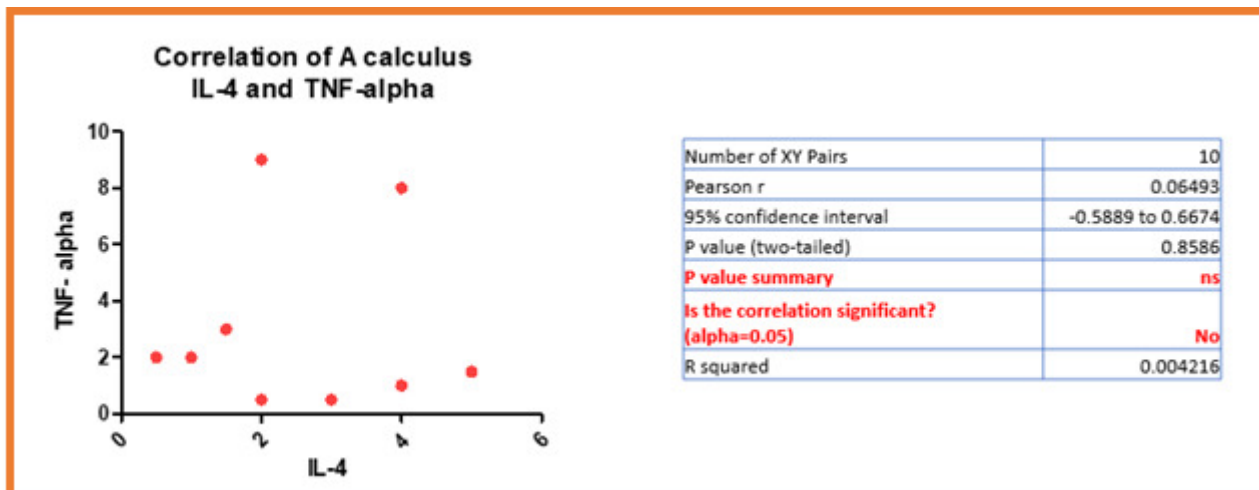


Fig. 2 : TNF-á and IL-4 Correlation among CAC, non-significant.

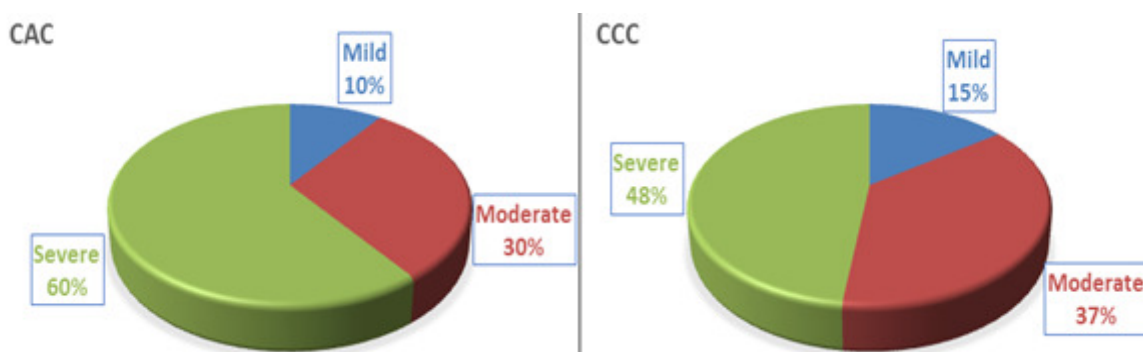


Fig. 3 : Degrees of inflammation among the studied population.

Table 1 : TNF- α and IL-4 expression among calculus and acalculous cholecystitis.

Group Statistics						
	Type	No.	Mean	Std. Deviation	ANOVA	p-value
TNF- α	Calculus	95	18.5579	15.97652	149.716	0.0005
	A calculus	10	3.0000	2.98142		
IL4	Calculus	95	7.7684	10.96460	3.942	0.050
	A calculus	10	3.8000	3.08401		

defense against parasite, virus and bacteria. TNF- α has a vital role in response to the infection, but excessive formation causes harm (Bradley, 2008).

TNF- α and IL-4 correlation among CCC and CAC patients is none, when protein expression of proinflammatory cytokines (TNF alpha) higher than anti-inflammatory cytokine (il4) this indicated the presence of immune predisposition in patients for gallstone. IL-4 protects gallstone production, TNF- α is causing an increase in the gallbladder inflammation and causes accelerating gallstone production (Ebadi *et al*, 2013). A previous study showed that TNF alpha high expression than IL4 levels of pro-inflammatory cytokines (IL1, TNF- α & IL-6) were significantly increased in gallstone patients sera, while anti-inflammatory cytokine IL-4 concentrations in gallstone patients sera showed significant reduced (Issa and Muthena, 2014).

CONCLUSION

Immunohistochemical expression of TNF- α and IL4 may suggest the role of these cytokines in the pathogenesis of cholelithiasis. TNF- α was detected in most patients with CCC and play a role in gallstone pathogenesis. IL-4 protects gallstone production and some gallbladder illness.

Recommendation

Further studies with the large samples are required to elucidate the role of anti-inflammatory cytokine and another proinflammatory cytokine in gallstones formation and attempt to study immune -modulation to prevent gallstones formation.

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