Prevalence of Hepatitis C virus antibodies among different populations of relative and attributable risk

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ABSTRACT

Objectives: To determine the prevalence of hepatitis C virus (HCV) antibodies among 5 different population groups including; healthy individuals, blood donors, hospital health care workers, renal dialysis patients and multiple blood transfusion group. To compare the ratios, relative and attributable risk among these groups. To outline a specific policy to reduce the potential risk of HCV among the different groups studied.

Methods: A prospective study was carried out in the Department of Microbiology, Faculty of Medicine, Tripoli, Libya, over a 2 year period for 1999 to 2001, to determine the prevalence of HCV-antibodies in sera collected from 5 distinct groups using enzyme-linked immunosorbent assay test. The groups included 800 healthy adults, 1200 individuals of blood donors, 459 hospital health care workers, 200 patients on renal dialysis and multiple blood transfusion group which included 250 patients. The prevalence of HCV was correlated with relative and attributable risk that contributed to the infectivity of HCV.

Results: A total of 2909 individuals participated in this study with 1.6:1 male to female ratio. The prevalence of HCV varied from one group to another. It was found to be 1.6% among the general population, 1.2% among blood donors, 2% among hospital health care workers, 20.5% among renal dialysis patients and 10.8% in the multiple blood transfusion group. The relative risk and attributable risk among these groups varies from 1.25 to 12.8 and from 0.4 to 18.9.

Conclusions: This study underlines the prevalence of HCV among different groups. The prevalence varies from one group to another, being the lowest among the blood donors and general population and the highest among the higher risk group in particular the renal dialysis patients. Specific measures should be implemented to reduce such risks. These may include specific programs for medical education, a meticulous infection control system in the hospitals, a registry program and clinical follow-up for patients positive for HCV.

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Hepatitis C virus (HCV) has been recognized to be the principle cause of parenterally transmitted non-A, non-B hepatitis. Following its discovery in 1989, the consensus of opinion has been that it is 2nd to human immuno-deficiency virus (HIV) among the emerging infectious diseases.[1] Serological tests to detect antibodies to HCV (anti-HCV) and HCV ribonucleic acid (RNA) has allowed detection of HCV-infected persons and screening of blood used in transfusion in the last decade. Hepatitis C virus infections usually persist due, in part, to the rapid replication of the virus and its tendency to mutate and hence to form variants not contained by immune response, resulting in the HCV quasi-species.[2] While

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antibodies may neutralize some quasi-species, as of this viral diversity, HCV antibody-containing immunoglobulin doesn't reliably prevent HCV infection. The host cellular immune response is important in viral clearance. Early emergence and maintenance of CD4+, T-helper lymphocytes in addition to MHC Class II genotype are associated with HCV clearance and loss of such cells correlates with the failure to control HCV infection.[3] It is estimated that more than 170 million persons are chronic carriers of HCV and HCV RNA can be persistently detected in 85% of infected patients.[4] The illness and economic impact of HCV are primarily caused by the complications of chronic infection. Duration of infection and occurrence of co-factors such as alcohol, exposure to toxins and pesticides, concurrent hepatitis B or HIV-1 infection, or the HCV genotype causing the infection affect hepatitis C prognosis.[5] It is estimated that 20% of those with chronic HCV infections develop cirrhosis. Annual incidence of hepato-cellular carcinoma (HCC) has been reported to be 2-4% in 20-30 year HCV carriers. Due to such delayed impact on the health of infected persons, its estimated that disease caused by HCV will beak during the first decade of this new millennium. The epidemiology of HCV varies greatly from one country to another. In the western nations is estimated to be less than 1%, although it is higher than that in the eastern countries.[4,5] Data suggest that certain populations are at a higher risk of acquiring HCV, such as hemophiliacs, those necessitating hemo-dialysis, persons injecting illicit drugs and others who received multiple transfusion of blood and plasma products.[6] Hepatitis C virus has also been considered as professional risk for hospital health care workers (HHCW) as a result of their daily practice in dealing with blood and blood products. The aims of this study were; to evaluate the prevalence of anti-HCV antibodies using a wide sample of subjects vary in relative and attributable risk factors. They include healthy adults, blood donors and those who at a higher risk of acquiring HCV including hospital health care workers, and renal dialysis patients.

Methods. ***Study population.*** Between 1999 and 2001, a prospective study were carried on 2909 subjects of adult individuals aged from 18-65 years. Each subject completed a questionnaire regarding the previous history and the predisposing factors of viral hepatitis including gender, age, pervious blood transfusion and other factors.[7,8] A venous blood sample from each patient was collected and the serum was separated and tested for HCV and then stored at -80°C for further laboratory analysis. The analyzed subjects came from 5 groups as shown in **Table 1**, they consist of different populations; group I; 800 healthy adults who were accompanying the patients. Group II; 1200 individuals of blood donors. Group III; 459 HHCW working in close contact with patients at different teaching hospitals, Group IV; 200 patients on renal dialysis and group V; multiple blood transfusion group includes 250 patients from oncology and hematology (non-hemophilic) patients with multiple blood transfusion. Patients with known history of drug addiction, jaundice or those with acute or chronic liver diseases were excluded from the study.

Laboratory tests. Laboratory analysis was carried out at the Department of Medical Microbiology, Faculty of Medicine, Tripoli, Libya. Each serum was screened for anti-HCV antibodies by an enzyme-linked immunosorbent assay (ELISA) (Ortho diagnostic system). The sensitivity of these ELISA tests was estimated to be between 97% and 100%. Samples were considered reactive according to the manufacturers specifications. Hepatitis C infection was defined as the presence of HCV antibodies in the serum detected by ELISA.

Statistical analysis. The chi-squared (X^2) test for examining data derived from HCV analyses in order to determine the significance of difference in the groups analyzed. Further more we compared the prevalence of infection between groups on the bases of prevalence ratios and P values to evaluate statistical significance, with 95% confidence interval. The risks of acquiring HCV among these groups were determined by calculating the risk difference (attributable risk) and the relative risk (risk ratio) among the studied populations according to the formula postulated by Fletcher et al.[9]

Results. The populations studied consisted of 5 different groups as shown in **Table 1**, with 1.6:1.0 male: female ratio. The largest group studied being between 35-60 years. The prevalence of HCV-antibodies among the groups studied is summarized in **Table 2**. The over all prevalence of HCV-infection among the populations studied was variable. The highest prevalence was reported among the renal dialysis patients (group IV; 20.5% with confidence interval [CI] = 0.192-0.410) followed by the multiple blood transfusion group (group V; 10.8 % CI= 0.051-0.141). The least prevalence were among blood donors (group II; 1.2 %, CI = 0.010-0.021), HHCW (group III; 2.0%, CI = 0.103-0.237), and the community individuals (group I; 1.6%, CI = 0.012-0.030); despite the slight variation in the prevalence of HCV among groups I and II ± 0.2%, though this was statistically insignificant (P>0.01). The positivity rates in the different populations were also analyzed according to sex. No significant difference was observed in the subjects studied (P>0.01) despite the number of positive cases were higher in males than that in females. Individuals who were found to be positive for HCV were analyzed according to the age

Table 1 - Populations studied.

Groups	Male	Female	Total
Healthy adults	540	260	**800**
Blood donors	710	490	**1200**
Hospital health care workers	275	184	**459**
Renal dialysis patients	120	80	**200**
Multiple blood transfusion*	163	87	**250**

* Patients with multiple blood transfusion of oncology/hematology underlyings

Table 2 - Prevalence of hepatitis C virus antibodies among different populations.

Groups	HCV positive	Prevalence	95% CI
Healthy adults	13	1.6	0.012-0.030
Blood donors	14	1.2	0.010-0.021
Hospital health care workers	9	2.0	0.103-0.237
Renal dialysis patients	41	20.5	0.192-0.410
Multiple blood transfusion	27	10.8	0.051-0.141

HCV - hepatitis C virus, CI - confidence interval

Table 3 - Distribution of hepatitis C virus antibodies by age group in the populations studied.

Groups	Age group (years), individuals tested positive at age of					Total
	18-25	26-35	36-45	46-55	>56	
Healthy adults	1	3	2	3	4	**13**
Blood donors	3	5	6	*	*	**14**
Hospital health care workers	0	0	1	4	4	**9**
Renal dialysis patients	3	7	14	9	8	**41**
Multiple blood transfusion	1	2	10	7	7	**27**

* No one donates blood at this age

distribution as shown in **Table 3**. Compared to individuals aged 18-24 years, all older age groups were more likely to be infected with HCV. This was clearly evident in high-risk group who showed the highest prevalence of HCV represented by renal dialysis and the multiple blood transfusion groups. The analysis showed that only age was significantly related to HCV sero-markers, as the older groups were 2-4 times more likely to be infected with HCV. Grouping the subjects to different groups showed a significant difference in anti-HCV antibody prevalence between the subjects in groups I and II and that in groups III, IV and V. Those in category I can be considered to be representative for an a symptomatic general adult population with various possible route of contact with HCV. This population differs from blood donors as well as from any risk group, which are target populations chosen for analysis. Analysis of comparing risks among these groups showed that the relative risk was found to be [12.8] among the renal dialysis patient, [6.75] among multiple blood transfusion group and then [1.25] in HHCW. On the other hand the attributable risk was found to be [18.9] in renal dialysis, [9.1] among multiple blood transfusion group and [0.4] in HHCW comparable to the community individuals.

Discussion. Hepatitis C has great deal of impact on both public and health authorities all over the world. Hence then conducting studies which could determine its prevalence among population groups is particularly important especially in countries where such information is scant. Here we report the results of seroepidemiologic investigation into HCV infection among a large group of subjects. The prevalence of anti-HCV antibodies was evaluated in different population, which included general healthy individuals, blood donors, HHCW, renal dialysis patients and oncology/hematology patients. The prevalence of HCV in our general

population was found to be 1.6%. This is in an agreement with other studies carried in KSA and Syria but less than that reported in Egypt where it reached up to 30% being the highest in the world.[10] This could be contributed to socioeconomic as well as other etiologic factors that are likely to be relevant to the observed variations.[11,12] Anti-HCV prevalence has usually been shown to be relatively low among blood donors where it found to be 1% in Europe and in North America, though higher than that the Middle East and Asia,[13] Here in we found only 1.2% among blood donors were HCV positive. Our data is in concordance with that reported among the Saudi blood donors (1%) but less than that reported among Egyptians (16%), Sudanese (2%) and Syrian (2%) blood donors.[13] Health care workers are on a continuo exposure to the risk of contracting HCV. The prevalence of HCV among the HHCW in this study was 2% that is in an agreement with other studies reported on the prevalence of HCV among HHCW worldwide. Furthermore there was a difference between HHCW and the other 2 previously mentioned groups (blood donors and healthy individuals). The prevalence of HCV among patients undergoing renal dialysis was 20.5% being the highest among the different groups studied. Our data are in agreement with other centers worldwide where it varies from 1-30%.[14] Such high prevalence were related to the fact that these patients are at increased risk of HCV infection depending on the duration of treatment, extended exposure to transfusion and possible nosocomial transmission. The prevalence of HCV among the various pathologies represented in the multiple blood transfusion groups was found to be 10.7%, higher than that of healthy individuals, blood donors and HHCW, and less than that of renal dialysis patients. This however, is similar to that reported in medical world literature[15] which could be contributed to the clinical status of these patients. Accordingly those patients subjected to multiple transfusion are at greater risk of acquiring HCV infection as the prevalence increased according to number of transfusion independently of age and sex.

Different studies concerning viral hepatitis have found a certain correlation between viral infectivity, age and sex. In this study however, no significant difference was observed in the prevalence of anti-HCV according to the gender of the population studied. The prevalence of HCV antibodies has risen during the ages 46-55. This however, is in agreement with other studies that showed a steady increase in HCV prevalence with age.[16]

Our study represented a large number of individuals from various sectors, where the prevalence HCV varies significantly among them. Healthy individuals and blood donors can be reasonably considered a representative of the general population where the prevalence of HCV was found to be considerably low. This however, should be interpreted with caution as far as the specific HCV modes of transmission are concern. However, available information indicate that most part of the anti-HCV subjects with no history of obvious parenteral exposure. Relative and attributable risks were calculated for the groups who are at higher risk of acquiring HCV; either as of their jobs (professional risk) as HHCW, where the prevalence is comparably low which might reflect the awareness of such group and meticulous precautions augmented in the hospitals particularly when the patients are known to be positive for HCV. The oncology and dialysis patients were the other risk group in our study that showed the highest prevalence of HCV due to the nature of their clinical status which appears evident that it imposes them at extended exposure of viral hepatitis. Although, when compared with other risk groups from other centers, they were found to be less than that of hemophiliacs or drug abusers, however such groups are not representative of the general population.[17] The prevalence of HCV was found to be lower than that of HBV among general population, blood donors and HHCW. This however, is in accordance with the results from other centers. In a recent comparative epidemiological studies carried by Daw et al[18] found that the prevalence of HBV was the highest among HHCW followed by general population and the least was among blood donors. Despite a lower prevalence of anti-HCV antibodies compared with other viral of hepatitis such as hepatitis B, infection with HCV is very likely to become chronic.[19,20] The clinical spectrum of such chronicity varies from a symptomatic carrier status without liver damage to clinically apparent and rapidly progressive hepatitis advancing to cirrhosis.[21] Hepatitis C virus infection has enormous clinical, social, and economic impact. Hence, prevention and treatment strategies should be clearly formulated by both public and health authorities in order to tackle such a problem. A registry program concerning regular follow up, clinical management and treatment should be available.[22] Hepatitis C virus positive individuals should be evaluated for presence and severity of chronic liver diseases. Initial evaluation for presence of diseases should include multiple measurement of alanine transferase (ALT) at regular intervals, as ALT activity fluctuates in persons with hepatitis C. Such patients should be evaluated for severity of their diseases and for possible treatment.[23] Antiviral therapy is recommended for patients with hepatitis C who are at greatest risk for progression to cirrhosis. These persons include anti-HCV-positive patients with persistently elevated ALT levels, detectable HCV RNA, and a liver biopsy that indicates portal or bridging fibrosis or at least moderate degree of inflammation or necrosis.[24]

Available data regarding the prevention of HCV infection with Immunoglobulin (IG) indicate that IG is not effective for post exposure prophylaxis of

hepatitis C. Further more assessments have been made of post-exposure use of antiviral agents (namely interferon) to prevent HC infection.[25] Post exposure to HCV with acute hepatitis C and positive HCV-RNA polymerase chain reaction can be treated with 6 months of interferon. The sustained response with undetectable PCR, 24 weeks after finishing therapy is 98%.[26] Mechanisms of the effect of interferon in treating patients with hepatitis C are under evaluation, and an established infection might need to be present for interferon to be an effective treatment. The current approved therapy is either conventional interferon or pegylated interferon plus Ribavirin for 6-12 months according to the genotype of HCV. At the moment, there is no place for single therapy with interferon alone. Pegylated interferons have a superior effect than non-pegylated interferon in the management of chronic hepatitis C.[27,28] Further more health authorities should plan clear national programs to rise up public a wariness concerning HCV and other related pathogens. Hospitals on the other hand should adhere themselves to strict guide lines concerning sharps, disinfection, sterilization and firm screening for blood and blood products in order to minimize the extent of exposure to viral hepatitis among their HHCW.[29,30] Further to educational programs which should target both public and hospital personnel.

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