Epidemiology of viral hepatitis B and C in Iraq: a national survey 2005-2006.

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Abstract

Background and objective: Viral Hepatitis Type B&C is serious public health challenge throughout the world.Hepatitis B and C viruses still remain to be the major causes of chronic hepatitis.It is estimated that around 350-400 million people in the world are chronic carriers of HBV, which represents approximately 7% of the total populationwhereas infection with HCV is found in approximately 3% of the world population, which represents 160 million people. Hepatitis B infection has a wide range of seroprevalence in the Mediterranean countries ranging from intermediate (=>2%) to high prevalence (=>7%). World Health Organization estimated a prevalence rate for HCV infection of about 4.6% in Eastern Mediterranean in 1999. During the eightieths years of the last century, Iraq was considered to be of intermediate endemicity with hepatitis B as reflected by 3% seroprevalence of HBsAg in normal population. Hepatitis C was found to be of low endemicity among blood donors 0.5%. There were no national wide epidemiological studies regarding the prevalence of hepatitis B&C accordingly we conduct this study to determine the prevalence of both types all over the Iraq.

Methods: From the 1st of January 2005 to 31st of December 2006, a community based cross-sectional study was conducted all over Iraqi governorates. A total of 9610 persons, recruited by surveying a nationally representative random sample of households were analyzed. A stratified random sample proportional to size of each of the 18 Iraqi governorates, both urban and rural areas were included. Prevalence estimates were therefore weighted and age-adjusted. Five (5ml) of blood samples were taken from the study subjects, and tested for hepatitis B surface antigen, antibody to hepatitis B core antigen antibody to hepatitis B surface antigen and hepatitis C antibodies .

Results: The national prevalence rate of HBs Ag was 1.6% and correlated positively with age. The prevalence rate of anti-HBs antibodies was 17%. The prevalence of anti-HBc was 9.7%. The prevalence of anti-HCV was low (0.4%). The prevalence rate of anti-HBs antibodies in <10 years children is only 32.2%, which raise the issue of incomplete coverage of hepatitis B vaccine during the years preceding the study years.

Conclusion: The findings revealed that Iraq is of low prevalence with HBsAg.On the other hand,hepatitis C was found to be of very low prevalence. As a marker of exposure to hepatitis B, Anti HBcIgG was found to increase with age.

Keywords: hepatitis B, hepatitis C, Iraq.

Introduction

Infection by the hepatitis B (HBV) and hepatitis C (HCV) viruses is the most common cause of post-transfusion hepatitis[1, 2]. Furthermore, HBV and HCV are also the most frequent causes of chronic hepatitis diseases in the world, and their transmission occurs, mainly, through direct contact

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with blood, through the utilization of intravenous drugs, blood transfusions and/or blood products, and through sexual relations. However, sexual relations seem not to be the most frequent mode of HCV transmission [3]. Infection by these two viruses may induce chronic hepatitis, which may progress to cirrhosis, and eventually to hepatocellular carcinoma [4, 5]. It is estimated that around 350-400 million people in the world are chronic carriers of HBV, which represents approximately 7% of the total population [6], whereas infection with HCV is found in approximately 3% of the world population, which represents 160 million people [7,8]. This high prevalence of HBV and/or HCV certainly results in high medical and social impact, due to a great number of cases of fulminating hepatitis, hepatic cirrhosis and carcinoma, and also provokes the death of a significant part of the population by these pathologies. Hepatitis B virus (HBV) is the most important causative agent of blood borne hepatitis in humans [9]. It is an important public health concern in both developing and developed countries affecting approximately 3.5 billion of the world's population and additionally ≥ 400 million are chronic carriers [10,11]. It has been estimated globally that each year ~1-2 million people die from HBV related complications such as chronic hepatitis, cirrhosis andhepatocellular carcinoma (HCC) [12,13]. HBV was of moderate endemicity in Iraqi population with a rate of 3% [14]. The highest concentrations of infectious HBV are in blood, serum and serum-derived body fluids, such as semen and saliva [15]. It has been reported earlier in 2002 that the hepatitis B virus can live for several days in dried blood on table surfaces, needles, syringes and razors [16, 17]. The World Health Organization (WHO) estimates that hepatitis B result in 563 000 deaths annually from the estimated 350 million carriers, while hepatitis C result in 366 000 deaths annually from 165 million infected individuals [18,19]. The hepatitis B virus is transmitted by contact with infected blood or body fluids of an infected person. Chronic infection after exposure to hepatitis B virus (HBV) has been observed in 30% to 90% of children aged less than five years. On the other hand, exposed adults become chronic carriers of HBV in only 2 to 5% of cases [23]. Based on the prevalence of HBV chronic carriers (individuals positive for hepatitis B surface antigen) amongst adults in the general population, countries are classified as having low endemicity<2%, intermediate endemicity 2 - 8% or high endemicity>8% of infection) [24]. Even with three effective doses of the vaccine available, hepatitis B remains a stubborn, unrelenting health problem, especially in Africa and other developing areas. The disease and its complications cause an estimated one million deaths globally each year [25]. Studies in the Middle East showed that the prevalence of HBs Ag ranged from 3% to 11% in Egypt [26]. Hepatitis B vaccination is the most effective measure to prevent HBV infection and its consequences. However, for persons already infected with HBV, antiviral agents are available that may prevent the serious sequel of chronic liver disease, which highlights the importance of identifying infected individuals. Hepatitis C virus (HCV) infection is a significant contemporary health problem in the United States and elsewhere. Because it is primarily transmittedvia blood, hepatitis C infection presents risks for both nosocomial transmissions to patients and occupational spread to health care workers. Hepatitis C virus (HCV) is the major cause of transfusion associated non-A, non-B hepatitis and continues to be a major cause of human liver disease throughout the world.World Health Organization estimated a prevalence rate for HCV infection of 4.6% in Eastern Mediterranean in 1999. Egypt had the largest scale of HCV infection prevalence ranging from 6% to 28%. In Iraq, hepatitis C is considered of low endemicity with a rate of 0.5% in blood donors [26]. The prevalence rates reported from other Mediterranean countries were 1.8% in Turkey, 0.55-0.66 % in Israel and 2.2% in the Gaza Strip[27]. Hepatitis C is gradually being

recognized as a major health problem even in developing countries. The prevalence of HCV infection varies throughout the world, with the highest number of infections reported in Egypt. The use of parenteral antischistosomal therapy in Egypt is thought to have contributed to a prevalence of antibodies against HCV in various regions ranging from 6 to 28 percent (mean, 22 percent) [28]. In the United States, 1.8 percent of the population is positive for HCV antibodies. Given that 3 of every 4 seropositive persons also have viremia, as assessed by currently available tests, an estimated 2.7 million people in the United States have active HCV infection.

The objectives of the present work was designed to assess the importance of HBV and HCV as a possible diagnosis in apparently healthy individuals. The second objective was to calculate a national estimate for point prevalence of markers of HBV markers (HBsAg, anti HBs and anti HBc antibodies) and third objective was to assess hepatitis C antibodies (Anti HCV antibodies). Other objectives were to evaluate the vaccination program for children in different governorates during the period preceeding the study years. In addition, to study the association of HBV and HCV with age, gender and place (according to governorates).

Methods

The data of the present study were part of a national survey conducted by the MOH (Ministry of Health) in Iraq in the period 1st of January 2005 to 31st of December 2006. The study used a nationally representative random sample of households. A total of 9610 persons, were recruited by surveying. All apparently healthy family members of the household were eligible for inclusion in the study. The sample of households was provided by the Ministry of planning using a stratified random sample proportional to size of each of the eighteen Iraqi governorates, both urban and rural areas. The proposed total national sample size was 12,000, which was expected to yield a sample estimate for proportion at its most extreme magnitude of 0.5, with a 95% confidence interval of +/-2% of the estimate employing the highest power of study possible of 99%. At the governorate level considering an average sample size of 650 per governorate, one would expect to yield a sample estimate for proportion at its most extreme magnitude of 0.5, with a 95% confidence interval of +/-8% of the estimate employing the highest power of study possible of 99%. The 20% non-response rate, being non-differential and affected only by poor level of security or logistic problems is not expected to affect the validity of the estimates to any important extent. Blood samples were taken from study subjects. Three to five (5) ml of blood was collected from each included individual. Serum was deep frozen by -20 c. All the samples were tested for antibody to hepatitis B core antigen (anti-HBclgG), hepatitis B surface antigen (HBsAg), and antibody to hepatitis B surface antigen (anti-HBs) by using ELISA technique (3rd generation). Also serum was tested for Anti HCV to find hepatitis C infection. Identifying information including age, sex and residence were also secured.

Statistical analysis

Statistical analysis was computer aided using SPSS version13 and EPI-Info version 3.5.1 (create map module). The 95% confidence interval of a proportion was used to calculate the population parameters. The prevalence ratio was used to calculate the magnitude of risk in a group compared to a reference category in a cross-sectional design. The formula used in its calculation and its 95% confidence interval (natural logarithm based method) are similar to that of risk ratio used in a cohort design (26). P value equal or less than the 0.05 level of significance was considered statistically significant.

Results

As shown in Table 1, the national estimate of HBs antigen prevalence rate was 1.6%, while that of HCV antibodies was only 0.4%. Anti-HBs IgG (total) had a higher

prevalence rate of 16.9% and HBc antibodies 9.8%. As shown in table 2, the prevalence of HBsAgwas lowest in the first decade of life (0.9%), and increase with age to reach a maximum prevalence rate of 2.4% in the fifth decade of life. The risk of testing positive for HBs antigen is almost doubled in the 3rd decade of life compared to 1st decade of life. Being in the fifth decade of life significantly increased the risk of having positive HBs antigen by 2.6 times compared to 1st decade of life. Male gender significantly increases the risk of having positive HBs antigen by 41% compared to females. The prevalence rate of positive HBs antigen was lowest in Maysan, DhiQar, Al Qadisiyah and Al Muthanna (<0.5%). The prevalence rate was highest in An Najaf, Dahuk, Salah ad Din and Babil (>3%), Figure 1. As shown in table 3, the prevalence of anti-HBs antibodies was lowest in the 3rd decade of life (12.2%), and is slightly, but not significantly higher in older ages. The prevalence rate of positive anti-HBs antibodies is highest in the first decade of life 32.2%. Compared to the 3rd decade of life the risk of testing positive is significantly increased by 38% in the 2nd decade of life and by 2.63 times in the first decade of life. Male gender significantly increased the risk of having positive anti-HBs IgG antibodies by 33% compared to females. The anti-HBcIgG antibodies shows a positive age trend as opposed to the negative age trend observed with anti-HBs IgG antibodies, figure 2. The anti-HBcIgG antibodies prevalence rate was lowest in the first decade of age (3.8%) and highest in the 5th decade of life (14%). Gender showed no important or statistically significant association with anti-HBc antibodies, table 4. As shown in table 5, the prevalence of anti-HCV IgG antibodies was lowest in the 1st decade of life (0.3%), and is slightly, but not significantly higher in older ages. The prevalence rate compared to the 1st decade of life the risk of testing positive is increased by 1.85 times in the 5th decade of life, but this risk estimate was not significant statistically. Male gender increased the risk of having positive anti-HCV IgG antibodies by 75% compared to females, but this association was again not significant statistically. The prevalence rate of Anti HCV was lowest in Erbil, Sulaymaniyah, Karbala, Al Qadisiyah, Al Muthanna, Al Basrah and Dahuk (<0.3%). The prevalence rate was highest in Babil, Najaf and The Qar (> 0.9%) Fig. 3.

Table 1: Iraq's National prevalence rate of selected viral hepatitis marker (2005-2006).

Overall	Total examined N	+ve N	+ve %	95% CI for prevalence rate (%)
HBs Ag	9610	155	1.6	(1.3 - 1.9)
Anti – HBs IgG**	4229	714	16.9	(15.8 - 18)
Anti – HBcIgG**	4196	410	9.8	(8.9 - 10.7)
Anti – HCV	9610	38	0.4	(0.3 - 0.5)

****Note:** The sample size for anti-HBs IgG and anti-HBcIgG antibodies was a subsample of the original national sample because some provinces failed to perform these serological tests, because of unavailability of materials.

Table 2: The HBs antigen prevalence rate by age and gender.

	Total examined N	HBs Ag +ve N	%	95% CI for prevalence rate (%)	Prevalence ratio (PR)	95% CI for PR	P (Chi-quare)
Age group (years)							
(1-10)	1641	15	0.9	(0.4 - 1.4)	Ref		
(11-20)	2235	22	1.0	(0.6 - 1.4)	1.08	(0.56 - 2.07)	0.82[NS]
(21- 30)	2374	43	1.8	(1.3 - 2.3)	1.98	(1.1 - 3.55)	0.019
(31- 40)	1603	33	2.1	(1.4 - 2.8)	2.25	(1.23 - 4.13)	0.007
41+	1757	42	2.4	(1.7 - 3.1)	2.62	(1.46 - 4.7)	<0.001
Gender							
Male	4754	90	1.9	(1.5 - 2.3)	1.41	(1.03 - 1.94)	0.031
Female	4856	65	1.3	(1 - 1.6)	Ref		

Note: CI=confidence interval PR=Prevalence ratio

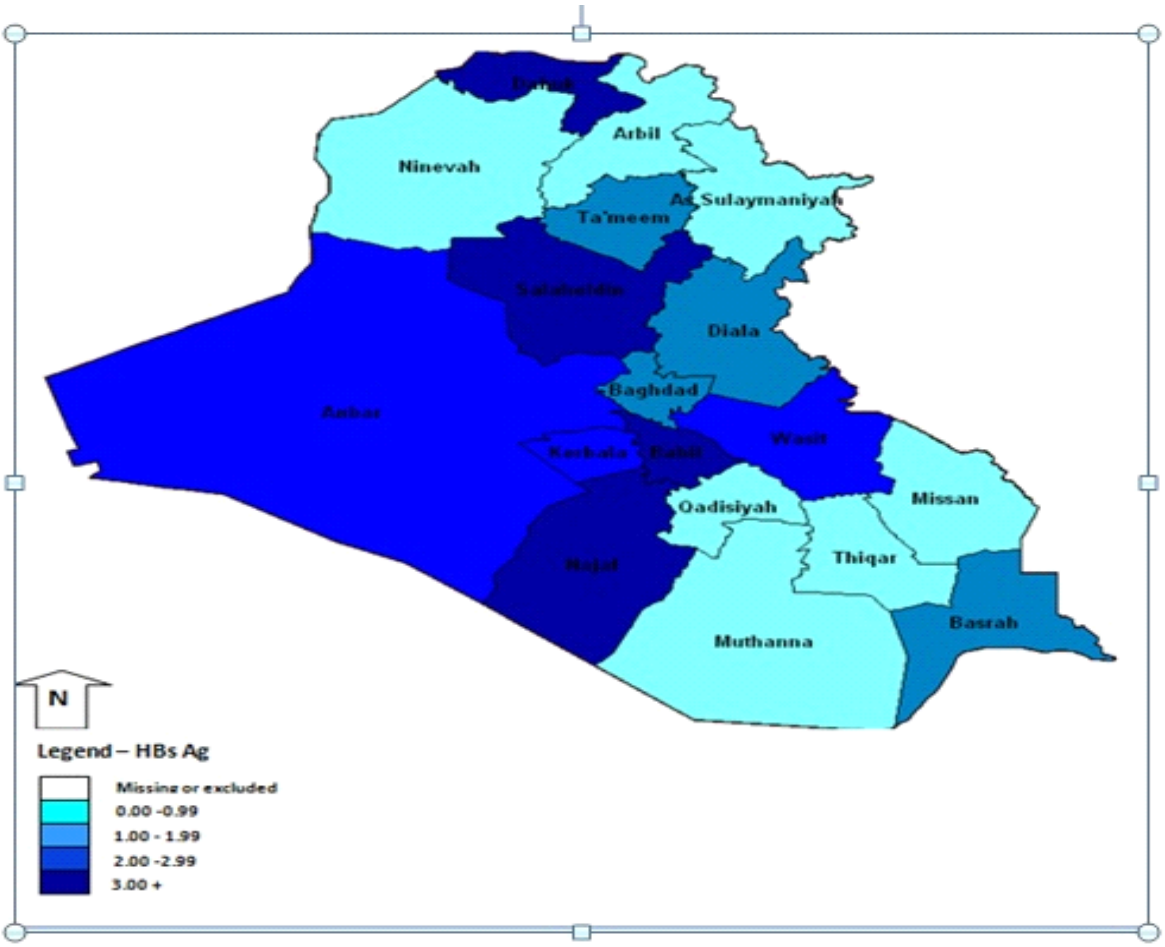

Figure 1: Map diagram showing the HBs antigen prevalence rate in 18 Iraqi provinces (2005-2006).

Table 3: The anti-HBs IgG antibodies prevalence rate by age and gender.

	Total examined	Anti-HBs IgG +ve		95% CI for prevalence rate	Prevalence ratio (PR)	95% CI for PR	P (Chi-square)
	N	N	%	(%)			
Age group (years)							
(1-10)	639	206	32.2	(28.6 - 35.8)	2.63	(2.16 - 3.21)	<0.001
(11-20)	1097	186	17	(14.8 - 19.2)	1.38	(1.12 - 1.71)	0.002
(21- 30)	1029	126	12.2	(10.2 - 14.2)	Ref		
(31- 40)	617	78	12.6	(10 - 15.2)	1.03	(0.79 - 1.34)	0.81[NS]
41+	847	118	13.9	(11.6 - 16.2)	1.14	(0.9 - 1.44)	0.28[NS]
Gender							
Male	2007	389	19.4	(17.7 - 21.1)	1.33	(1.16 - 1.52)	<0.001
Female	2222	325	14.6	(13.1 - 16.1)	Ref		

Note: CI=confidence interval PR=Prevalence ratio

Table 4: The Anti-HBcIgG antibodies prevalence rate by age and gender.

	Total ex-amined	Anti-HBcIgG +ve		95% CI for prevalence rate (%)	Prevalence ratio (PR)	95% CI for PR	P (Chi-square)
	N	N	%				
Age group (years)							
(1-10)	639	24	3.8	(2.3 - 5.3)	Ref		
(11-20)	1097	92	8.4	(6.8 - 10)	2.23	(1.44 - 3.46)	<0.001
(21- 30)	1019	102	10	(8.2 - 11.8)	2.67	(1.73 - 4.11)	<0.001
(31- 40)	607	75	12.4	(9.8 - 15)	3.29	(2.11 - 5.14)	<0.001
41+	834	117	14	(11.6 - 16.4)	3.74	(2.44 - 5.72)	<0.001
Gender							
Male	1966	204	10.4	(9.1 - 11.7)	1.12	(0.93 - 1.35)	0.22[NS]
Female	2230	206	9.2	(8 - 10.4)	Ref		

Note: CI=confidence interval PR=Prevalence ratio

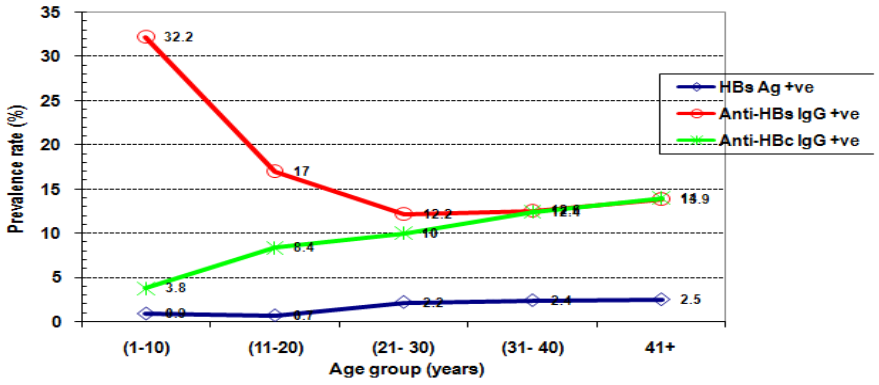

Figure 2: Line graph showing the prevalence rate of 3 markers for hepatitis B by age.

Table 5: The anti-HCV antibodies prevalence rate by age and gender.

	Total examined N	Anti-HCV IgG +ve N	%	95% CI for prevalence rate (%)	Prevalence ratio (PR)	95% CI for PR	P (Chi-square)
Age group (years)							
(1-10)	1621	5	0.3	(0 - 0.6)	Ref		
(11-20)	2235	6	0.3	(0.1 - 0.5)	0.9	(0.27 - 2.85)	0.82[NS]
(21- 30)	2374	9	0.4	(0.1 - 0.7)	1.23	(0.41 - 3.66)	0.71[NS]
(31- 40)	1603	8	0.5	(0.2 - 0.8)	1.62	(0.53 - 4.94)	0.39[NS]
41+	1757	10	0.6	(0.2 - 1)	1.85	(0.63 - 5.39)	0.25[NS]
Gender							
Male	4754	24	0.5	(0.3 - 0.7)	1.75	(0.91 - 3.38)	0.09[NS]
Female	4856	14	0.3	(0.1 - 0.5)	Ref		

Note: CI=confidence interval PR=Prevalence ratio

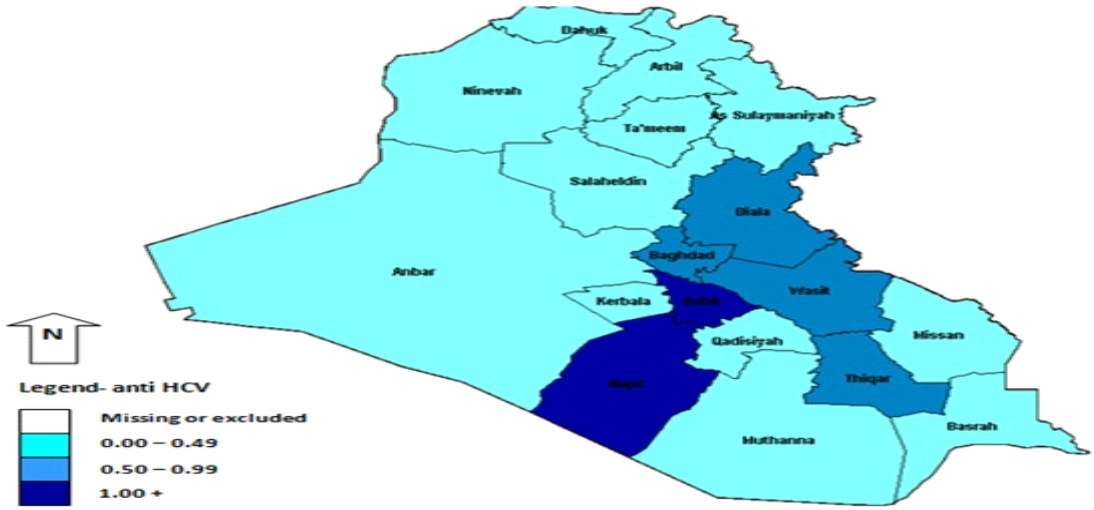

Figure 3: Map diagram showing the anti-HCV antibodies prevalence rate in 18 Iraqi provinces (2005-2006).

Discussion

HBV and HCV infections are among the most prevalent infectious diseases in humans worldwide. Both 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. [31] The prevalence of infection with HBV varies from one country to another depending upon a complex mixture of behavioral, environmental and host factor. The prevalence of HBs antigen (HBsAg) positivity in different populations ranges from less than 0.5% to as high as 20%. A study conducted in Aurangabad reported 6.42% carriage in resident doctors [32]. Another study conducted in Delhi reported 6.9% transfusion associated hepatitis (TAH) among patients receiving blood transfusion for cardiac surgery; of the total TAH cases 20% were related to HBV [33]. The spread of hepatitis B virus continues to be at an alarming rate worldwide and this created an impact on many countries.Although the rate of exposure to HBV in Pakistan is not fully confirmed, Awan et al (2010) reported ~38% prevalence of different hepatitis B markers, with a 4% HBs Ag carrier rate and 32% with anti-HBV surface antibodies (Anti HBs Ab) by natural conversion [20]. High prevalence of HBV was observed in geographical areas of low economic status, which underscores the importance in controlling this disease [21,22]. The present study gives a highlight on HBV activity in Iraq. It demonstrated that the prevalence rate of HBsAgin apparently healthy individuals was 1.6%. It was more frequent in age group above 40 years and in males more than females. The results of this survey comply with the results of other published articles in neighbor populations. Schreiber el al. (1996) reported an intermediate prevalence of 2-8% for HBV infection in Egypt. Another study reported the prevalence of HBsAg among Kuwaiti national and non-Kuwaiti Arab at 1.1 and 3.5%, respectively [34] High prevalence results of HBV in males compared to females have been observed in earlier studies in Pakistan [24,35]. Similar results have also been obtained in Bangladesh where the researchers reported higher prevalence in males (67.86%) than females (32.14%)[36].The aforementioned gender disproportion may be explained by the increased frequency of high risk jobs and behavior in men, like multiple sexual partners, drug use and unhygienic barber shaving practices. The prevalence of HBV infection rises gradually with age.Higher

risk of infection was found in the older subjects as compared to the younger ones. The higher prevalence among older age groups may be attributed to the more frequent and continuous exposure to risk factors of hepatitis B (HBV infection). The prevalence of HBV infection and immunity was determined in a representative sample of the US population for the period 1999–2006. National Health and Nutrition Examination Surveys participants ≥6 years of age were tested for antibody to hepatitis B core antigen (anti-HBc), hepatitis B surface antigen (HBsAg), and antibody to hepatitis B surface antigen (anti-HBs). The prevalence of anti-HBc increased from 0.6% in children aged 6–19 years to 5.9% among adults 20–49 years of age, and further increased to 7.2% among older persons (≥50 years) [37]. In our study the prevalence of antibody to hepatitis B core antigen (anti-HBc) showed a weak positive age trend. Anti-HBc antibodies is expected to increase with age in a pattern that is similar to HBs Ag marker, since this type of antibodies is only produced by natural infection and not by vaccination Prevalence of Anti-HBs IgG was negatively correlated with age, ranging from 53.5% (95% CI, 50.8%–56.3%) among persons aged 6–11 years to 5.1% (95% CI, 4.3%–6.0%) among persons ≥60 years of age [37]. In the current study of Iraqi community the prevalence rate of positive anti-HBs was highest in children and lowest in the 3rd decade of adult life and then rises again. The main reason for this increase in prevalence rate of anti- HBsAb in the first decade of life is the vaccination program, however vaccination give antibodies to HBs Ag at a lower titer than that of natural infection, in addition Anti HBs IgG in natural infection is always associated with anti-HBc antibodies. Another fact is that about 60% of vaccinated individuals have no detectable antibody in their blood after 9 to 15 years after vaccination, although they were still immune due to availability of memory cells [(38)]. In Iraq, hepatitis B vaccination was introduced on 1993 for the first time as a part of Expanded Program of Immunization (EPI) and was applied on children below 5 years of age [39], accordingly those Iraqi whom were above 30 years of age at the time of conducting the study were not vaccinated. In Egypt,it was found that, 0.2 to 4% of blood donors were found to be anti HCV positivedepending upon the type of the test used for screening and confirmation [40]. In addition the national prevalence rate of HCV antibody positivity has been estimated to be between 10-13% of the total population[40], they thought that this high prevalence of Anti HCV Abs might be attributed to a now-discontinued mass-treatment campaign for schistosomiasis, using improperly sterilized glass syringes[41]. In our study the prevalence of anti-HCV antibodies was 0.4% only. It was more frequent in age group above 40 years and in males than females. It is obvious that HCV is of low prevalence in Iraq, possibly of strict rules of testing blood for hepatitis markers. While in a study done in south India hepatitis C was found in 3% cases. Prevalence of 8.33% HCV infection among patients of chronic active hepatitis and cirrhosis has been reported from Calcutta [41].Most of hepatitis C cases (70 to 80%) progress to chronic infection.

Conclusion

- Hepatitis B as reflected by HBs Ag is of low endemicity 1.6% (below 2%) and most infection occurs in young adults.
- Hepatitis C as reflected by Anti HCV Abis of low endemicity with prevalence rate of about 0.4% in apparently normal population.
- The prevalence rate of anti-HBs antibodies in <10 years children is only 32.2%, which raise of incomplete coverage of hepatitis B vaccine during the years preceding the study years(2005-2006) due to unstable situation in Iraq at that time.
- **Recommendation**
  - More epidemiological studies and research are needed in the field of

in the field of HBV & HCV prevalence especially in risk groups.

- Genotyping & subtyping studies are needed to find which genotype or subtypes are more prevalent in Iraq.
- The performance of Iraqi vaccination program for hepatitis B need to be reviewed and universal vaccination of infants; screening of all pregnant women for HBV, with post-exposure prophylaxis provided to infants born to infected women; catch-up vaccination of adolescents; and vaccination of adults who are at increased risk of infection
- Careful screening of blood, blood products, adequate sterilization of reusable surgical and dental instruments, professional and public health education in addition to implementation of infection control practices in all health facilities should be followed to control spread of hepatitis

Conclusion

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