



Correlation between the Prevalence of Hepatitis B and C Viruses against Tumor Necrosis Factor- α among Patients in Babylon Province

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Authors' contributions

This work was carried out in collaboration between both authors with joint designed of the study. They managed the literature searches, wrote the protocol, performed laboratory study and manuscript. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Hepatitis is a liver disease caused by infectious and non-infectious agents. Hepatitis B and C are major public health problems worldwide. Hepatitis B (HBV) and C virus (HCV) infections are known to occur in the general population due to their multiple mode of transmission mainly through blood.

Aim: This study aimed to estimate the prevalence of hepatitis B and C virus among population in Babylon province and evaluation of the levels of the TNF-alpha in infected patients with hepatitis B and C

Methods: The study was conducted on individuals referred to the Central Public Health Laboratory to investigate the prevalence of HBV and HCV infections in Babylon province. A total of 6061 samples was included in this study, they screened by VIDAS test for detection of both viruses, then

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confirmed by real-time PCR. Concentration of TNF- α was measured in patients with hepatitis B and C and control group (Control group consisted of the healthy subjects with no history of renal or liver diseases and negative results for HBV and HCV test) by using ELISA test.

Results: A total of 6061 individual were screened, amongst them, 18 (0.29%) were positive for HBV and 16 (0.26%) were positive for HCV by both VIDAS test and real-time PCR.

Most of HBV infections seen among hemodialysis patients followed by haemophilia, while most HCV infections seen among thalassemia and haemophilia patients than others groups.

The prevalence of both viruses was higher among male than female, and in urban than rural region. Most of HBV infections were high in individual with age ranging between 20-29 and 30-39 years, while most HCV infections in individual with age ranging between 20-29 years, although it is statistically insignificant.

The mean serum level of TNF- α was significantly higher in individual with HBV and HCV infection (68.7 ± 12.84 pg/mL) and (89.1 ± 22.017) as compared with control group (43.1 ± 5.87 pg/mL).

Conclusion: The prevalence of HBV and HCV was relatively low. There are increasing level of TNF- α in the serum of patients with viral hepatitis B and C.

Keywords: Hepatitis; hepatitis B virus; hepatitis C virus; tumor necrosis factor-alpha.

ABBREVIATIONS

HBV: Hepatitis B virus, HCV: Hepatitis C virus, TNF- α : tumor necrosis factor-alpha, VIDAS: Vitec Immuno Diagnostic Assay System; ELISA: Enzyme linked immunosorbent assay, ELFA: enzyme-linked fluorescent immunoassay, PCR: polymerase chain reaction, HBsAg: Hepatitis B surface antigen, IFN- γ : interferon- γ , IL-2 interleukin-2, IL-10: interleukin-10, IFN- α : interferon- α , Th-1: T helper-1, IU: International unit.

1. INTRODUCTION

Hepatitis means inflammation of the liver. Viral hepatitis is a major public health problem worldwide. Different viruses including hepatitis A, B, C, D and E viruses cause viral infections of human liver [1].

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the most common causes of liver disease worldwide. Both Hepatitis B and C virus are transmitted through infective blood and body fluids (semen, saliva or vaginal secretion). Other modes of transmission including sexual transmission and vertical transmission. Sexual activity is the major route for transmission of HBV, while HCV is transmitted primarily through infective blood and drug injection [2]. Infections are associated with a broad range of clinical presentations ranging from acute or fulminant hepatitis to chronic infection that may be clinically asymptomatic or may progress to chronic hepatitis and liver cirrhosis [3]. The prevalence of HBV and HCV infections has a wide geographical variation depending on the rate of chronic carrier and the predominant route of transmission. The estimated global prevalence of viral hepatitis is 3%-5%, approximately 400 million people are infected with HBV and around 170 million with HCV. HBV and HCV infections

are of major public health concern; infected individuals carry a substantial risk for chronic liver disease, 5%-10% for HBV and more than 50% for HCV [4]. Iraq is among the intermediate HBV endemic countries, because the carrier rate of HBV between (3%-4.5%) among normal population [5].

The liver is an important site of synthesis cytokines and major clearance organ for various cytokines [6]. HBV causes an inflammatory hepatic illness characterized by mononuclear and polymorphonuclear cellular infiltrates with evidence of hepatic macrophage activation. Macrophage activation represents one of the first events of innate resistance against intracellular infection. In response to pathogens, macrophages and other inflammatory cells secrete cytokines, which mediate the inflammatory process and contribute to the successful clearance of the virus, avoiding the progression of infection and persistence of the virus [7]. Tumor necrosis factor (TNF- α) is a principal mediator of inflammation and cellular immune responses with multiple biological functions, including cytotoxicity towards tumor cells and virus-infected cells, several immunomodulatory actions and initiation of the inflammatory response [8]. TNF- α is a proinflammatory cytokine released mainly from

monocytes and lymphocytes in response to inflammatory stimuli. The production of TNF- α by mononuclear cells shown to be increased in patients with chronic liver disease [9].

2. MATERIALS AND METHODS

2.1 Study Subjects

This cross sectional study was carried out on different groups of population, attended to the Central Public Health Laboratory through period of one year (2013). All of them from different districts belong to the Babylon Province, Iraq. A total of 6061 samples (2828 female and 3233 male with age ranged between (less than 1 to 59 year) was investigated for the prevalence of HBV and HCV. The risk factors of surveyed subjects were recorded: Blood donors, contact, thalassemia and hemophilia patients, patients undergo: hemodialysis, previous surgeries, previous coronary catheterization and patients have history of jaundice and acute hepatitis cases. In addition, the following data were gathered from patients and control groups; Name, age, gender and residence.

Ten ml (10) of blood sample was obtained from each participant, then transported to two tube, one with EDTA and other tube without any anticoagulants, sera were separated by centrifugation at 2000 RPM for 10 minutes, and then stored at -20°C until used.

2.2 Laboratory Test of HBV and HCV

Detection of HBsAg and anti- HCV antibodies was carried out by enzyme-linked fluorescent immunoassay (ELFA) kit that was performed in the automated VIDAS system (BioMerieux, France). The assay principle combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection. The viral load was measured by RT-PCR using Exiprep™ viral DNA/RNA kit (Bioneer-Koria) for extraction of the nucleic acid of the two viruses and RT-PCR Amplification kit (Sacace-Italia) was used for amplification.

2.3 Estimation the Level of TNF- α

The serum level of (TNF- α) in patients with hepatitis B and C infection and control group was investigated. Measurement of TNF- α was done by immunosorbent assay using ELISA test with commercial kits of Boster, USA.

2.4 Statistical Analysis

Statistical analysis was carried out. Data were presented as mean and standard deviation or number and percentage as appropriate. The Chi square test was used to analyze the significance of the results. P value <0.05 was considered significant.

3. RESULTS AND DISCUSSION

3.1 Prevalence and Risk Factors Associated with HBV and HCV Infections

A total of 6061 individuals was involved in this study and examined for the prevalence of HBV and HCV. This study was carried out through period of one year (2013). The results of this study showed that the prevalence of hepatitis B and C virus among different groups of population was (0.29%) and (0.26%) respectively.

The seroprevalence of anti-HBsAg and anti-Hepatitis C virus antibody was detected using enzyme-linked fluorescent immunoassay (ELFA) that was performed in the automated VIDAS system with values ranged between (15.5-40.19) and (1.42-24.10) with mean value (23.52) IU/ML and (10.46) IU/ML respectively and these results was confirmed by RT-PCR with values that ranged between (1.34×10^3 - 15.6×10^4) and (4.60×10^3 and 5.80×10^7) with mean viral load was 4.286×10^4 IU/ML and 3.380×10^7 IU/ML respectively Table 1.

Regarding distribution of HBV according to the different risk groups, the highest rate of prevalence was seen among hemodialysis group (10%), followed by haemophilia (3.8%), thalasemic (2.8%), previous surgeries (1.2%), contact (0.78%), acute hepatitis (0.5%), previous coronary catheterization (0.23) history of jaundice (0.21%) and blood donor (0.06%) groups, While the distribution of HCV according to risk groups of population, The rate of prevalence was highest among thalasemic group (8%), followed by haemophilia (7%), previous surgeries (0.9%), previous coronary catheterization (0.6%), acute hepatitis (0.5%), contact (0.2%) and history of jaundice (0.1%). No positive cases with HCV were detected among hemodialysis, and blood donor groups (Table 2). The difference in the distribution of HBV and HCV by risk groups was not significant ($\chi^2 = 7.412$ and $P > P=0.945$).

Table 1. Results of mean value of VIDAS and RT-PCR among patients with viral hepatitis B and C

Patient groups	VIDAS mean value IU/ML	RT-PCR viral load mean value IU/ML
HBV	23.52	4.286*10 ⁴
HCV	10.46	3.38 *10 ⁶

The results of current study was very close to other studies like [10], in which its showed that the overall rate of HBsAg and anti HCV antibody using ELISA technique was (0.89%) and (0.93%) respectively. The author [11] in his study also found similar prevalence (0.2%) of HCV in Babylon province.

These figures can be compared with other figures found in Baghdad, which recorded prevalence rate (3.0%) and (2.4%) for hepatitis B and C respectively [12]. HBV varies in different countries, the prevalence of HBV was found as (1.5%) in Kingdom of Saudi Arabia, (4.3%) in Egypt, (1.38%) in Turkey, (0.82%) in Nepal and 3.3% in Brazil. On the other hand, HCV prevalence rate in same countries was found to be (0.4%), (2.7%), (0.35%), (0.47%), and (5.9%) respectively [13].

Viral hepatitis is a major health problem in all parts of the world especially in tropical and subtropical areas. It is among the leading causes of morbidity, and actually heads the list of communicable diseases reported in many countries [14].

The prevalence of both viruses in present study was relatively low. This is probably due to developing public awareness about these virus, and route of transmission, not sharing the razors, use of disposable syringes and proper screening of blood and blood products, vaccination of individuals at risk, improvement in hygienic, social and educational conditions.

3.2 Blood and Blood Products Risk Factor

The results revealed that 10% of patients subjected to hemodialysis have hepatitis B and no one of haemodialysis patients suffered from hepatitis C. Similar results recorded in study [15], in which its found that (10.2%) of haemodialysis patients have HBV. Studies like [16] revealed that prevalence of HBV and HCV among hemodialysis patients was (1.2%) and (5.2%) respectively. Hemodialysis patients have high risk for viral hepatitis infections due to the high number of blood transfusion session, prolonged vascular access and the potential for exposure to infected patients and contaminated equipment [17].

Although many studies like [18,19] showed the presence of HCV cases in hemodialysis patients, Yet these absence in current study can be explained due to: 1. HCV infection characterized by low plasma viral load and Long incubation period that may extend to 3 months. 2. The majority of infections is asymptomatic, and have high chronicity rate. All these factors can delay the seroconversion and consequently the serological diagnosis of HCV infection [20].

Table 2. The Prevalence of HBV and HCV among different risk groups of population attending Central Public Health Laboratory in Babylon province

Groups	No. examined	HBV No.	Positive %	HCV No.	Positive %
Blood donor	3088	2	0.06%	0	0
Thalasemia patients	35	1	2.8%	3	8%
Haemophila patients	26	1	3.8%	2	7%
Hemodialysis	10	1	10%	0	0
Previous coronary catheterization	430	1	0.23%	3	0.6%
Acute hepatitis	521	3	0.5%	3	0.5%
History of Jaundice	933	2	0.21%	1	0.1 %
Previous surgeries	325	4	1.2%	3	0.5%
Contact	384	3	0.78%	1	0.2%
Total	6061	18	0.29%	16	0.26%
Statistical analysis	$\chi^2 = 7.412$ and $P=0.945$				

The prevalence of HBV among the blood donors was (0.06%). Similar results were recorded by others studies in this field [10]. In opposite, this finding was lower than results previously recorded [14]. No positive cases with HCV detected among blood donor. In contrast, other studies like [21,1,13] recorded positive cases with HCV among these group. The common route of HCV transmission is parenteral and most infected individuals are blood recipients or intravenous drug users [22]. In developing countries like Iraq to minimize the risk of transmission of HBV and HCV infections through blood transfusion; we used a sensitive screening methods like PCR that detected infectious agents.

The prevalence of HBV and with HCV among thalassemic patients was (2.8%) and (8%) respectively. Similar percentage (1.5%) and (4%), (3.69%) and (8.97%) of HBV and HCV positivity was reported respectively in other studies [23,24]. On other side, results reported in other studies like [25,26] showed that the prevalence of hepatitis B and C in thalassaemic patients was significantly high. Exposure of thalassaemic patients to the multiple injections increased the risk of getting HBV and HCV with age and has led to high morbidity in thalassaemia patients [24].

In haemophilia group, (3.8%) and (7%) of patients have HBV and HCV infections. The authors [27] recorded related ratio of positivity (6.67%) of HCV in hemophilia patients, but don't found anti-HBs Ag seropositive cases among haemophilia patients. Studies like [28,29] revealed similar results. Hemophilia patients have a high risk of acquiring hepatitis B, C and other viral infections because of the large number of blood transfusions and clotting factor concentrates received [30].

The prevalence of hepatitis B and C among blood diseases patients means that long exposure to blood and blood products has high risk for infection with these virus, contaminated needles and unscreened blood products are the major factors contributing to transmission of hepatitis B and C. Contaminated needles and surgical instruments can transmit infection even after a month of being soiled by virus [31]. The risk of bloodborne transmission is dependent upon the amount of blood, virus titer and virulence of pathogen [32].

Individuals have coronary catheterization were susceptible to infection with HBV and HCV, at

the present study the rate of prevalence among them was (0.23%) and (0.6%). These findings were compatible to finding seen in study [33], in which its found that infection with HBV among these groups was (0.08%). The researchers [34] in his study, reported higher finding, in which (14%) of these patients were positive for HBV and (8%) positive for HCV.

3.3 Contact Group

In the present study, the prevalence of HBV and HCV among contact group was (0.78%) and (0.2%). Studies like [10] revealed similar results, in which the infection rate with HBV and HCV among contacts groups was (1.84%) and (1.38%). Household or sexual exposure to a contact who had hepatitis were found as a significant risk factors for acquiring HBV and HCV [23].

3.4 Acute Hepatitis and History of Jaundice Risk Factor

Among patients with acute hepatitis, (0.5%) have HBV and HCV. The authors [35,36] also reported related rate of positivity of both viruses among patients with acute and chronic hepatitis, which reflects the association of HBV with liver disease, high rate of infection associated with chronic liver diseases and hepatocellular carcinoma.

The results of the present study shows that the prevalence of HBV and HCV among patient with history of jaundice was (0.21%) and (0.1%). Related result (2.5%) was mentioned in study [37]. These results were lower than results of (14), in these study its recorded (19.2%) and (3.8%) infection rate with HBV and HCV among these patients respectively.

3.5 Surgical Risk Factor

Among patients have previous surgery, the positivity rate with HBV and HCV was 1.2% and 0.9%. The authors [38] in his study recorded (3.6%) and (5.1%) prevalence rate of HBV and HCV among these patients. Exposure to invasive procedures was associated with presence of hepatitis infection. Certain operations are associated with increased exposure rates, given the high incidence of these infections; strategies such as shapeless surgical techniques should be evaluated and implemented to protect surgeons from blood-borne pathogens. Hepatitis viruses were seen in several common operations like

lymph node biopsies, soft tissue excision biopsies, abscess-drainage, etc. [38].

3.6 Distribution of HBV and HCV According to the Gender, Residence and Age

Regarding the gender, The prevalence of HBV and HCV was different according to gender, the results showed that the prevalence of HBV was higher in males (0.4%) compared to females (0.17%). Likewise, the HCV prevalence was higher in males (0.34%) compared to females (0.17%), the difference was statistical significant ($\chi^2 = 13.176$, $P = 0.022$) as shown in Table 3. These results was accordance with results of others studies like [10] in which its showed that the positivity rate of HBV was higher in males compared to females (0.96% vs 0.62%). Likewise, the HCV positivity rate was higher in males compared to females (1.0% vs 0.57%).

Male predominance was seen in other studies like [39-41]. The reason for this may be due to larger number of samples from males than females used in the study. It is also probably due to lifestyle variations between both gender groups, males are actively more exposed to risk factor such as sexual activity with multiple partners and contact with contaminated blood or blood prods than the females.

The prevalence of HBC and HCV in urban was significantly higher in urban (0.33%) and (0.27%) than rural rejoin (0.25%) and (0.25%) respectively ($\chi^2=9.647$, $P= 0.041$) as shown in Table 4. These results was agrees with results of [40], who found high percentage of prevalence with HBV and HCV in patients living in urban

area. The authors [37] stated that (51.6%) of HBV infection found in urban residence. Living in urban area was associated with HBV and HCV infections and its may be due to the nature of living in which urban areas are densely populated as compared to rural areas and this might expose urban dwellers for different risk factors.

The age-specific prevalence's of hepatitis B d C are presented in Fig. 1. The results shows that most of individuals have HBV belongs to age group ranging between 20-29 and 30-39, while most of individuals have HCV belongs to age group ranging between 20-29 years than other age. The difference in the distribution of HBV and HCV infections by age groups ($\chi^2 =5.333$, $P =0.377$ and $\chi^2 =3.500$, $P =0.623$) was not significant. High prevalence of HBV and HCV at age group ranging between (20-29) and (30-39) years was recorded previously [20]. Studies like [11,39] shows that the vast majority of hepatitis infections are within age group ranging between (30-39, 40-49) years, these age groups have high chances for exposure to HBV and HCV infections because individual usually becoming sexually active at an early age and ignorance may not indulge in safe sexual practice that lead to disseminating the virus in this an active period of life [42].

The difference in the prevalence of HBC and HCV and it's distribution according to the gender, age and residence among different studies and among different countries may be due difference of sample size and using different methods of screening with variable sensitivity and specificity which give high false positive results [21].

Table 3. Distribution of HBV and HCV according to the gender

Gender	No. examined	Hepatitis B positive		Hepatitis C positive		$\chi^2 =13.176$ $P=0.022$
		No.	%	No.	%	
Female	2828	5	0.17	5	0.17	
Male	3233	13	0.4	11	0.34	
Total	6061	18	0.29	16	0.26	

Table 4. Distribution of HBV and HCV according to residence

Residence	No. examined	Hepatitis B positive		Hepatitis C positive		$\chi^2 =9.647$ $P= 0.041$
		No.	%	No.	%	
Urban	3291	11	0.33	9	0.27	
Rural	2770	7	0.25	7	0.25	
Total	6061	18	0.29	16	0.26	

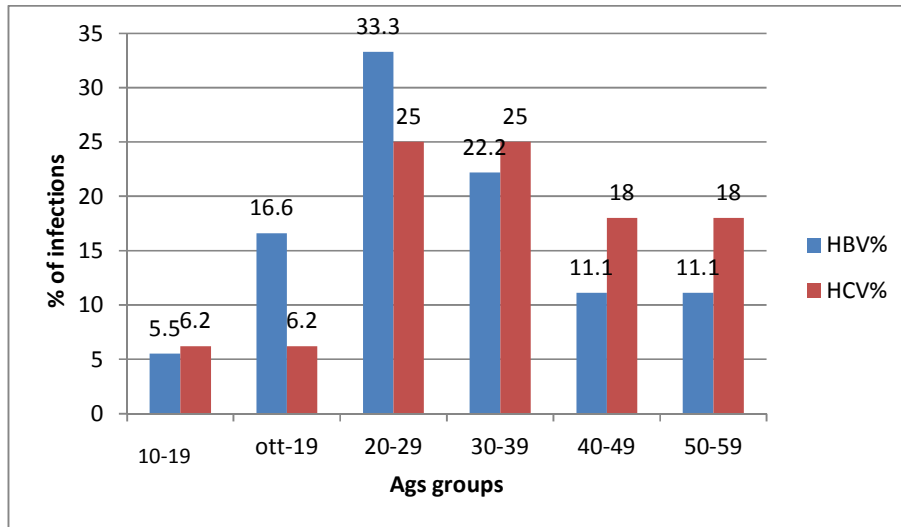


Fig. 1. Distribution of HBV and HCV according to age group

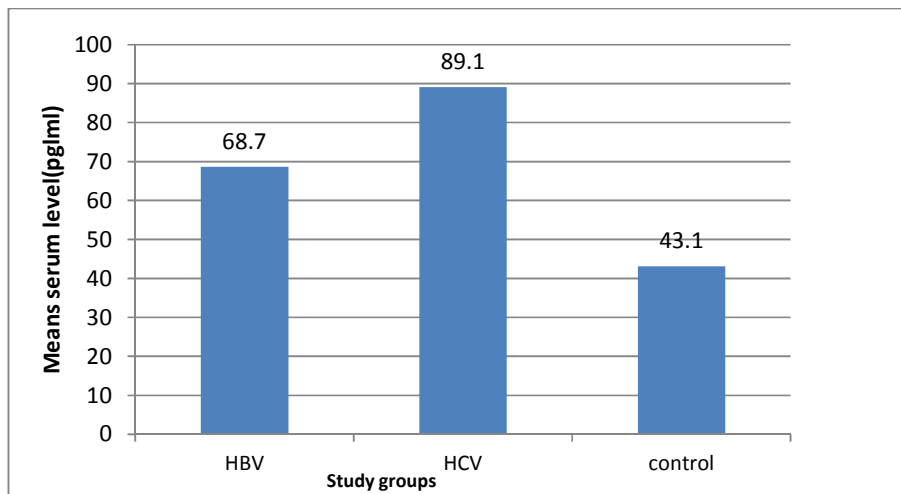


Fig. 2. Mean serum levels of TNF-α in patients with viral hepatitis B and C and healthy control groups

3.7 Estimation of TNF- α in Patient with Hepatitis

The present data in above Fig. 2 revealed that means(means±SD) serum levels of TNF-α concentration were significantly higher (68.7±12.84 pg/ml) and (89.1± 22.017 pg/ml) in patients with HBV and HCV infection compared to its concentration (43.1±5.87 pg/ml) in the healthy controls (P= 0.0002, P =0.00012). Many studies support the result of the current study like [43], in which its found that their is a elevation in the levels TNF- α in patients with HBV(211.27±28 pg/ ml), and in patients with HCV(189.77±23.5 pg/ ml) in comparison to

control group (59.45±22 pg/ ml). In addition, studies like [44,6] revealed that serum levels of TNF-α were significantly increased in patients with viral hepatitis.

There are many factors that affect the clinical state of patients with hepatitis such as the age, the presence of other diseases, drugs and immunological factors like cytokines from these cytokines TNF-α. TNF- α plays a central role in the host's immunomodulatory response to infective agents [45]. TNF-α system also implicated in the pathogenesis of viral hepatitis, in HCV infections the viral particles induces the expression of the TNF- α in human liver (HCV specific CTL have

been showed to secret TNF- α in vitro). Plasma TNF- α level is increased in the patients with chronic HCV infections. In HCV infection, the disease sings and liver injury occur as a result of both cytopathic effects of the viral particles and replication and the immune response to the process of viral multiplication and viral proteins in the liver. As a result of the infection and liver injury, there is a clear changes in the concentrations of some cytokines, mainly TNF- α , IL-1 α , and IL-6, IFN- γ , IL-8 [43]. We look to these results as the high level of cytokines production stimulates in both types of hepatitis, the levels of these cytokines and other chemokines depending on the clinical stage of the disease.

4. CONCLUSION

The results of the present study concludes that the prevalence of Hepatitis B and C Virus was relatively low in Babylon province in Iraq. These findings were comparable to others studies at other areas of Iraq and neighbor countries. Our study shows that prevalence of hepatitis B and C virus was insignificantly varies with different risk factor groups, the risk group associated with transmission of HBV was hemodialysis followed by haemophila diseases, while the risk group associated with transmission of HCV was thalasemia and haemophila diseases. We reported higher infection of both viruses among males than female and also in urban than rural rejon. The most of infection with HBV seen among individual with age ranged between 20-40 years old, while most HCV infection seen among age 20-29 years old. The difference was not significant. Patients with hepatitis B and C exhibit increase in plasma levels of TNF- α compared to control group. These data indicate that the TNF- α system is activated in patients with chronic HCV infection.

CONSENT

All patients' consents were taken before inclusion in the study.

ETHICAL APPROVAL

Ethical Committee of the Central Public Health Laboratory Ministry of health approved the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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