Comparative study of the impact injury by (Toxoplasma, Rubella virus and cytomegalo virus) on some liver enzymes in diabetic women in Kirkuk Governorate.

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Abstract

Igm and IgG antibodies for Toxoplasma ,Rubella virus , and Cytomegalovirus infections were assessed in a total 100 diabetics and 30 non diabetics women serum samples .On the other hand IgG positive serum samples for Toxoplasma ,Rubella virus , and Cytomegalovirus were evaluated by determination (GPT ,GOT, TSB and ALP).Results revealed increased levels activity of liver function tests in infected women , due to liver cell damage that have occur during virulent and low virulent infection . Increaed levels activity of liver function tests in infected women.

CONCLUSION

This study concluded that the higher prevalence of seropositivity for human (Toxoplasma, Rubella virus and cytomegalo virus)in diabetic patients comparing with normal individuals which means that patients with diabetic were at high risk for these infections.

Keywords: Biochemical, *Toxoplasma gondii*, Liver function, Women, Rubella andcytomegalovirus,

Introduction

Toxoplasma Gondi is considered one of the most widespread parasites in the world causing abortion it is intracellular protozoan that infects humans and other warm_blooded animals [1].The organism transmitted to humans by accidental ingestion of water, food, or soil contaminated with T. gondii oocysts or consumption of meat containing T. gondii cysts that is eaten raw or undercooked .This disease is clinically insignificant in immunocompe-tent adults. [2].Toxoplasma gondii is a ubiquitous parasite whose definitive hosts are members of the Felidae cat family. Cat shed millions of environmentally resistant oocysts in their feces after primary infection and are usually without clinical manifestations of disease[3]. Intermediate hosts include almost all warm- blooded mammals and birds,including humans, who accumulate infectious, quiescent stages (bradyzoites) of the parasite in their tissues particularly in the skeletal muscle and the brain

[4,5].Cytomegalovirus(CMV) belongs to the herpes virus group of infections. It can be transmitted through body secretions, as well as by sexual contact; some newborns which acquire CMV through the mother's breast milk Infected infants may have severe problems, such as hearing loss, mental retardation, pneumonia, hepatitis, or blood disorders[6]. Cytomegalovirus (from the Greek cyto-, "cell", and -megalo-, "large") is a viral genus of the Herpesviruses group: in humans it is commonly known as HCMV or Human Herpesvirus 5 (HHV-5) [7] .Human Cytomegalovirus (CMV) is a herpes virus and the most common cause of congenital viral infection and malformation in the developed countries resulting from viral intrauterine infection [8] .Cytomegalovirus like all herpes viruses undergoes latency and reactivation in the host. Although HCMV has been shown to infect a broad-spectrum of cells in vivo and has been isolated from saliva, urine, blood and human milk [9]. However, in immune compromised individuals owing to the lack of immunologic control, the virus is able to reactivate and to cause severe CMV disease. Viral activity can be observed in all organs, including the pancreas [10] demonstrating that the virus has a broad cellular tropism. This broad cellular tropism is because widely spread receptors, such as integrin's and the epidermal growth factor receptor, serve as entry receptors [11]. These are also found on pancreatic cells making them putative targets for CMV infection [12]. However, in immune compromised individuals owing to the lack of immunologic control, the virus is able to reactivate and to cause severe CMV disease. Viral activity can be observed in all organs, including the pancreas demonstrating that the virus has a broad cellular tropism. This broad cellular tropism is because widely spread receptors, such as integrins and the epidermal growth factor receptor, serve as entry receptors. [13,14].Up to 15% of intrauterine CMV infections result in symptomatic congenital disease at birth and 10 to 15%of those born with asymptomatic congenital CMV will develop significant clinical squeal in infancy [15]. The presence of CMV-specific Immunoglobulin M (IgM) may not be indicative of primary infection, since it is also produced during reactivation and re infection[16] .Rubella (German measles) [17] .The name rubella is derived from Latin mening " Little red " rubella was initially considered to be a variant of measles or scarlet fever and was called " Third disease " it was first described as a separate disease in the German medical literature .[18].Rubella is an acute febrile illness ,which caused by rubella virus ,from Togavirus family genus Rubivirus . The disease is characterized by a rash and lymphadenopathy that affect children and adults .It is the mildest of common viral exanthemas.[19].Rubella is a mild viral infection of childhood caused by non-arthropod born member of family togaviridae .At least half of all primary rubella infections are subclinical . However if it is acquired during pregnancy it may cause abortion , stillbirth , premature delivery , low birth weight and a number of congenital anomalies .[20]

Infections caused by TORCH – toxoplasma, rubella virus, cytomegalo virus (CMV) and herpes simplex virus (HSV) – is the major cause of BOH . Infections by TORCH agents in women are usually asymptomatic and chronic. Fetus TORCH

infections cause a syndrome characterized by microcephaly, sensor neural deafness, chorioretinitis, hepatosplenomegaly and thrombo-cytopenia. Symptoms of a TORCH infection may include fever and poor feeding. The newborn is often small for gestational age.[21] A petechial rash on the skin may be present, with small reddish or purplish spots due to bleeding from capillaries under the skin. An enlarged liver and spleen (hepatosplenomegaly) is common, as is jaundice. However, jaundice is less common in Hepatitis B because a newborn's immune system is not developed well enough to mount a response against liver cells, as would normally be the cause of jaundice in an older child or adult. Hearing impairment, eye problems, mental retardation, autism, and death can be caused by TORCH infections. The mother often has a mild infection with few or no symptoms [22]. Infections caused by TORCH – toxoplasma, rubella virus, cytomegalo virus (CMV) and herpes simplex virus (HSV) -- is the major cause of BOH . The aim of the current work is to assess the impact injury of (Toxoplasma, Rubella virus and cytomegalo virus) on some liver enzymes in diabetic women in Kirkuk Governorate by comparison with the healthy controls.

Patients and Methods

A total of 130 serum samples were optained from women 100 diabetic and 30 non - diabetic as control cases who attended to the private laboratories in Kirkuk city . A total of 130 women were investigated including 100 diabetic and 30 non –diabetic clinically normal women . All sera samples (130 samples) of DM and non diabetic women were analyzed for serological evaluation for IgM and IgG antibodies for (Toxoplasma, Rubella virus and cytomegalo virus) infections according to manufacturer's instructions usingImmunochromatography method (CTK BioteckInC : USA) .Liver function for positive IgG for (Toxoplasma, Rubella virus and cytomegalo virus)were evaluated by estimation the activities of GPT ,GOT, TSB , and Alkaline Phosphatase by using diagnostic kit (BIOLABO :FRANCE).

RESULTS

Out of 100 DM samples samples positive results by Immunochromatography method detected in 2 samples 2.0%IgM only 22 samples 22% IgG only for Toxoplasma,in one samples 1.0 %IgM only 25 samples 25.0% IgG only for rubella virus andin 3 samples 3.0 %IgM only 35 samples 17.0% IgG for cytomegalovirus only and 1(0.9%) sample showed positive results for both IgM and IgG for CMV virus . No positive results detected among control group for all three studied viruses Table 1 . Liver function tests showed elevation among diabetic patients whom infected with Toxoplasmosis ,rubella virus and cytomegalovirus compared with control group ...Table 2, Table 3, Table 4 respectively .

Discussion

Results of this study showed the presence of considerable differences between the mean values of IgG of diabetics and non diabetics controls, pointing to the possible role of microbial infection (in general) in diabetes mellitus. The infections by a given

virus may involve different cell types and present different clinical pictures..Study by Yasir mentioned that the higher prevalence of seropositivity for human CMV in diabetic patients comparing with normal individual which mean that cytomegalovirus patients with diabetic were at high risk for CMV infection .Higher prevalence of CMV antibodies was observed in diabetic patients of all age – group as compared with control group .[23] Study by Robert who mentioned a greater seroprevalence of anti-CMV IgG antibodies among patients with diabetes (97.6%), compared with control subjects (86.7%), and the difference was statistically significant [OR = 6.2, 95% CI: 1.1 to 36.0, $P < 0.05$]. Three draws on a subset of 91 patients produced still greater odds [OR = 12.4, 95% CI: 1.3 to 117, $P < 0.05$]. There were significantly more ($P <$ or $= 0.001$) vascular complications among patients with diabetes. There was a colinearity of trends between diabetes, seropositivity to CMV, and age his findings indicated an up to 12 times greater odds of having type 2 diabetes for persons previously exposed to CMV. Since accelerated atherosclerosis is also associated with diabetes and CMV, past CMV infection may be a common factor that links atherosclerosis and diabetes. No other viruses tested in this study, either coxsackie B viruses or parvovirus, showed a significant association with type 2 diabetes[24]. Study by Al-baitushi reported that neither the CMV nor the EBV has relation with T1D ,while the infection with hepatitis c virus may be contributed to T1D since there is a significant differences between the number of T1D patients and the number of control who have anti HCV Abs.[25] .In addition, the liver can be affected as part of a generalized host infection with viruses that primarily target other tissues, particularly the upper respiratory tract. Examples of this phenomenon include the herpes viruses (Epstein-Barr virus, cytomegalovirus [CMV], and herpes simplex virus), parvovirus, adenovirus[28],and severe acute respiratory syndrome (SARS)-associated coronavirus[28].Liver involvement in non hepatotropic viral infections can range from mildly deranged liver biochemistry to fulminant liver failure. In most of these infections, hepatitis is thought to be a consequence of an immune response to viral antigens with a close topographic association between the presence of viral antigens and the associated inflammatory infiltrates in the liver. Loss of immune control may be responsible for the development of hepatitis in CMV hepatitis[29]and other opportunistic viral infections such as adenovirus .Similar activities may also be involved in SARS-associated hepatitis, which is characterized by focal lobular lymphocytic infiltrates [30].Serum AST and ALT activities are excellent markers of hepatocellular injury [31] and serum ALT activity is more specific than serum AST for assessing liver injury [32] . The significantly elevated serum activities of aminotransferases in the serologically positive cases of toxoplasmosis in this study are in agreement with several studies[33]. These results also agree with the studies performed on experimental animals [34] . These elevations suggest the involvement of liver cells. Hepatic necrosis is a well established complication of toxoplasmosis where this infection can cause round cell infiltration in the portal areas, cholestasis, swollen endothelial cells and focal necrosis of liver cells [35]. However, despite the

significant increase of AST and ALT activities compared with the controls, the levels are still within normal ranges suggesting a mild effect on the liverSerum ALP activity was significantly higher in the patients group than that the control . Our finding is in agreement with that reported by several studies and could be explained by the presence of Toxoplasma gondii parasites in the bile duct cells since hepatic ALP is reported to be present on the canalicular and luminal domain on bile duct epithelium .In conclusion, the liver enzymes activities are statistically elevated but they are still within normal acceptable ranges suggesting that toxoplasmosis may affect the liver in a way that this effect is not sufficient to produce clinical signs and symptoms[33]Liver function tests in toxoplasmosis by Nadwa A. J. Mahmood to highlight the possible effects of toxoplasmosis on serum activities of liver enzymes. Repoted thatLiver enzymes activities were higher in patients compared with those of the controls. A probable involvement of the liver in the disease process was noticed for the toxoplasmosis patients although not sufficient to produce clinical signs and symptoms of liver disease.[36]The present study demonstrates a strong association between the infectious agents (Toxoplasma gondii ,Rubella and CMV) and diabetics in women. It is therefore recommended that all cases with such history should be routinely screened for these agents (IgM and IgG). Early diagnosis will help in proper management of the cases. This study also emphasizes the need for immunization in prospective mothers and adolescent girls who have not received vaccine in their childhood that give there acquired immunity to prevent infection that will reducing chance of abortion

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Table 1:Results of IgM and IgG of rubella virus among diabetic women .

Studied Groups	Name of the Pathogen	Total Number of Examined Cases	Results			
			Igm		IgG	
			Positive Results		Positive Results	
			No.	%	No.	%
Diabetic women	Toxoplasma	100	2	2	22	22
	Rubellavirus	100	1	1	25	25
	CMV	100	3	3	35	35
Controle	Toxoplasma	30	0	0	2	6.6
	Rubellavirus	30	0	0	4	13.3
	CMV	30	0	0	6	20.0

Table 2: Comparison of measured serum (ALT,AST,ALP and TSB) activities between Toxoplasma IgG positive patients and controls

Tests	Patients (n=20)			Control (n=15)		
	Number of Samples	Range Iu/l	Mean ±SD	Number of Samples	Range	Mean ± SD
AST (IU/L)	20	11.7-23.0	17.6±3.82	15	7.7-13.3	9.4±3.03
ALT (IU/L)	20	13-22.3	17.6±5.022	15	5.4-9.3	7.48±2.54
ALP (IU/L)	20	77-130	86.2±14.57	15	63-92	74.06±12.46
TSB mg/dl	20	0.3-4.4	1.16±5.46	15	0.2-0.7	0.4±1.39

SD. = Standard deviation

Table 3: Table 1. Comparison of measured serum (ALT,AST,ALP and TSB) activities between Rubella IgG positive patients and controls

Tests	Patients (n=20)			Control (n=15)		
	Number of Samples	Range	Mean ±SD	Number of Samples	Range	Mean ±SD
AST (IU/L)	20	27.1-46.4	35.98±17.74	15	16.3-24.1	19.02±5.08
ALT (IU/L)	20	19.2-49.3	40.6±5.46	15	12.1-33.3	21.46±1.35
ALP (IU/L)	20	72.3-122.2	127.6±44.45	15	55.1-87.1	73.6±2.79
TSB mg/dl	20	0.9-3.0	1.6±1.24	15	0.2-1.2	0.6±2.46

SD. = Standard deviation

Table 4: Table 1. Comparison of measured serum (ALT,AST,ALP and TSB) activities between CytomegalovirusIgG positive patients and controls

Tests	Patients (n=20)			Control (n=15)		
	Number of Samples	Range	Mean ±SD	Number of Samples	Range	Mean± SD
AST (IU/L)	20	17.1-33.3	24.6±5.01	15	7.6-20.1	12.3±5.03
ALT (IU/L)	20	19.39	29.2±14.29	15	9-18	13.2±4.43
ALP (IU/L)	20	77-100	85.1±20.23	15	47.3-87.3	64±6.60
TSB mg/dl	20	1.0-2.9	1.71±8.05	15	0.3-1.2	0.7±3.07

SD. = Standard deviation