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Hepatitis C and B Viruses Among Some High Risk Groups of Egyptian Children

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The aim of this study was to detect seroprevalence of hepatitis C virus antibodies (anti-HCV), hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) among some high risk groups of Egyptian children and its effect on liver functions. We clinically examined 100 children who were classified into 4 groups; group 1:34 children with Insulin Dependent Diabetes Mellitus (IDDM), group 2:31 children having Chronic Renal Failure (CRF) on regular hemodialysis, group 3:15 patients with Systemic Lupus Erythematosus (SLE) and group 4:20 control healthy children. Anti-HCV antibodies, HBsAg and anti-HBs antibodies were detected in all children using ELISA technique. Anti-HCV seropositivity was found in 15 (44.1%) diabetic children, 16 (51.6%) CRF patients, 6 (40%) SLE patients and in one (5%) healthy child ($p<0.05$). One CRF patient was seropositive for both HBsAg and anti-HCV and simultaneously was anti-HBs seronegative. Ten CRF patients were anti-HBs seropositive. Two SLE patients were HBsAg seropositive and anti-HBs seronegative; one of them was also anti-HCV seropositive. Five SLE patients were anti-HBs seropositive. Comparing anti-HCV seropositive patients versus seronegatives of the three patients groups revealed that, disease duration, dialysis duration, AST and ALT were significantly increased only in anti-HCV seropositive versus seronegative CRF patients ($p<0.05$). In conclusion a significantly high anti-HCV seroprevalence was found in IDDM, CRF and SLE children with risk of chronic liver disease development suggesting the need of more stringent measures for prevention of HCV transmission with implementation of education programs identifying risk factors associated with inappropriate therapeutic modalities, periodic HCV screening and hepatitis B vaccination with booster inoculations to previously vaccinated children.

Key words: Hepatitis C virus, Hepatitis B virus, children, prevalence, insulin dependent diabetes mellitus, chronic renal failure, hemodialysis, systemic lupus erythematosus

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INTRODUCTION

Hepatitis C Virus (HCV) is a global health problem, with 170 million carriers worldwide and 3-4 million new cases per year and overall global prevalence 1-3%, with a significant risk of progression to cirrhosis and hepatocellular carcinoma (WHO, 2000; Lauer and Walker, 2001; Hassan *et al*., 2001; McHutchison, 2004). In children, HCV seroprevalence is 0.2-0.4% (Committee on Infectious Diseases, 1998). The highest HCV prevalence among adult Egyptians is due to the history of parenteral antischistosomal therapy, with high morbidity and mortality (Frank *et al*., 2000).

Similarly, Hepatitis B Virus (HBV) is a major cause of chronic liver disease, particularly cirrhosis and hepatocellular carcinoma; though HBV incidence and infection has been markedly reduced after mass vaccination programs (Wang *et al*., 2002).

The main transmission route of HCV is parenteral, however approximately 10% of the cases are sporadic, without well-defined transmission routes. Since the introduction of blood and organ donor screening by antibody testing in 1991, HCV has rarely been transmitted by transfusion of blood products (Center for Disease Control and Prevention, 1998; Alter, 2002).

Hepatitis C virus infection is a persistent public health concern in hemodialysis patients (Center for Disease Control and Prevention, 2001; Tokars *et al*., 2002), because of the risk for exposure to HCV associated with the dialysis procedure and the compromised immune system of them at both B and T-cell levels (Fabrizi *et al*., 2003, 2004). Also, HCV is associated with different extrahepatic disorders including autoimmune disorders (Galossi *et al*., 2007; Zignego *et al*., 2007). It was suggested that HCV is associated with diabetes mellitus because of the high frequency of injections (Rudoni *et al*., 1999) and the progression of autoimmune diabetes might have been accelerated due to infection of HCV (Chen *et al*., 2005; Masuda *et al*., 2007). Moreover, HCV was associated with systemic lupus erythemetosus and can induce various autoantibodies (Ramos-Casals *et al*., 2000a).

Patients infected with HCV often have minimal clinical evidence of disease (Mohan *et al*., 2007). Accurate testing for HCV is complicated by regional variation in the HCV genome and by variation in screening tests (Lauer and Walker, 2001; Pawlotsky, 2002).

Acute HCV infection is rarely recognized in children outside special circumstances and most chronically infected children are asymptomatic and frequently with normal or borderline Alanine Transaminase (ALT) values (Jonas, 2002; Mohan *et al*., 2007). Although the natural history of HCV infection acquired in children seems benign in the majority of instances, the infection takes an aggressive course in a proportion of cases leading to cirrhosis and end-stage liver disease during childhood and even hepatocellular carcinoma (Strickland *et al*., 2000).

The prevalence of infection with HCV among Egyptian children, in relation to lifestyle is poorly understood and recent studies of HCV prevalence in risk groups of children are scarce. Since HCV treatment become increasingly effective, it is important to identify silently infected individuals.

The aim of the present study was to detect seroprevalence of hepatitis C virus antibodies (anti-HCV), hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) among some high risk groups of Egyptian children and its effect on liver functions.

MATERIALS AND METHODS

This study was carried out on 100 children (44 males and 56 females) with age range from 4.5-19 yeas; for a period of 2 years starting at December 2004. The majority of them were referred from rural areas (72%), 18% from semi-urban areas while 10% from urban areas. Parental consent was obtained for all children included in the study.

Group 1 consisted of 34 children suffering from Insulin Dependent Diabetes Mellitus (IDDM) (type 1 diabetes; according to WHO (1985), criteria. They were 12 males and 22 females with age range from 4.5-19 years. They were recruited from the outpatient clinic of Diabetes, Endocrinology and Metabolism Pediatric Unit at Cairo University Children's Hospital as well as from the Pediatrics Clinic of the National Research Center. All diabetic children were on Insulin regimen and disease duration ranged from 1.5-17 years. All of them have used finger stick devices. None of them had received blood transfusion or were on hemodialysis.

Group 2 consisted of 31 children suffering from Chronic Renal Failure (CRF) on regular hemodialysis at the Center of Pediatric Nephrology and Transplantation, at Cairo University Children's Hospital. They were 20 males and 11 females and their ages ranged from 5-15 years. Disease duration ranged from 0.33-4 years. Dialysis sessions were performed 3 times/week using polysulfone dialyzers, bicarbonate-based dialysate and controlled ultrafiltration. Duration of each dialysis session varied between 2.5 to 3.5 h according to the patients. Vascular access used for hemodialysis was arteriovenous fistula. Infection control measures recommended by

Center for Disease Control and Prevention (2001) were applied in the hemodialysis unit; including dedicated machines for identified HCV infected CRF patients.

Group 3 consisted of 15 patients with Systemic Lupus Erythematosus (SLE) (2 males and 13 females) and their ages ranged from 4.5-19 years. They were selected from the Collagen Vascular Clinic at Cairo University, Children's Hospital. Duration of disease ranged from 2-16 years. The patients were fulfilling the revised criteria of the American College of Rheumatology for SLE (Tan *et al*., 1982). All patients were on antimalarial drugs and steroids and 14 were on immunosuppressive drugs. None of them had received blood transfusion nor were on hemodialysis.

Group 4 consisted of 20 healthy children matched in age and sex (10 males and 10 females) with age range from 5-19 years. They were chosen from the Pediatrics Clinic of the National Research Center. None of them had received blood transfusions or were on hemodialysis and they had no history of connective tissue disease or diabetes mellitus.

None of the children enrolled in the study had a history of previous jaundice or other signs of hepatitis and all of them were subjected to the following:

- Full history taking, with emphasis on personal or family history of hepatitis, jaundice, vaccination, injections, past hospital admission, surgical procedures, blood transfusions, haemodialysis, dental care, tattooing, ear piercing and circumcision by informal health care provider.
- Thorough clinical examination including weight, height and proper examination of the liver size and the skin.

Laboratory investigations: Venous blood samples 5 mL were withdrawn from all children and centrifuged and then the separated sera were kept frozen at -20°C until analysis of hepatitis markers. Those samples for routine laboratory investigations were immediately transported to the laboratory for assay.

The following laboratory investigations were done:

- Complete Blood Count (CBC)
- Aspartate Transaminase (AST)
- Alanine Transaminase (ALT)
- Total and direct bilirubin
- Urea and creatinine
- Hepatitis C antibodies (anti-HCV)
- Hepatitis B surface antigen (HBsAg)
- Hepatitis B surface antibody (anti-HBs)

Hepatitis C antibodies (anti-HCV), Hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) were detected by Enzyme Linked Immunosorbent Assay (ELISA) using Equipar Kits (made in Italy) catalog No. 2000CB-2000CBA, 1900 BG and 1900 BBC, respectively (Fody and Johnson, 1987; Fazekas *et al*., 1980; Mushawar *et al*., 1981).

Statistical methods: Statistical Package for Social Sciences (SPSS) program version 11 was used for analysis of data. Data were summarized as mean±SD and percentage. Comparison between 2 groups was done by using Student's t-test for quantitative independent variables and Chi square test for qualitative variables. ANOVA test was used for analysis of more than two groups followed by Post Hoc test if significant. Correlations between various variables were done using Pearson correlation coefficient (r). p-value is considered significant if <0.05.

RESULTS

A total of 100 children were enrolled in this study (44 males and 56 females), with mean age (12.06±3.84 years). Descriptive data of the 4 studied groups are shown in Table 1.

Table 1: Descriptive data of the studied groups included in the study

Items	Group 1 (N = 34)	Group 2 (N = 31)	Group 3 (N = 15)	Group 4 (N = 20)	*p-value
(Male/female) No. (%)	12/22 (35.3/64.7)^{a}	20/11 (64.5/35.5)^{ab}	2/13 (13.3/86.7)^{bc}	10/10 (50/50)^{c}	0.005
Age (years)	12.44±4.48	10.95±2.67	13.10±3.51	12.38±4.31	0.250
Weight (kg)	38.38±16.08	23.53±7.12	37.40±10.80	44.95±13.93	0.0001§
Height (cm)	136.46±18.28	121.37±15.06	139.20±16.59	142.35±20.02	0.0001§
Disease duration (years)	6.55±3.85	1.72±1.08	4.75±3.52	-	0.0001§
Hb (g dL^{-1})	12.06±0.73^{abc}	10.09±1.73^{ad}	10.92±1.88^{be}	12.87±1.05^{cde}	0.0001
AST (U L^{-1})	25.32±11.08	30.48±28.34	27.21±9.27	19.86±7.90	0.220
ALT (U L^{-1})	23.77±12.12	45.97±37.45	23.84±13.11	15.99±5.96	0.0001§
Total bilirubin (mg dL^{-1})	0.55±0.18	1.06±1.04	0.50±0.15	0.50±0.11	0.001§
Direct bilirubin (g dL^{-1})	0.15±0.05	0.24±0.15	0.15±0.05	0.13±0.04	0.0001§
Urea (mg dL^{-1})	11.76±3.04	74.13±17.70	15.97±6.42	8.80±2.17	0.0001§
Creatinine (mg dL^{-1})	0.68±0.19	7.39±1.63	0.73±0.31	0.52±0.17	0.0001§

Data were expressed as Mean±SD, except for numbers between parentheses, *: p-value is significant if <0.05, Similar symbol indicates significant difference
§: Significant difference between Group 2 and other groups

All males included in the study were circumcised while circumcision was done to only 16 females. All females had ear piercing and none of the children had tattooing. All children had injections either sporadically or regularly, 80 children had undergone dental care, 78 children had been hospitalized and 35 children had undergone surgery. Concerning vaccination history all children had been vaccinated according to schedule but regarding hepatitis B vaccination we found that 21 children were not vaccinated.

Etiological causes of CRF were urinary tract disorders in 14 (45.2%) patients, idiopathic in 11 (35.5%), congenital or hereditary in 4 (12.9%) and glomerulonephritis in 2 (6.5%). Mean dialysis duration was (1.22±0.64 years). Past history of blood transfusion was found in 26 (83.9%) CRF patients.

The seroprevalence of anti-HCV antibodies of all children incorporated in the study was 38%. There was no difference of anti-HCV seropositivity in relation to age or sex of the studied children ($p>0.05$). The overall mean serum levels of AST and ALT were statistically significantly higher in anti-HCV seropositive than seronegative children (35.13±24.59 U L^{-1} versus 20.58±8.67 U L^{-1} for AST and 43.40±35.36 U L^{-1} versus 20.34±8.92 U L^{-1} for ALT, respectively) ($p<0.05$); still they were within normal range. Also, a positive correlation was found between HCV seroprevalence and AST and ALT ($p = 0.0001$, $r = 0.395$; $p = 0.0001$, $r = 0.444$, respectively).

Seropositivity of anti-HCV was found in 15 (44.1%) diabetic children, in 16 (51.6%) cases of CRF, in 6 (40%) SLE patients and in only one healthy child (5%) of the control group ($p<0.05$) (Table 2).

Regarding hepatitis B virus; only one CRF patient (3.2%) was seropositive for both HBsAg and anti-HCV antibodies and in the same time was anti-HBs negative. Furthermore, only 10 (32.3%) patients were seropositive for anti-HBs antibodies with a titer of >10 IU L^{-1} (Table 2).

Two (13.3%) SLE patients were HBsAg seropositive and anti-HBs seronegative; one of them was also anti-HCV seropositive. Only 5 (33.3%) SLE patients were anti-HBs positive (Table 2).

Neither the diabetic patients nor the healthy children of the control group were seropositive for HBsAg, with 25 (73.5%) diabetic patients and 19 (95%) healthy children were seropositive for anti-HBs antibodies (Table 2).

Cryoglobulinemia was found in 8 (53.3%) patients with SLE.

Comparison between the 3 patients groups (1-3) in relation to reactivity to HCV revealed that, there was no significant difference between anti-HCV seropositive versus seronegative patients of group 1 and group 3 ($p>0.05$). On the other hand, anti-HCV seropositive CRF patients (group 2) had a statistically significantly higher values of disease duration, AST and ALT than seronegative CRF patients ($p<0.05$). Also, dialysis duration was statistically significantly longer in anti-HCV seropositive than seronegative CRF patients ($p = 0.003$) (Table 3).

There was no significant difference between anti-HCV seropositive CRF patients and seronegatives regarding history or number of blood transfusion ($p>0.05$).

Table 2: Seroprevalence of hepatitis C and B viruses in the four studied groups

Items	Group 1 N = 34	Group 2 N = 31	Group 3 N = 15	Group 4 N = 20	Total N = 100
	----------N (%)----------				
Anti-HCV +ve	15 (44.1)	16 (51.6)	6 (40)	1 (5)	38 (38)
HBsAg +ve	0 (0)	1 (3.2)	2 (13.3)	0 (0)	3 (3)
Anti-HBs +ve	25 (73.5)	10 (32.3)	5 (33.3)	19 (95)	59 (59)
HBV/HCV co-infection	0 (0)	1 (3.2)	1 (6.67)	0 (0)	2 (2)

Table 3: Comparison between anti-HCV seropositive and seronegative Chronic Renal Failure (CRF) patients

Items	Anti-HCV seropositive CRF N = 16	Anti-HCV seronegative CRF N = 15	*p-value
Disease duration (Years)	2.36±1.00	1.03±0.65	0.0001
Dialysis duration (Years)	1.54±0.63	0.88±0.46	0.003
§AST (U L^{-1})	43.94±34.37	16.13±5.26	0.006
†ALT (U L^{-1})	66.44±43.25	24.13±3.48	0.001

Data were expressed as Mean±SD, *: p-value is significant if <0.05, §: Aspartate transaminase, †: Alanin transaminase

DISCUSSION

The current study demonstrated a significantly high seroprevalence of anti-HCV in the 3 patients groups (1-3) as compared to the control group (4). This finding reflects prior HCV infection but not necessarily a current liver disease and indicates that parenteral transmission, either through intravenous or subcutaneous route is a major risk factor for infection (Center for Disease Control and Prevention, 1998).

The present results revealed that, anti-HCV seroprevalence in children with IDDM (Group 1) was higher than the reported prevalence in a previous Egyptian study (El-Nanawy *et al.*, 1995), which was 29.4%. The higher prevalence in our diabetic patients may be attributed to the larger sample size of our study (almost the double of the previous one), or due to the increased use of finger stick devices by all diabetic children we studied. Also, the prevalence in our study was higher than that found in diabetic children and adults in different countries (Ozyilkan *et al.*, 1994; Simo *et al.*,

1996; Mason *et al*., 1999; Rudoni *et al*., 1999; Sotiropoulos *et al*., 1999). On the contrary, other studies in children revealed that HCV was not associated with diabetes in spite of the high frequency of injections (Cerutti *et al*., 1999; Atabek *et al*., 2003).

We found no differences between anti-HCV seropositive versus seronegative diabetic patients in terms of type of treatment, hospital admissions and use of finger stick devices which was in agreement with Rudoni *et al*. (1999) who stated that these medical practices play no role in nosocomial transmission of HCV in diabetic patients.

It is not known exactly whether IDDM results in an increased HCV prevalence in diabetic children or vice-versa. Cerutti *et al*. (1999) mentioned that autoimmune complications are common in chronic diseases as a result of the continuous stimulation of the immune system, the reactivity of which is reduced in children compared with that in adults. Chronic HCV infection may give rise to a large array of extahepatic autoimmune diseases including endocrinologic disturbances besides the indolent but progressive liver damage (Mayo, 2003; Galossi *et al*., 2007; Zignego *et al*., 2007). Existing evidence indicates that the progression of HCV infection is slower in children, presumably as a result of their weaker immune response (Tovo and Newell, 1999). Therefore, the occurrence of HCV related disorders is expected to be lower in children than in adults. Furthermore, there is a long latency period between acquisition of HCV infection and appearance of autoimmune diseases (Cerutti *et al*., 1999). Accordingly, HCV does not seem to represent a significant risk factor for type 1 diabetes in childhood.

So, the increased anti-HCV seroprevalence in our patients with IDDM suggests that multiple injections play an important role in addition to the possibility of patient-to-patient transmission during hospital admission or during attending the outpatient clinics with wrong handling of the same finger stick device. Hence, it is recommended to use individual disposable materials for insulin injection, finger stick devices and an insulin delivery system.

We observed that, anti-HCV seroprevalence was the highest in CRF patients on hemodialysis (Group 2) than the other groups, in spite of the use of preventive measures recommended by Centers for Disease Control and Prevention (2001). The exact mode of transmission of HCV within dialysis units is as yet incompletely defined, but there is evidence to support nosocomial transmission (Fabrizi *et al*., 2002, 2004). Present results were higher than the prevalence reported by other studies among pediatrics and adult patients in the same geographic region and in other far regions (Bdour, 2002; Molle *et al*., 2002; Sivapalasingam *et al*., 2002; Saxena *et al*., 2003; Saxena and Panhotra, 2004; Di Napoli *et al*., 2006; El-Amin *et al*., 2007; Santos and Souto, 2007).

The current study revealed that, there was no significant difference between both anti-HCV seropositive CRF patients on hemodialysis and seronegatives regarding history of blood transfusion or number of transfused units, which coincides with other investigators who mentioned that, patients who were receiving maintenance hemodialysis had no significant association with blood transfusion (Molle *et al*., 2002; Saxena *et al*., 2003; El-Amin *et al*., 2007). So, HCV seropositivity was not most probably related to patients' transfusional history.

On the contrary, it was reported that the prevalence of anti-HCV correlated with a history of blood transfusion before the introduction of blood donor screening for HCV (Bdour, 2002). Even, after the introduction of blood donor screening for HCV; Santos and Souto (2007) reported that blood transfusion remains a major risk of HCV transmission.

We further noticed that the mean hemodialysis duration and disease duration were significantly longer among anti-HCV seropositive compared to serongative CRF patients (Group 2). A positive association between HCV prevalence and length of time on hemodialysis has been found in many other studies (Bdour, 2002; Molle *et al*., 2002; Santos and Souto, 2007).

So, the present results suggest a nosocomial transmission in the hemodialysis unit, which could be due to a failure to identify carriers of this disease and thus might favor patient-to-patient transmission or because of a lack of truly effective biosafety measures implemented in the dialysis units. Several investigators stated that, the sharing of facilities in a high risk hemodialysis environment facilitates nosocomial transmission of HCV infection (Saxena *et al*., 2003; Moreira *et al*., 2005; El-Amin *et al*., 2007).

Therefore, additional efforts should be made to minimize the risk of HCV infection before and during long-term dialysis, with implementation of a surveillance system and retraining units' personnel on recommended infection control measures in hemodialysis units.

The present study demonstrated that, seroprevalence of anti-HCV antibodies and cryoglobulinemia in SLE patients (Group 3) were higher than that mentioned in earlier adult studies (Ramos-Casals *et al*., 2000a; García-Carrasco *et al*., 2001; Qin *et al*., 2002; Ahmed *et al*., 2006a). The cause of this high prevalence of anti-HCV antibodies in our lupus patients may be due to frequent hospitalization and injections in addition to unhealthy behavior. It was

reported that viruses might be one of the elements that trigger SLE and HCV appears to be most often associated with the presence of autoimmune disorders (Ramos-Casals *et al*., 1999; Rivera and García-Monforte, 1999; Ramos-Casals *et al*., 2000a, b).

There was no significant difference of cryoglobulins in SLE patients in relation to reactivity to HCV which is against what was mentioned in other studies (Ramos-Casals *et al*., 2000a; Perlemuter *et al*., 2003).

So, HCV testing should be done when the diagnosis of SLE is considered. Ramos-Casals *et al*. (2000a), further recommended HCV testing for SLE patients, especially who lack the typical features of SLE or who have cryoglobulinemia, or liver involvement, in order to identify this subset of patients for prognostic and therapeutic reasons.

Seroprevalence of anti-HCV antibodies in the control group (Group 4) of our study was much lower than the observed prevalence of an earlier Egyptian study in children (11.8%) (El-Nanawy *et al*., 1995). On the other hand, present results were higher than that reported by EL-Raziky *et al*. (2007), which was 2.02% in Egyptian children. However, these present results lie within the recorded range of anti-HCV prevalence (3-9%) in other studies (Habib *et al*., 2001; Medhat *et al*., 2002). This variation in seroprevalence can be attributed to the smaller number of healthy children of group 4 in the current study; or may be attributed to the different laboratory methods used for detection of anti-HCV (Pawlotsky, 2002).

The cause of anti-HCV seropositivity in the healthy child (who was a girl from a semi-urban area) was not clear. There was no family history of HCV. However, ear piercing, circumcision by informal health care provider, dental care or use of contaminated syringes may be assumed, as they are known to be risk factors and a history was obtained from the parents about them.

We found no significant difference in seroprevalence of anti-HCV antibodies in relation to age or sex of all children which was in agreement with many investigators (Molle *et al*., 2002; Mudawi *et al*., 2007), while others found that prevalence was higher in males than females (Sivapalasingam *et al*., 2002; El-Sadawy *et al*., 2004). The former reported that it was associated with younger age, while El-Sadawy *et al*. (2004) reported that it increased sharply with age.

Regarding hepatitis B virus; only 3% of total children were HBsAg seropositive (one CRF patient and two SLE patients). This prevalence lies within the Egyptian range from 3.2-4.3% (Zaki *et al*., 2003; El-Gilany and El-Fedawy, 2006). This low prevalence supports the success of the scheduled hepatitis B vaccination program of Egyptian 3children, which has been approved in Egypt in 1992, but some of our studied children have missed the vaccination. This together with the low anti-HBs antibody concentrations found in the majority of the children make HBV vaccination of patients and staff (in addition to booster inoculations for all previously vaccinated children) an effective way of limiting the risk of transmission of HBV infection.

The three HBs-Ag seropositive patients were also seropositive for anti-HCV leading to more aggressive liver disease as reported by several authors who further mentioned that this is probably because of impaired immune function and high risk of parenteral exposure with a prevalence of dual infection ranging from 3 to 56% (Antonova *et al*., 2001; Anima *et al*., 2001; Devi *et al*., 2004; Reddy *et al*., 2005; Siagris *et al*., 2006).

There was no significant difference of AST and ALT levels between anti-HCV seropositive and seronegative patients with diabetes and SLE. On the other hand, significantly elevated levels of AST and ALT were found only in anti-HCV seropositive CRF patients versus seronegatives with higher ALT levels than normal range, which pointes out to the high risk of continuous parenchymal hepatic damage in these children. But, Molle *et al*. (2002) has shown that all affected CRF children had normal serum levels of ALT and also Moreira *et al*. (2003) observed that the monthly determination of ALT does not aid in the early detection of HCV infection and they recommended not to employ elevated transaminases to predict HCV infection in this cohort of patients.

In general there are conflicting data about the role of AST and ALT in the diagnosis and follow up of HCV. Some investigators found that all affected children had normal levels of transaminases (Gismondi *et al*., 2004); others reported that most chronically infected children with HCV have mildly elevations in ALT levels (Jonas, 2002) and also, it was stated that chronic hepatitis C may even occur in adult patients with persistently normal ALT levels with slow or absent progression to cirrhosis after 10 years of follow-up (Persico *et al*., 2006; Shiffman *et al*., 2006). In contrast, persistently elevated ALT levels was recorded in several Egyptian pediatric and adult studies and consequently HCV infection is not always benign in Egyptian children, hence the authors suggested those tests to be useful and dependable markers in the non-invasive diagnosis of HCV (El-Raziky *et al*., 2004; Wahib *et al*., 2005).

In conclusion a significantly high anti-HCV seroprevalence was found in children with IDDM, CRF and SLE which carries a considerably high risk for development of chronic liver disease in these patients and suggests the need of more stringent measures for prevention and control of HCV.

The silent evolution of HCV infection in children makes periodic screening of HCV in risk groups mandatory, with follow up of all anti-HCV positive patients associated with Polymerase Chain Reaction (PCR) technique, in addition to implementation of education programs of infection control based on the identified risk factors associated with inappropriate therapeutic modalities, besides improvement in certain lifestyle patterns and customs to reduce the spread of HCV.

Application of HBV vaccination of patients and staff members who have missed it and booster inoculations for all previously vaccinated children to limit the risk of transmission of HBV infection, with completing the vaccination course.

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