University of Khartoum
Faculty of medicine
Graduate College
Health & Medical Studies Board

PREVALENCE OF HEPATITIS C VIRUS ANTIBODIES AMONG CHILDREN WITH CHRONIC RENAL FAILURE IN KHARTOUM STATE

By
Dr. Hind Abd El Rahman Mohmmed Ahmed Elansari
MB,BS University of Elgazira

A thesis submitted in partial fulfillment for the requirements of the

Clinical MD in Paediatrics and Child Health, 2005

Supervisor
Dr. Ilaham M. Omar
Assistant Professor
MPC (U of K)

بسم الله الرحمن الرحيم

قال تعالى:

((وَمَا أُوتِيتُم مِّن الْعِلْمِ إِلاَّ قَلِيلاً))

صدق الله العظيم
الإسراء – آية 85

Dedication

At times it is hard to find away to pick the perfect words.

To say to those whose loving kindness never ends just like
How much we need them to share our joys.

To my parents, sisters and brothers for their patience
encouragement and care.

To the soul of my late father who introduced me to
the field of medicine

Acknowledgement

I would like to express my sincere appreciation to my supervisor Dr. El Tahir Medani Elshibly, Associate Prof. of Pediatrics, University of Khartoum for his supervision, valuable advice and helpful support.

My grateful thanks to Dr. Ilham M Omer. It has been a great pleasure working with her and I am very grateful to her.

My special thanks to Dr. Eltigani MA Ali, Pediatrics Nephrologist, who allowed me to have an access to the patients in the Renal Units.

I would like to thank Dr. Abd El Aziz Mohammed Hammed, Khartoum Blood Banks Directorate, for sponsoring this work.

My great thanks to the Lab. Technician, Shaza Mahgoub El Siddig for her keen help and support.

I am most grateful to all people working in Dr. Salma M Suliman Kidney Dialysis & Transplantation Center, Bahry Renal Center.

My thanks also extend to all people who contributed to my training, teachers and consultants, colleagues and patients.

Abstract

Hepatitis C virus infection (HCV) is emerging as the world's predominant cause of chronic liver disease. Variable prevalence of hepatitis C (HCV) infection has been reported in adult patients with chronic renal failure on renal replacement therapy. So we have studied the prevalence of anti- HCV infection in children in the renal units.

The objectives of this study were to determine the prevalence of anti-HCV antibodies in patients with chronic renal failure, then to study the risk factors for acquiring HCV infection and to correlate the presence of anti-HCV antibodies to liver disease activity.

Records were reviewed for demograghic, clinical, biochemical data and risk factors .Sera from 50 patients under going haemodialysis, peritoneal or conservative management and 50 control were tested for antibody to HCV by 3rd generation Enzyme – linked immunosorbent assay. From a total of 50 patients (33 male and 17 female), aged 0-18 yrs, two were anti-HCV positive (4.0%) All the anti-HCV positive patients had been on haemodialysis for a mean of 27 months, while the anti- HCV negative patients had been on dialysis for 15 months ($p<0.003$).

All the anti-HCV positive patients had been transfused with 2-8 units, a mean of 5 units ($p<0.000$). No one of them has had prior or recent HBV or HIV infection.

The most predictive risk factor for HCV infection was the length of time on haemodialysis.Three out of the 50 patients had high alanine amino transferase levels. Two were patients with chronic renal failure; one of them was positive while the other was negative for anti-HCV, the third one was in the control group with negative anti-HCV.

ملخـص الأطروحـة

إلتهاب الكبد الفيروسي (س) أصبح باغتاً سيادة على الأسباب الأخرى لأمراض الكبد المزمنة في العالم .

هنالك تباين في معدل انتشار الأجسام المضادة لفيروس التهاب الكبد الوبائي (س) في الكبار المصابين بمرض الفشل الكلوي المزمن الذين يتلقون بدائل العلاج الكلوي ، لذا قمنا بدراسة التهاب الكبد الفيروسي (س) في وحدات الكلى للأطفال .

أهداف هذه الدراسة هي تحديد معدل انتشار إيجابية اختبار الأجسام المضادة لفيروس التهاب الكبد (س) ومن ثم دراسة عوامل الخطر له وأيضاً إيجاد علاقة ما بين ايجابية اختبار الاجسام المضادة بفيروس التهاب الكبد الوبائي (س) ونشاط إمراضية الكبد .

تمت مراجعة سجلات المرضى للاطلاع على المواصفات الاجتماعية والسكنية والسريرية والكيمياء الحيوية وعوامل الخطر وتم أخذ أمصال دم من 50 من المرضى الذين يتلقون بدائل العلاج الكلوية إما في شكل غسيل دموي أو بروتوني أو علاج تحفظي وكذلك أخذت عينات من 50 من الأطفال الأصحاء غير المصابين بمرض الفشل الكلوي المزمن .

تم اختبار الأمصال للكشف عن وجود الأجسام المضادة لفيروس التهاب الكبد الوبائي (س) بواسطة الجيل الثالث من ELISA . من عدد 50 مريض (عدد الذكور فيهم 33 والإناث 17) تتراوح أعمارهم ما بين (0-18) ، اثنين فقط منهم ايجابي الاختبار (4%) وهم كانوا يتلقون الغسيل الدموي لمدة 27 شهر في المتوسط . أما هؤلاء الذين كانوا يتلقون الغسيل الدموي وأظهروا سلبية الاختبار متوسط فترتهم كانت 15 شهر (الاحتمال < 0.003).

وقد أظهرت الدراسة أن الغسيل الدموي هو المتكهن بعامل الخطر كما يوجد 3 فقط من المرضى المصابي بالفشل الكلوي المزمن لديهم معدلات مرتفعة لإنزيم الكبد ALT واحد منهم فقط كان ايجابي الفحص.

كل ايجابي الاختبار كانوا قد تلقوا عمليات نقل دم بأعداد تتراوح من 2 – 8 وحدات على أنه لا يوجد أحد من سالبي الفحص قد تلقى نقل دم (الاحتمال 0.000). كما انه لا يوجد تاريخ سابق أو حالة للاصابة بالتهاب الكبد الفيروسي (ب) أو فيروس عوز المناعة البشري المكتسبة.

Contents

List of Tables

List of Figures

List of Abbreviations

ACE	Angiotensin Converting Enzyme
Anti-HCV	Anti-hepatitis C virus Antibodies
CAPD	Continous Ambulatory peritoneal Dialysis
CCPD	Continous Cycling peritoneal Dialysis
CHC	Chronic Hepatitis C
CRF	Chronic Renal Failure
CRI	Chronic Renal insufficiency
CRI	Chronic Renal impairment
EIA	Enzyme Immuno Assay
EIA (IR)	EIA reactive
ELISA	Enzymed linked immunsorbant assay
ESRD	End-stage renal disease
HAI	Histological Activity Index
HBsAg	Hepatitis B Surface Antigen
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HGF	Hepatocyte Gross Factor
KKDC	Khartoum Kidney Dialysis Center
KSA	Kingdom of Saudi Arabia
NANBH	Non-A, Non-B Hepatitis
NAPRTCS	American pediatric Renal Transplant Cooperative
NS	Non-Structural
PCR	Polymerase Chain Reaction
RIBA	Recombinant immunsorbant assay
RR	Repeatebly Reachic

1. INTRODUCTION AND LITERATURE REVIEW

1. Chronic renal failure

1.1. Historical background

During the late 1970s, whether any child was candidate for any form of renal replacement therapy was questioned because the risk of therapy was not thought to justify the potential benefit. Since that time, dialysis followed by renal transplantation became routine therapy for treatment of children with end-stage renal disease ESRD.[1]

1.2. Incidence

The incidence of chronic renal disease in children is steadily increase in US followed by Japan. Current data suggest that 1.5 to 3.0 children per one million populations per year develop ESRD. The North American Pediatric Renal Transplant Cooperative Study Group (NAPRTCS) initiated a registry of children treated with dialysis; 2, 828 patients had been registered. NAPRTCS initiated a registry to collect data from children with chronic renal insufficiency (CRI) in 1994 and since then 2.529 patients have been registered.[1,2]

When haemodialysis and transplantation progress were being developed, the first figures produced the frequency of terminal renal failure in children, provisionally estimated to be in the region of one or two cases per million inhabitants per year. [3]

1.3. Prevalence

1.3.1. Prevalence of HCV infection in haemodialysis in Sudan

In December 1994, the prevalence of HCV antibodies in haemodialysis patients in Khartoum Kidney Dialysis Center (KKDC) in Sudan was (34.9%) in the patients group and (5.41%) in staff members.[4, 5]

1.3.2. Prevalence of HCV infection in Arab countries.

The prevalence of HCV in haemodialysis population in survey of 273 adult haemodialysis patient in 3 haemodialysis units in Jordan (Amman) was (1.7%) in healthy blood donors and (24.5%) in haemodialysis population, a percentage similar to what has been reported around the world and in the neighboring countries.[6]

Also it is found that the prevalence of anti-HCV antibodies among 5 different population groups including; healthy individuals, blood donors, hospital health care workers, renal dialysis patients and multiple blood transfusion in Libya,(1.6%) among the general population, (1.2%)among blood donors, (2%) among health care workers, (20.5%) among renal dialysis and(10.8%) in the multiple blood transfusion group.[7]

In January 1991 and December 1993 the prevalence of positivity of anti-HCV antibodies in the haemodialysis patients was

Sixty-four patients (24.4%) in Al-Jazerah hospital, Abu Dhabi, United Arab Emirates.[8]

In Hamad General Hospital, Doha, Qatar they screened 130 patients on regular dialysis for anti-HCV antibodies by enzyme linked immunosorbant assay (ELISA) and confirmation by recombinant immunosorbent assay (RIBA). 58 (44.6%) were antibody positive.[9]

At prevalence of (2.7%) in the early 1990s, it is estimated that approximately 500,000 people in Saudi Arabia have been exposed to HCV. Over (80%)of such individual remain infected and most of them progress to chronic hepatitis (CHC), cirrhosis and/or hepatocellular carcinoma (HCC). The recent reported prevalence of HCV infection in Saudi Arabia was approximately (1%). This decline is largely due to the early implementation of testing of blood donors for HCV.

However, it is peritent that measures are taken to identify patients already infected and offer treatment to those with good prognostic factor.[10]

The age specific prevalence of antibody to HCV was studied. The prevalence of anti-HCV in apparently healthy Saudi (without overt liver disease) increased with the age, with a peak of 5% in

those over 50 years of age. The range which was (2.2 – 5%) is higher than that reported from any western countries.[11]

In another study, one hundred and forty nine patients with end-stage renal disease on regular haemodialysis were screened for antibodies against HCV and HBs Ag. The overall prevalence of anti-HCV antibodies was (84.6%.[12]

Twenty percent of pediatrics haemodialysis patients were found to be anti-HCV antibodies positive using first generation testing. It is possible that higher prevalence may be found using detection of viraemia by poly merase chain reaction (PCR) as the standard method of diagnosis. Screening of 20 Saudi children with renal failure showed a prevalence of (45%).)[13, 14]

1.3.3. Prevalence of HCV infection in Europe and South America:

They screened a haemodialysis population in central Brazil by PCR method to assess the prevalence of HCV infection. An overall prevalence of(46.7%) was found.[15]

In another study done by J A Oliva and et al in Creu Raja hospital, Barcelona, Spain. They examined the prevalence of the IgG C virus 100-3 antibody (anti-HCV) in a group of 43 patients on haemodialysis, the anti- HCV prevalence was (30%).[16]

Anti-HCV antibodies in haemodialyzed versus non-dialyzed patients was compared in kidney centre in Aga khan University Hospital in Karachi using enzyme immunoassay (EIA) (C 100-3-AbboH) in 68 patients with chronic renal failure (CFR) who were on maintenance haemodialysis and 48 patients on conservative management. In haemodialysis group 31 patients (46%) and in conservative group only 3 patients (6%) were anti-HCV positive.[17]

1.4. Definitions and pathophysiology:-

1.4.1. Definition:-

The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines chronic kidney disease (CKD) as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 for 3 or more months. Whatever the underlying etiology, the destruction of renal mass with irreversible sclerosis and loss of nephrons leads to a progressive decline in GFR. The different stages of CKD form a continuum in time; prior to February 2002, no uniform classification of the stages of CKD existed. At that time, K/DOQI published a classification of the stages of CKD, as follows:

- Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2)
- Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m^2)

- Stage 3: Moderate reduction in GFR (30-59 mL/min/1.73 m^2)
- Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m^2)
- Stage 5: Kidney failure (GFR <15 mL/min/1.73 m^2 or dialysis)

The K/DOQI definition and the classification of CKD allow better communication and intervention at the different stages.

The term chronic renal failure(CRF) is used to describe a patient who has residual renal function of less than 30%.

ESRD is term reserved for the stage of renal disease when replacement therapy, whether dialysis or transplantation is required.[1]

1.4.2. Pathophysiology:-

According to Bicker's hypothesis residual renal function derives from the remaining healthy nephrons in a kidney parenchyma in which all the diseased nephrons have ceased to function. In support of this hypothesis, the classic experimental protocol of unilateral pyelonephritis provides two pieces of evidence, first is that the ratio of the majority of tubular function to glomerular filtration remains very similar in both healthy and the diseased sides that means, the glomerulotubular balance is preserved in experimental (CRF). The next evidence is the demonstration of the homogeneous character of the population of residual nephrons in the diseased kidney.[2,18]

1.5. Etiology:-

The NAPRTCS registry confirms that different forms of obstructive uropathy (including reflux and dysplasia) account for almost 50% of the etiologies of renal failure. Other relatively common causes of ESRD in children that are rare in adults include renal hypoplasia and dysplasia, hereditary nephritis, infantile polycystic disease, cystinosis and uremic medullary cystic disease. Focal glomerulosclerosis is the most common glomerulopathy leading to CRF in young children (accounting for 14.8% of all children with ESRD), but older children may suffer from many form of chronic glomerulonephritis.[1]

In conclusion, there are certain special features about the etiological distribution of CRF in children, such as the incidence of hereditary nephropathy, of renal hypoplasia and of vascular nephropathy and the absence of intestinal nephropathy of infectious origin without associated malformation of the urinary tract.[18]

1.6. Signs of progressive loss of renal function:-

The databases have confirmed that children with chronic renal disease present in a different manner from similarly affected adults. The uremic syndrome is the hallmark of renal failure. It includes such non-specific symptoms as lethargy drowsiness, itching, nausea, vomiting and paresthesias. Although at times the

pediatrician sees these late symptoms, for the child with renal insufficiency, earlier diagnosis and initiation of therapy, when subtler symptoms occur are advantageous.

The most common finding that should alert the pediatrician to the possibility of chronic renal disease is growth impairment. The mean height of children entering the NAPRTCS CRI database is 1.4 standard deviations below the mean. For the NAPRTCS dialysis database, mean height at entry is 1.75 SD below the mean. Short stature, particularly if associated with other symptoms, such as polyuria frequent bouts of dehydration, salt craving, bone deformities, abnormal tooth development, or anemia, should suggest that the affected patient might have chronic renal disease. A previous history of urinary tract infection or glomerulonephritis adds further support to this suspected diagnosis.[1, 18]

1.7. Treatment:-

Numerous changes is recommended therapy have been made over the past few years and will continue to be made as more information becomes available about the metabolic abnormalities and the requirements for growth in these children.

1.7.1. Non dialytic therapy for chronic renal insufficiency:-

1.7.1.1. Diet:-

Provide at least 100% of recommended daily allowance of caloric intake. Protein intake is controversial; range 0.5 – 1.5 g/kg/d .Medium chain triglyceride should be added.

1.7.1.2. Renal osteodystrophy:-

1, 25 dihydroxy cholecalciferol and calcium carbonate as a calcium supplement and PO_4 binder.

1.7.1.3. Anaemia:-

*M*ay require iron or erythropoietin.

1.7.1.4. Hypertension:-

Contro lsodium intake. If hyperreninemic, consider angiotensin – converting enzyme (ACEs) inhibitor.

1.7.1.5. Acidosis:-

may improve with reduced protein &lipid intake, sodium citrate or $NaHCO_3$, 2-4 mEq/kg/day**.**

1.7.2. Dialytic therapy:-

In children, two techniques of maintenance dialysis are used, peritoneal and haemodialysis. Several publications have been devoted to the pediatric problems of kidney transplantation. Now, maintenance haemodialysis and transplantation are linked in the treatment of chronic uremia and cannot be considered separately.[19]

1.7.2.1. Peritoneal dialysis:-

In the 1950s and 1960s, peritoneal dialysis was used to treat acute renal failure. Treatment of CRF with peritoneal dialysis was not successful until reliable peritoneal access was developed in the late 1960s. At that time several pediatric programs using intermittent peritoneal dialysis were developed.[1]

1.7.2.2. Continuous Ambulatory peritoneal dialysis and continuous cycling peritoneal dialysis:-

In 1976, a new form of peritoneal dialysis that later became known as (CAPD) was described. CAPD overcomes the relative inefficiency of the peritoneal membrane by exposing it continually to dialysate in the early 1980s; this form of dialysis was introduced as a form of therapy for children with CRF. In 1981 another form of peritoneal dialysis was introduced and was named Continuous Cycling Peritoneal Dialysis (CCPD). Both of them can be done at home. So permitting the patient to attend school and have relatively normal peer interactions. Both forms of therapy are less costly than in-centre haemodialysis and either one can be used to treat even the smallest infant.[1]

Complication:-

Hernias may occur, because of persistently increased intra abdominal pressure. The most common complication of peritoneal

dialysis is peritonitis, most often with coagulase-negative staphylococcus.[1]

1.7.2.3. Haemodialysis*:-*

The History of Haemodialysis:

The idea of removing solutes from body fluids by dialysis dates back to the beginning of the century. Adel et al, 1983 at the Johns Hopkins Medical School in Baltimore, performed the first experimental haemodialysis in dogs. George Haas from Geissen, Germany performed the first human dialysis. He dialyzed four patients with terminal renal failure between 1924 and 1928 using large celloidin tube mounted in glass containers.

Willem Kolff at the Groningen University Hospital in the Netherlands introduced the first dialysis suitable for use in man in 1943. The first patient whose life was saved by treatment with the artificial kidney was a woman with acute renal failure.[20]

Technical aspects of renal replacement therapy:-

The major components of a haemodialysis system include the blood circuit and the dialysate circuit, the central part of both circuits is the dialyser, where waste product, excess electrolyte and water are removed from the patient's blood. Dialysis fluid and blood are pumped through the dialyser in a counter current direction, separated by the semi permeable membrane.[20]

Composition of dialysate:-

The composition of dialysis fluid should be similar to that of normal interstitial body fluid, appropriately corrected for the protein content of the latter. The basic principles, procedures and complications of haemodialysis are the same as in adult.[20]

The fact that kidney function can be replaced in part by maintenance haemodialysis, peritoneal dialysis or transplantation means that patient with end-stage renal failure can expect a much long survival than patients suffering from other sever disease such as cancer. However, they have medical complication of the long-term dialysis, which are:-

1. Cardiovascular complications are worldwide a cause of mortality in patients on renal replacement therapy. The European dialysis and transplantation association reports indicated that 52.6% of deaths in dialysis patients are due to cardiovascular complication. In Canada, 39.9% of deaths in patients with end-stage renal failure were of cardiac origin and in New Zealand and Australia 46% of dialysis patient died from heart disease.
2. Cerebrovascular accident:- The incidence of cerebrovascular accidents in dialysis patient's increase with age. Patients aged 15 to 34 years have prevalence of cerebrovascular accident 250 times greater than that in general population. Cerebrovascular

accidents are slightly more common in adult with polycystic kidney disease (19.3%) due to the presence of vascular malformation.

3. Infections diseases:- Viral hepatitis plays only a minor role in the mortality of haemodialysis patients. If Hbs Ag+ve positive patients are dialyzed in separate rooms with appropriate sanitary measures, the incidence of hepatitis B and its complication decrease. The availability of hyper immune serum and hepatitis B vaccine, careful screening for infectious blood products and reducing the number of blood transfusion also decreases the incidence of hepatitis B and of hepatitis C in dialysis patient. Bacterial infections and septicemias are more common in patients with CRF than in normal population.[20]

2. Hepatitis C Virus:-

Hepatitis C is a viral infection of the liver which in 1974 had been referred to as parenterally transmitted hepatitis C until identification of the causative agent in 1989 by Choo et al. The discovery and characterization of the HCV led to the understanding of its primary role in post-transfusion hepatitis and its tendency to induce persistent infection [21]. *HCV* is a major cause of acute hepatitis and chronic liver disease, including cirrhosis and liver cancer. Globally, an estimated 170 million persons are chronically

infected with HCV and 3 to 4 million persons are newly infected each year. No vaccine is currently available to prevent HCV infection and treatment of chronic hepatitis C is too costly for most persons in developing countries to afford. Thus, from a global perspective view, the greatest impact on hepatitis C disease burden will likely be achieved by focusing efforts on reducing the risk of HCV transmission from nasocomial exposure (e.g. blood transfusions, unsafe injection practices) and high-risk behaviors (e.g. injection drug use).

2.1. Prevalence:-

WHO estimates that about 170 million people, 3% of the world's population, are infected with HCV and are at risk of developing liver cirrhosis and/or liver cancer. The prevalence of HCV infection in some countries in Africa, the Eastern Mediterranean, South-East Asia and the Western Pacific is high compared to some countries in North America and Europe.[10,21]

2.2. Pathogen:-

Hepatitis C virus is one of the viruses (A, B, C, D, and E), which together account for the vast majority of cases of viral hepatitis. It is an enveloped RNA virus in the flaviviridae family

which appears to have a narrow host range. Humans and chimpanzees are the only known species susceptible to infection, with both species developing similar disease.

An important feature of the virus is the relative mutability of its genome, which in turn is probably related to the high propensity (80%) of inducing chronic infection. HCV is clustered into several distinct genotypes which may be important in determining the severity of the disease and the response to treatment [21]

Table 1. 1. Hepatitis C estimated prevalence and number infected by WHO region

WHO Region	Total population (millions)	Hepatitis C prevalence rate %	Infected populations (millions)	No of countries by WHO region where data are not

				available
Africa	602	5.30	31.9	12
Americas	785	1.07	13.1	7
Eastern Mediterranean	466	4.60	21.3	7
Europe	858	1.03	8.9	19
South-East Asia	1500	2.15	32.3	3
Western Pacific	1600	3.90	62.2	11
Total	5811	3.10	169.7	57

Hepatitis C virus is one of the viruses (A, B, C, D, and E), which together account for the vast majority of cases of viral hepatitis. It is an enveloped RNA virus in the flaviviridae family which appears to have a narrow host range. Humans and chimpanzees are the only known species susceptible to infection, with both species developing similar disease.

An important feature of the virus is the relative mutability of its genome, which in turn is probably related to the high propensity (80%) of inducing chronic infection. HCV is clustered into several distinct genotypes which may be important in determining the severity of the disease and the response to treatment.[21]

2.3. Isolation of HCV:-

The HCV was cloned from the plasma of an experimentally infected chimpanzee with chronic NANBH. The genetic material (DNA & and RNA) was extracted and reverse transcribed in order to construct a complimentary library [8] .The resultant complementary DNA was inserted into a cloning vector (Phage gt 11). The vector containing the viral genome was then expressed in Escherichia Coli.

The protein expressed by the cloned DNA sequence was screened using an immunoblot assay against serum from a patient with chronic NANBH, presumed to contain antibodies to the responsible virus. After approximately 10-clones had been screened, an antigenic protein encoded by the HCV was isolated. Expression of the corresponding HCV complementary DNA in yeast allowed the development of an immunologic assay to detect antibody reactive against the protein.[22,23]

2.4. HCV Genome:-

The entire HCV genome has been sequenced and all viral proteins encoded by the genome have been expressed. HCV appears to be a unique viral pathogen (novel type of virus) because little overall homology exists between the sequence of both the HCV genome and it's encoded polypeptides and other known viral sequences.[24]

HCV is a small (30-60 nm), single stranded RNA virus with a lipid envelope and a genome length of approximately 10-kilo bases that code for approximately 3000 amino acids.[8,11] HCV is inactivated by heating (60° C for 30 min or 100° C for 2 min.) or UV exposure.[22,25]

The genome structure is similar to that of Flaviviruses Family (Human Flavi and Animal Pesti Viruses).[12] The Flaviviruses are mostly transmitted by arthropods such as mosquitoes and ticks.[24]

HCV structural proteins are encoded by contiguous sequences from the 5' terminus, and non-structural (NS) proteins are encoded by sequences at the 3' end.[27]

Hepatitis C virus nucleotide structure includes a single large open region frame that produces a polyprotein precursor. This in turn is cleaved into several polypeptides: a nucleocapsid core ©, various envelope structural regions (E1 & E2 / NS1) and several

non-structural proteins (NS2, NS3, NS4, NS5), involved in viral replication, protein modification and assembly, thus the coding regions of the genome are flanked by non-coding regions at both ends (fig 1:1).[12]

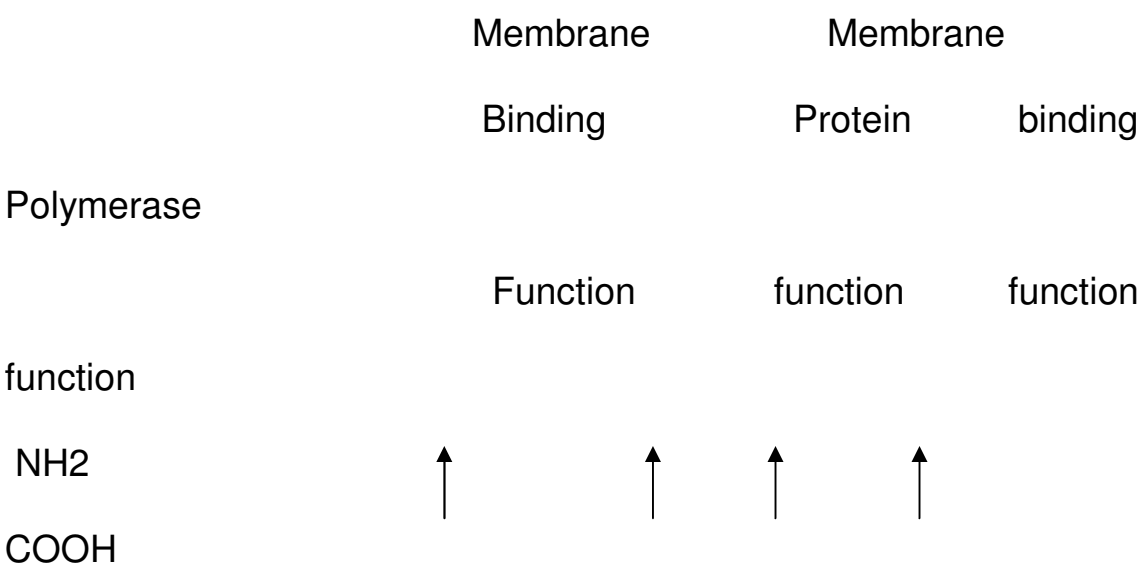
The 5' NCR is a highly conserved non-coding region, which has approximately 300 amino acid bases; located to the left of the nucleocapsid region and the 3' non –coding sequence of about 50 amino acid bases follows the NS coding region.

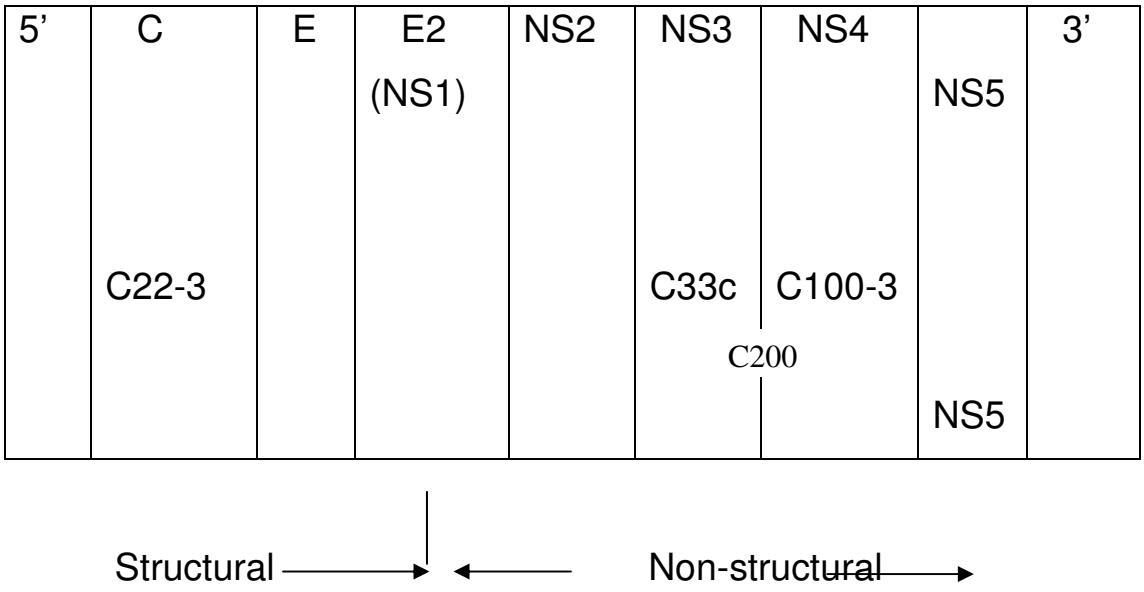
The 5' NCR presumably exerts a regulatory influence upon replication and translation of the RNA genome. This region is the target of choice for PCR assays to detect HCV RNA.[13]

A feature of the E2 / NS1 region is a hyper variable domain of significant sequence heterogeneity.[26] There appears to be significant genetic diversity and several distinct subtypes have been distinguished with definite geographic distribution. This heterogeneity depend on the homology of the nucleotide sequences or there deduced amino acids sequences among different HCV isolates. HCV, which replicates, circulate as a heterogeneous mixture of closely related genomes containing a master (most frequently represented) sequence and a large spectrum of mutants, a genomic distribution referred to as Quasispecies.[26,28] Thus, HCV like many RNA virus, exhibit a high mutation rate and can therefore

escape immune surveillance .This has implications for both vaccine development and responsiveness to anti-viral agents.[27]

Fig 1.1. Structure of HCV genome





C: Core antigen

E: Envelope

NS: Non-structural region

Source:-A- Kader H-H, Balistreri WF Pediatr Inf Dis J 1993;12: 853-867.

2.4.1. Implications of HCV heterogenesis:-

Rigorous phylogenetic analysis of the NS 5 region has found clustering of nucleotide sequences into 6 major genotypes and a series of definable subtypes.[29] The heterogeneity of certain regions , such as the E2 region, which has the highest mutation rate, may be the basis for the unreliability of antibody test, the phenomena of reinfection due to incomplete immunity and the difficulty in development of a useful vaccine[24].The high mutation rate in the E2/NS1 region allows the virus to elude host defense ,

which explains persistent and flare up of the disease .Thus at any one time , an individual may harbor several mutants , some of which are neutralized and others are free ; the latter may be transmissible from mother to neonate , this state also explains the aggressive behavior of HCV noted in immune suppressed patients.[30]

There is also a high mutation rate in infected individuals during anti-viral therapy.[31] These variations may explain the unpredictable, highly capricious response of patients, to treatment with interferon. There are also diagnostic implications where the subtypes of HCV possess different antigenic potential owing to the production of this similar protein. Thus the variability of HCV subtypes renders detection by PCR of questionable reliability if primers are chosen from a variable region of the genome [26].Perhaps the most significant clinical implication is the potential for repeated bouts of acute hepatitis with different subtypes and acute HCV super infection with a different subtype in a person with established HCV infection.[32]

2.4.2. Genotypes of HCV:-

Currently there are 9 major genotypes and over 30 subtypes. Genotype 1 is widely distributed through out the world.

In the United State and Western Europe, patients with chronic hepatitis and blood donors were found to be infected with subtypes

1A, 1B .2B & 3A, while in Japan and Taiwan subtypes 1B, 2A & 2B are frequently found. In Thailand and Nepal, genotypes 1 & 3 are common where as genotype 4 are predominant in the Middle East, Egypt and Central Africa. Genotype 5 is found in South Africa, 6 in Hong Kong and Vietnam and recently new genotypes 7-9 have been identified in Vietnam. [33,34,35]

2.5. Hepatitis C Virus infection:-

2.5.1. Classification:-

HCV infection was classified according to persistence of abnormal liver function for less or more than 6 months to:-

2.5.1.1. Acute hepatitis:-

The acute response to HCV involves necrosis of the entire liver; most marked in the centrilobular areas and increased cellularity, which is predominant in the portal areas .The lobular architecture remains intact. Fatty change is rare, a diffuse mononuclear cellular inflammatory reaction causes expansion in the portal tracts, bile duct proliferation is common but bile duct damage is not often found. Diffuse kupffer cell hyperplasia is present in the sinusoids along with infiltration of polymorphonuclear leukocytes and esoinophils.[18]

The combination of bile duct damage and lymphoid aggregates should suggest infection with HCV; the single lesion thought to be most predictive of HCV infection is the presence of lymphoid aggregates.[36]

2.1.5.2. Chronic hepatitis:-

Individuals infected with HCV evidence a high percentage of chronic hepatitis on biopsy (35-63%), including lesions, suggesting the so called chronic persistent hepatitis , chronic active hepatitis, and chronic lobular hepatitis .The prevalence of cirrhosis or developing cirrhosis ranges from 20 to 58% [26,37] .

It is thought that the virus may promote cancer through cirrhosis although HCV mostly genotype 1B was found to be associated with hepatocellular carcinoma without the intermediate step of cirrhosis.[34] In children long-term studies are needed to confirm this association .

I- Chronic persistent hepatitis (CPH):-

This is benign inflammatory process of the liver. The lobular architecture is always normal. Inflammation is limited to portal triads, and no significant fibrosis or cirrhosis found. Prognosis is good in childhood.[18]

II- Chronic active hepatitis:-

It is characterized by resolving inflammation, necrosis and fibrosis with the possibility of progression to cirrhosis and liver failure.

The above classification was renewed in 1994 to Knodell et al scoring system. This scores; portal inflammation, piece meal necrosis, lobular inflammation and fibrosis .Also it was name Histological Activity Index (HAI).

2.5.2. Clinical features of acute infection:-

The clinical picture of HCV infection in children is indistinguishable from hepatitis A or B.[22]

The incubation period is 7-9 weeks (range 2-24weeks). Most pediatric patients are asymptomatic infections are usually mild (sub-clinical) and insidious in onset . Fatigue is the most commonly reported symptom.[26] Fever, malaise, nausea, often the presenting symptoms. Diarrhea often occurs and dark colored urine. Jaundice occurs in only 25% of patients.[38] An enlarged tender liver usually occurs during the acute stage following transfusion of HCV infected blood; hepatitis C develops in approximately 80% of recipients.[39]

Typically, a fluctuating pattern of amino transferase (ALT) elevation occurs in about 80% of those in whom chronic HCV develops. These episodes of fluctuations in ALT presumably reflect waves of liver cell inflammation and cell death .The pattern of the

ALT level may offer a prognostic indicator for progression to chronicity ; chronic hepatitis C occurs in 42% of patients with a transient ALT elevation, 87% of patients with fluctuating ALT levels, and 95% of patients with persistent ALT elevation[26]. Absence of HCV antibodies is seen in 10%of chronic hepatitis C, despite the presence of HCV RNA and evidence of liver disease.[26] Although chronic elevations of aminotransferase levels are common , chronic HCV will progress to cirrhosis in only about half of the patients or about 25% of all those initially infected.[18]

2.5.3. Natural Course of HCV infection:-

The true natural history of HCV remains a major area of controversy in hepatology, reflecting the indolent by the logistical difficulties inherent in studying a disease that typically takes decades to evolve.[40]

Liver disease tends to evolve silently and insidiously, unheralded by physical signs or abnormal liver function test and thus progression is difficult to assess with standard serologic, biochemical and physical criteria. Follow up is best with periodic liver biopsies and quantitative estimate of viral load with PCR or branched DNA-based quantitative assays.[41]

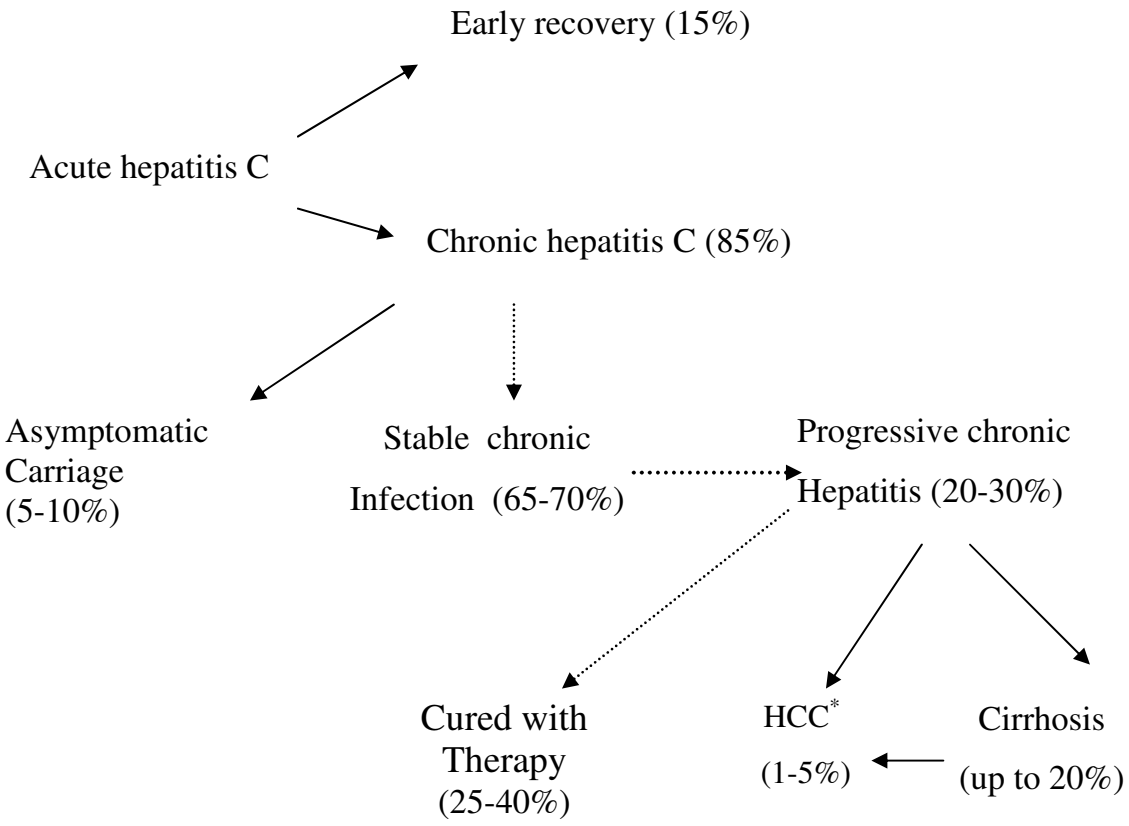
It has been proposed that there are four patterns of HCV infections. The first is the pattern of recovery, which is seen in 15%

of patients with viremia and acute hepatitis followed by resolution of viremia with persistence of antibody.

Next is the asymptomatic carriage and the stable chronic course in which patients have viraemia and acute hepatitis with subsequent decrease in ALT with intermittent ALT elevations and persistent viraemia over years. This is the predominant pattern seen in 70% of the patients. It is thought to be secondary to the emergence of quasispecies and relative in effectiveness of neutralizing antibodies. The third pattern is that of severe and rapid progression occurring in 20-30%of patients, which result in persistent elevation of hepatic enzymes, persistent viraemia and a more rapid progression to cirrhosis. The last pattern is that of acute resolving hepatitis with persistent viral replication (asymptomatic carriage) .This occurs in 5-10 % of patients.[40,42] HCV generally develops chronic hepatitis in about5- 10 years, cirrhosis in about 10-20 and HCC in about 20-30 years.[40]

The natural history of hepatitis C in sporadic and low risk cases is that of a relatively benign and very slowly developing process. [41] The few published studies of chronic hepatitis C in children, are based on patients in the high risk category who manifest a disease spectrum that broadly resembles that course of hepatitis C in adults.

Figure 1.2: Natural course of hepatitis C



* HCC hepatocellular carcinoma

Source: - Alter H .Patterns of hepatitis C infection. 37th Annual

Meeting of the infectious diseases society of America; Philadelphia 1999 Session 70, S 111.

Little is known about the natural history of parentally acquired HCV infection. In a recent study by Palomba et al,[40] seven HCV positive children were followed up for a period of 65 months (range 26-90 months). Viraemia was evident in these children at the most recent follow up visit. Liver biopsies of five children showed chronic persistent hepatitis. These preliminary result suggest that perinataly acquired HCV may persist indefinitely, causing chronic indolent hepatitis.[40]

It was found that there were 5 situations associated with an accelerated course of infection .These included concurrent alcohol use , hepatitis B infection ,iron overload, aflatoxin exposure and immunosuppressive state such as HCV infection and chronic renal dialysis.[41]

2.5.4. Chronic infection and consequences:-

About 80% of newly infected patients progress to develop chronic infection. Cirrhosis develops in about 10% to 20% of persons with chronic infection, and liver cancer develops in 1% to 5% of persons with chronic infection over a period of 20 to 30 years. Most patients suffering from liver cancer who do not have hepatitis B virus infection have evidence of HCV infection. The mechanisms by which HCV infection leads to liver cancer are still unclear. Hepatitis C also exacerbates the severity of underlying liver disease when it

coexists with other hepatic conditions. In particular, liver disease progresses more rapidly among persons with alcoholic liver disease and HCV infection.[10]

2.5.5. Means of transmission:-

HCV spread primarily by direct contact with human blood. Transmission through blood transfusion that are not screened for HCV infection, through the reuse of inadequately sterilized needles, syringes or other medical equipment, or through needle-sharing among drug-users, is well documented. Sexual and perinatal transmission may also occur, although less frequently. Other modes of transmission such as social, cultural, and behavioral practices using percutaneous procedures (e.g. ear and body piercing, circumcision, tattooing) can occur if inadequately sterilized equipment is used. HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils, or casual contact.

In both developed and developing countries, high risk groups include injecting drug users, recipients of unscreened blood, hemophiliacs, dialysis patients and persons with multiple sex partners who engage in unprotected sex.

In developed countries, it is estimated that 90% of persons with chronic HCV infection are current and former injecting drug

users and those with a history of transfusion of unscreened blood or blood products.

In many developing countries, where unscreened blood and blood products are still being used, the major means of transmission are unsterilized injection equipment and unscreened blood transfusions. In addition, people who use traditional scarification and circumcision practices are at risk if they use or re-use unsterilized tools.[10,18]

2.5.6. Diagnosis:-

Diagnostic tests for HCV are used to prevent infection through screening of donor blood and plasma, to establish the clinical diagnosis and to make better decisions regarding management of a patient. Diagnostic tests commercially available today are based on EIA for the detection of HCV specific antibodies. EIAs can detect more than 95% of chronically infected patients but can detect only 50% to 70% of acute infections.[45,46]

A recombinant immunoblot assay (RIBA) that identifies antibodies which react with individual HCV antigens is often used as a supplemental test for confirmation of a positive EIA result.

Testing for HCV circulating by amplification tests RNA (e.g.: PCR or branched DNA assay) is also being utilized for confirmation of serological results as well as for assessing the effectiveness of

antiviral therapy. A positive result indicates the presence of active infection and a potential for spread of the infection and/or the development of chronic liver disease.[46]

2.5.6.1. Virology:-

The preferred sample for virological investigation is plasma from a tube anti-coagulated with ethylenediamine tetra-acetic acid (EDTA). The plasma is suitable for both antibody and HCV-RNA testing. If plasma is unavailable, then serum should be separated at low speed centrifugation and stored at -20^{o}C or lower.[10]

1. Detection of HCV antibodies by the enzyme immunoassays

The enzyme immunoassay (EIA) is the methodology of choice to detect antibodies against HCV specific antigens in individuals exposed to HCV. The EIA assays should have adequate sensitivity, appropriate specifity. A negative EIA test is sufficient to exclude a diagnosis of chronic HCV infection in immuno-competent patients. The initial EIA-reactive (IR) results have to be confirmed. Firstly, the test should be repeated so that the serological reaction is shown repeat ably reactive (RR). This sample is then considered to be "EIA-positive". The patient should be re-bled and re-tested using the same reagents to confirm that the first EIA-positive sample did indeed come from the patient. Then, the RR EIA-positive sample should be referred to a reference laboratory for confirmation of

infection by PCR. If HCV-RNA is detected. CHC is confirmed. In those cases where HCV-RNA is not detected, the patient could have either, resolved past HCV infection, or a false-positive HCV EIA test result.[10,45,46]

The EIA assays are considered to have very high specificity of over 99%. Studies of EIA-positive samples in KSA have shown that, they are very likely to be reactive by RIBA, and the positive predictive value of EIA assays reaches 97%. The EIA may be falsely negative in immuno-compromised patients (for example HIV, renal failure and post transplant) and in the stages of an acute infection. Therefore, the HCV-RNA detection should be carried out in suspected cases.[45,46]

2. HCV-RNA detection:-

Viral RNA detection tests for HCV can be either qualitative or quantitative. It is recommended that the blood sample should be taken into tubes with the anticoagulant (EDTA), which provides more stable RNA.

The HCV-RNA qualitative test is usually the more sensitive and can detect less than 50 IU/ml (<100 copies/ml) using target amplification assays such as reverse transcriptase-polymerase chain reaction (RT-PCR). Transcription mediated amplification (TMA), a newly developed technique has been shown to be more

sensitive with a limit detection of less than 5 IU/ml. Because of this relative sensitivity, a qualitative assay will confirm viraemia and assess the SVR. Quantitative tests should be used to determine the pre-treatment viral load and to assess the early response to therapy at 12 weeks.[46]

2.5.7. Treatment:-

Antiviral drugs such as interferon taken alone or in combination with ribavirin, can be used for the treatment of persons with chronic hepatitis C, but the cost of treatment is very high. Treatment with interferon alone is effective in about 10% to 20% of patients. Interferon combined with ribavirin is effective in about 30% to 50% of patients. Ribavirin does not appear to be effective when used alone.[47,48,49]

2.5.8. Prevention:-

There is no vaccine against HCV. Research is in progress but the high mutability of the HCV genome complicates vaccine development. Lack of knowledge of any protective immune response following HCV infection also impedes vaccine research. It is not known whether the immune system is able to eliminate the virus. Some studies, however, have shown the presence of virus-neutralizing antibodies in patients with HCV infection.

In the absence of a vaccine, all precautions to prevent infection must be taken including:-

- Screening and testing of blood and organ donors.
- Virus inactivation of plasma derived products.
- Implementation and maintenance of infection control practices in health care settings, including appropriate sterilization of medical and dental equipment.
- Promotion of behaviour change among the general public and health care workers to reduce over use of injections and to use safe injection practices .
- Risk reduction counseling for persons with high-risk drug and sexual practices.[10]

3. Hepatitis B Surface Antigens (Hbs Ag):-

It is common practice to look for HBsAg during the first assessment so that chronic carriers can be further investigated and special precautions can be taken in handling their blood samples [49].

It is a common infection worldwide although the prevalence varies considerably from country to country. The incubation period is between 6 weeks to 6 months, and it is common for CRF patients to have a relatively asymptomatic course while affected dialysis staff frequently have extreme fatigue, jaundice, arthritis and anorexia. Between 10% and 14% of non-uraemic patients who develop

hepatitis B will progress to chronic active or chronic persistent hepatitis, and between 1% and 3% will develop fulminant hepatitis, which carries a high mortality rate.[20]

The eighteenth combined report (Brunner 1987) on regular dialysis and transplantation in Europe patients and staff of hemodialysis units varied widely between countries, surprisingly, the majority of centers in Austria, Belgium and France were reported not to use separate rooms for haemodialysis of patients positive for the HbsAg. The reports indicated that the higher the number of HbsAg positive patients on treatment, the higher the number of new cases; however, the number of new cases of hepatitis B in staff appeared to be only weakly related to the number of HBs Ag positive patient on HD.few member staff were infected in most European countries but in some Eastern European countries, where there was a high proportion of HBsAg positive patients on haemodialysis centre, there were also high number of infected staff.

A dramatic decrease in the number of staff contracting hepatitis has been observed in countries where active immunization against hepatitis B has been introduced[20].

4.Hepatitis B&C screening:-

If the initial blood test for HbsAg was negative it should be repeated to confirm that the patient remain free of hepatitis B before decisions are made about the form of replacement therapy. If the initial test was positive it should be repeated and tests for HBeAg and anti-HBeAg performed. HBsAg positive have the same survival on regular dialysis as HBsAg negative patients but a poorer prognosis and higher incidence of hepatic disease after renal transplantation. Patients who are HBsAg positive, particularly if they are also HBeAg positive, are better managed by chronic ambulatory peritoneal dialysis or home dialysis, which reduces the risk of transmission to the staff and fellow patients, though this has become a less important considerations since the introduction of vaccine. Patients who are negative for HBsAg are offered vaccination if they do not have naturally acquired immunity; a test for anti- HBsAg is therefore performed. In many centers, those who have no detectable surface antibody are offered vaccination with serum derived or yeast derived vaccines before they undergo dialysis, or immediately after starting. It is essential to confirm that protective antibody levels have been achieved; prolonged courses of four or more injections, and high doses, are required in some uraemic patients, particularly those who have received immunosuppressive therapy.[49]

The recent development of an antibody test for hepatitis C has shown that previous exposure to this virus (probably by routes similar to those for hepatitis B) is not uncommon among patients on dialysis, an incidence of 5.5 percent in Germany. So far there are no available tests for infectivity comparable to those for HBsAg and HBeAg. When such a test becomes available it will become a routine part of predialysis assessment, since epidemics of hepatitis C occur in dialysis units. For the moment we have only the unsatisfactory option of treating all antibody positive patients as infectious, while this a reasonable policy for blood donors , since the incidence of permanent carriage of the virus is high in parenteral hepatitis C, it raises more ethical problem in the case of dialysis patients who may have their mode of treatment changed because the probability, not the certainty, that they are infectious.[49]

There are particular problem in areas of low prevalence, at a time when there is no confirmatory test for doubtful positives. Consequently one cannot be dogmatic but in our view screening for hepatitis C antibody should now become a routine part of predialysis assessment, but they should be used with discretion.[49]

5. HCV/HIV Co-infection:-

The prevalence of HCV infection in patients with HIV diseases has been reported to vary from 26% - 97 % [50]. HIV co-infection

result in an increased hepatitis C viral load and accelerate liver disease progression associated with CD4 decline due to HIV disease. The accelerated liver disease result in 16-fold increase in end stage liver disease, 5.6 fold increase in hepatocellular carcinoma and a 7-fold increase in mortality.[51] New data suggest more rapid development of AIDS in hepatitis C co-infected patient who developed liver disease.[51]

The mechanism of this may be due to change in the immune system. The expansion of T helper cell (Th) type 1 clone and Th recognition of multiple epitopes are important in the elimination of HCV. Co-infected lymphocytes produce a Th II response rather than the desire Th I, which impaired the host immune response to HCV.[40]

6. Hepatitis and CRF:-

Despite major improvements in renal replacement therapy the immune function of uraemic patients remains poor. In part, these immune aberrations are linked to the uraemic status and are present before the onset of any renal replacement therapy.[52]

However, treatment such as hemodialysis with cuprophan membranes may contribute to reduce immune capacity. From a practical point of view, these data strongly favour the use of more biocompatible membranes, which have fewer complement activating

properties, and non-pyrogenic, endotoxin-free, and eventually acetate-free, dialysates for renal replacement therapy. Moreover, recent knowledge of fundamental immunology, once fully applied to the study of the immune deficit of chronic uraemia, may lead to the definition of effective immuno-modulating strategies.[52]

Acute and chronic hepatitis can pose a difficult diagnosis in CRF patients .The clinical picture of viral hepatitis is indistinguishable form that of drug induced hepatitis, toxic hepatitis or alcoholic hepatitis. Identification of the causative virus is essential because it has implication on treatment and prognosis. Due to the immunosuppressive effect of ureamia, viral hepatitis in these patients is often mild compared to the infections in non-uraemic subjects, who mount more vigorous inflammatory responses.

As cell mediated immunity which is important for terminating hepatitis B infection is impaired there is increased tendency for the uraemic patient to develop chronic liver disease as a result of viral hepatitis[52]. Following acute viral hepatitis caused by the B or non-A, non-B, chronic liver disease may develop in the form of chronic active hepatitis. The latter is a serious complication which eventually progresses to cirrhosis.[52]

7. Hepatitis and Haemodialysis:-

Patients treated with haemodialysis usually show abnormal stored liver function test. Approximately 30% of haemodialysis patient present mild elevation of transaminase. Hepatitis B and C are the main cause of liver disease in such patients.

With the extensive use of haemodialysis in the 1960s it became apparent that viral hepatitis was major problem associated with this therapy. In 1972 it was found that patient submitted to chronic hemodialysis were at great risk of acquiring HBV infection. Subsequently, several studies confirmed the incidence of HBV infection in hemodialysis unit; at least one serological HBV marker was positive in about 40%; the prevalence of serological HBV markers in patient dialyzed at home is lower (5%-6%) suggesting that transmission of HBV from other patient or hospital personnel important in the spread of HBV infection in hemodialysis unit[52].

8. Hepatitis in renal dialysis unit:-

Out breaks of hepatitis affecting both patients and staff began to occur soon after intermittent hemodialysis units were established for the treatment of patient with CRF. In the beginning it was assumed that these outbreaks were due to hepatitis B and transfusion of the patient was restricted and washed frozen cell substituted for whole blood in an effort to prevent the virus entering the units. Stringent precautions against cross-infection were also

introduced (PHLS 1968) but did not terminate out breaks already in progress or prevent new ones from starting.[53] Infection control policy now is adopted.

JUSTIFICATION

1. Although many studies regarding the prevalence of HCV were conducted in Sudan, the prevalence of HCV in children with CRF is not known.
2. CRF patients are at risk of developing HCV infection i.e. those needing blood transfusions an appreciable number of hospital inpatients and outpatients and are a great burden to the health system, family and society.

3. With the increased facilities of haemodialysis, patients with ESRD are living longer. Consequently, the chance of acquiring infection is increased in these immunocompromised patients.
4. HCV has become the most common cause of chronic liver disease with no effective vaccine and non-sustained response to treatment
5. Higher risk of mortality in patients referred for renal transplantation who were anti-HCV positive compared to anti-HCV negative
6. Yet in Sudan there is no protocol to screen blood bank and donor for HCV.

OBJECTIVES

1. To determine the prevalence of HCV infection in children with chronic renal failure in Khartoum state.
2. To study the risk factors for transmission of HCV among children with CRF.
3. To correlate the presence of HCV antibodies to liver disease activity.

2. MATERIALS AND METHODS

2.1. Study design:-

This is a descriptive comparative hospital based study.

2.2. Study area:-

This study was conducted at the following six dialysis centers and hospitals:-

D_1 = Dr. Salma dialysis and kidney transplantation centre.

D_2 = Dialysis unit in Khartoum teaching hospital.

D_3 = Suba University hospital

D_4 = Renal Center in Khartoum North hospital.

D_5 = Ahmed Gasim Paediatric Hospital

D_6 = Dialysis unit in military hospital – Omdurman.

2.3. Study duration:-

This study was conducted during the period from the 1st of Dec 2004 – end of June 2005.

2.4. Study population:-

The study populations were children aged 0 – 18 years.

2.4.1. Patients:-

The study was conducted in children aged 0-18 years who presented to the above mentioned hospitals with chronic renal failure or end-stage renal disease and maintained on either conservative therapy or dialysis.

The study was conducted in three groups: -

1. Children on conservative management.

2. Children on peritoneal dialysis.

3. Children on haemodialysis.

2.4.2. Control group:-

Healthy children aged 0-18 years matched for age and sex were enrolled in the study; they were randomly selected from Basic Schools, neibourghers, Relatives& Co-patients.

2.4.3. Case definitions:-

Chronic renal failure is defined as an irreversible reduction in the GFR to less than 25% of normal level, for at least three months. It is staged according to residual renal function into:

- Stage 1:Kideny damage withnormal or increased GFR > 90ml/ min 1.73m
- Mild reduction in GFR:89 – 60ml min 1.73 m.
- Moderate reduction in the GFR: 59-30ml min 1.73
- Sever reduction in the GFR :29-15ml min 1.73m
- Renal Failure:15ml min 1.73m

2.4.4. Inclusion criteria:-

All children aged 18 years or below with a diagnosis of CRF or ESRD, after taking informed verbal or written consent from parents or caregiver.

2.4.5. Exclusion criteria:-

-Refusal to participate in the study.

-transplanted patient

2.4.6. Sample size:-

- Total coverage 50 patients.
- 50 cases control group.

2.5. Study techniques and tools:-

2.5.1. Questionnaires:-

Detailed questionnaire was completed for all the study subjects. This provided an account for:

- Data regarding medical record, type of center, Socio-demographic data, serology at the start of dialysis (Hepatitis B, C and HIV), number of HD sessions per week, time interval from diagnosis of (ESRD) to initiation of(HD) in months, number of blood transfusions, number of (HD) centers utilized, number of surgical procedures, hospital admissions, parenteral injection and traditional treatment and practices.

Clinical examination was conducted. Symptoms and signs were recorded with concentration on Pallor, jaundice and signs of chronic renal and liver diseases, anthropometric measurements such as weight and height using tape measurement were recorded.

The researcher collected the data personally by interviewing patients, parents or caretaker while the patients receiving haemodialysis treatment or came for follow up in the referred clinic. Additional information was obtained from the medical staff.

2.5.2. Blood Sampling:-

Sterile disposable syringes labeled for each case was used to collect 5cc venous blood. The blood was allowed to clot in a test tube (vaccu container), then transferred to the laboratory where it

was centrifuged and the serum separated in plain container. The serum was stored in –20 degrees C until further analysis.

Third Generation Enzyme Immuno- assay was used for analysis of the samples and the positive cases were retested with ELISA from different company.

2.5..3. Research team:-

- The author.
- The lab technicians.
- The computer technician.

2.5.3.1. The input of the author:-

- Selection of the cases.
- Filling the questionnaire.
- Physical examination of the patients.
- Collection of the samples& centrifugation.
- Analysis of the data.

Principle of the test:-

DIA. PRO were used in this study from diagnostic Bio probes Sol via columella ^ 31 20128 Milano – Italy.

This is based on highly sensitive technique, which detects antibodies against (HCV) in human serum and plasma. Thus immunodiagnosis of (HCV) infection is based on detection of host generated antibodies to viral proteins. This technique utilizes a

combination of recombinant proteins with the sequence of both (HCV) structural and nonstructural proteins i.e. core, NS3, NS4, NS5. It has improved sensitivity over the previous generations.

The recombinant antigens are coded onto the microwells, diluted samples and controls are then incubated. Antibodies to HCV, if present, bind to the immobilized (HCV) antigens in the microwell during the incubation period. The microcells are then thoroughly washed with a wash buffer to remove excess of unbound anti (HBV)or other human IgGs, which may interfere with the test. Enzyme conjugate, antihuman IgG conjugated with horse Raddish Peroxidase (HRPO) is added. The excess conjugate is again washed. At this stage the microcells hold only the bound antigen-anti (HCV) enzyme conjugate complex. In the next step, freshly prepared substrate solution incubated with complex in the microcells. The enzyme substrate reaction leed to development of yellow colour, which is indicative of the antigen- antibody reaction, which had occurred in the microcell. The last step is to add the stop solution and the optical density of the developed colour is read photometrically.

The samples also screened for(HBs) antigen and (HIV) by ELISA, and tested for liver enzyme (ALT).

2.7. Ethical consideration:-

Written consents were taken from:

- Directors of the different hospitals.
- Doctors on charge of CRF patients.
- Parents of the children.
- After diagnosis of HCV infection, information was given to each caring unit for further management.

2.8. Data entry & statistical methods:-

All data collected from each child were coded for subsequent computer processing and analysis. Frequencies and descriptive statistics were obtained for all variables. Chi-Square test was computed for selected variables. The level of significance was taken as $p< 0.05$ using T test for the risk factors.

2.9. Difficulties encountered:-

- Kits were expensive.
- Blood sample transportation.
- Convincing the parent and their children to take blood samples.

3. RESULTS

3.1. Socio– Demographic Characteristics of children in the study:-

3.1.1.Age distribution of the study group:-

Distribution of the study group according to their age. The age group between 0-18 yrs divided in to four groups. The majority, 31 patients (62.0%) were between 12 – <18 yrs, aged 6 - <12 years were 13 patients (26.0%), 3(6%) were 18 yrs old and 2 patients (4.0%) were less than six year. The same for the control group as shown in Fig (3.1.1).

3.1.2. Sex distribution of the study group:-

Distribution of the study group according to their gender. The majority of children, 33 (66.0%) were male and 17 (34.0%) were

female in the patients group and the same distribution for the control group, the male: femle ratio 1.8:1 as shown in Fig (3.1.2).

3.1.3. Educational level of the study group:-

The majority of cases in CRF group; 37 (74.0%) were primary school level, 10 (20.0%) were secondary school level and 3 (6.0%) were illiterate. Also in the control group, the majority 29 (58.0%) were primary school level, 16 (32.0%) were secondary school level , only three (6.0%) were illiterate , 1(2%)was from Quran school and one was university graduate (P 0.360) as shown in Fig (3.1.3).

3.1.4. Residence of the study group:-

Distribution of the study group according to their residence. Most of the patients, 23 (46.0%) were from urban area, 18 (36.0%) were from rural and 9 (18.0%) were from suburban area. While the majority of the control group 23 (46.0%) were from suburban area, 21 (42.0%) were from urban and 6 (12.0%) were from rural (P 0.002) as shown in Fig (3.1.4).

Figure 3.1.1. Age distribution of the study group

(n = 100)

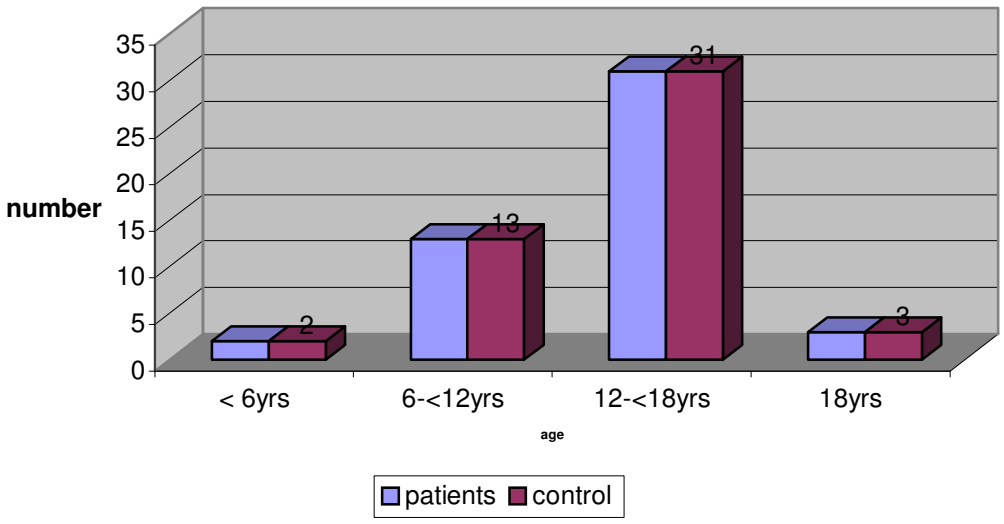


Figure 3.1.2. Gender distribution of the study group

(n = 100)

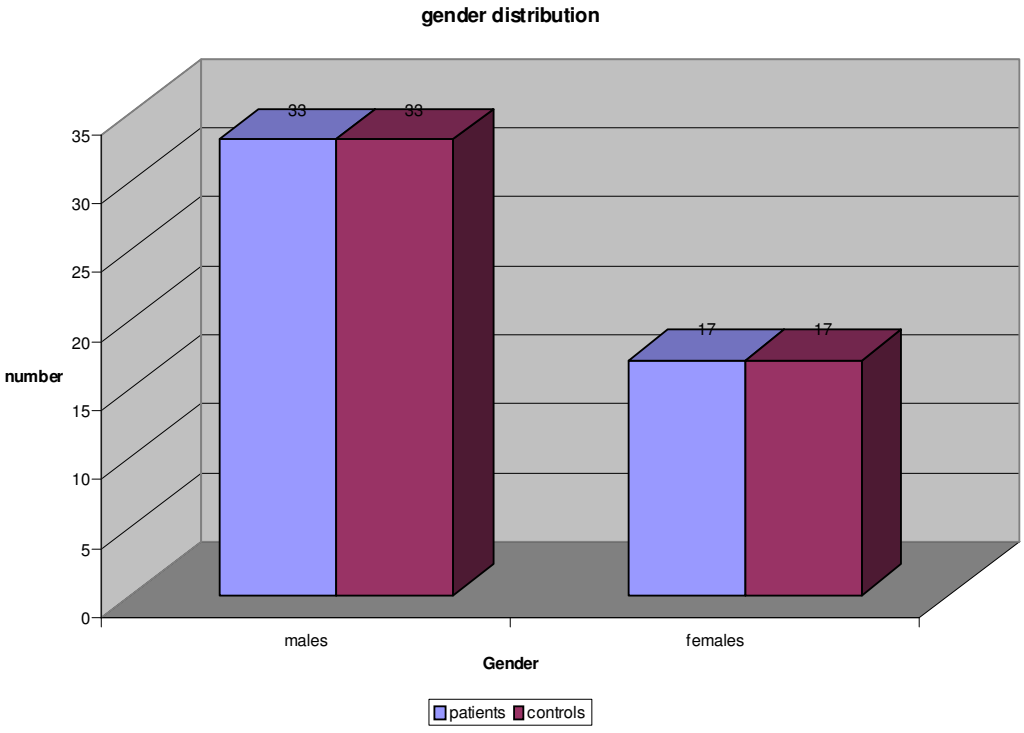


Figure 3.1.3. Educational level of the study group

(n = 100)

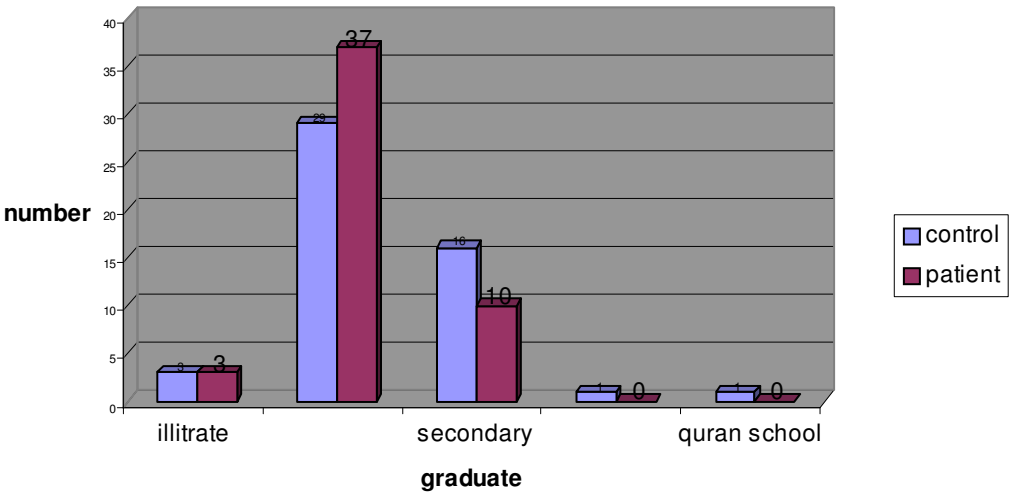
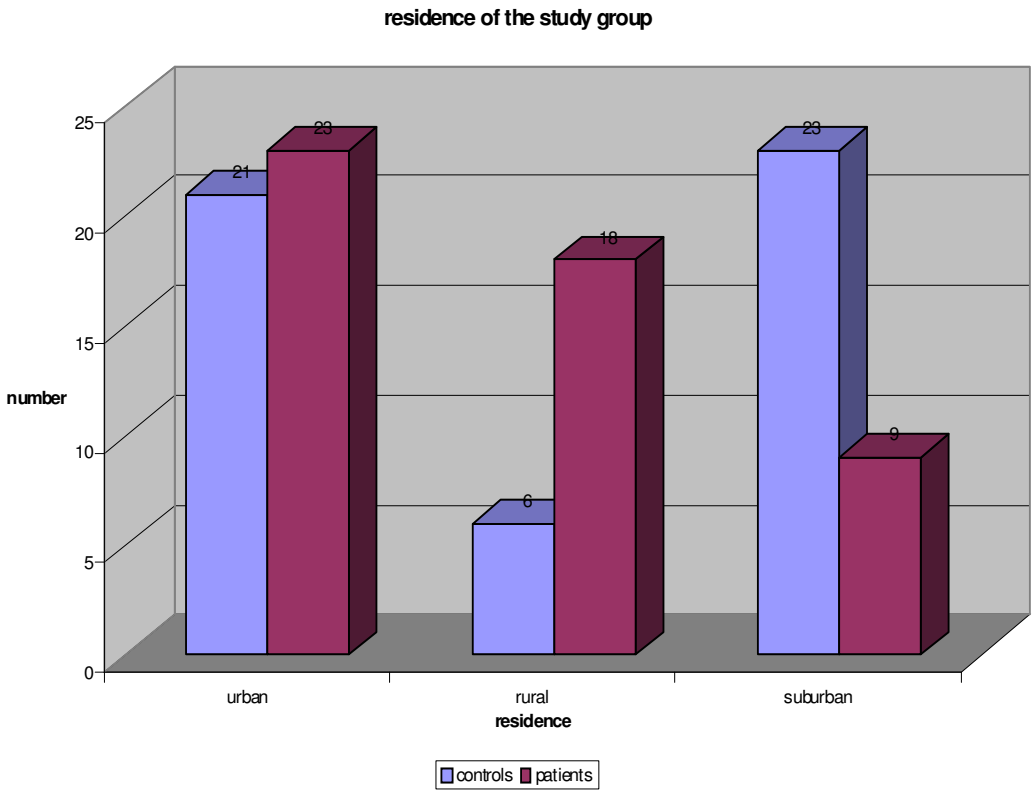


Figure 3.1.4. Residence of the study group

(n = 100)



3.1.5. Fathers' educational level:-

The educational level of the fathers in the study group. The majority 16 (32.0%) were primary school level, 12 (24.0%) were secondary level, 9 (18.6%) were illiterate, 8 (16.0%) were post secondary school and 5(10.0%) were Quran school. While in the control group the majority 16 (32.0%) were secondary school level, 12 (24.0%) were primary school level, 11 (22.0%) were post secondary level, 9 (18.0%) were illiterate and 2 (4.0%) were Quran school educated (p 0.566) as shown in table(3.1.5).

3.1.6. Mothers' educational level:-

The educational level of the mothers in the study group. The majority of the mothers of patients with (CRF) , 18 (36.0%) were illiterate, 16 (32.0%) were primary school level, 11 (22.0%) were secondary school level ,3 (6.0%) were post secondary school and 2 (4.0%) were Quran school. In contrast , in the control group the majority 19 (38.0%) were secondary school level, 13 (26.0%) were primary school level, 10 (20.0%) were illiterate ,7 (14.0%) were post secondary school level and 1 (2.0%) was Quran school graduated (P 0.052) as shown in table(3.1.6).

3.1.7. Fathers' occupation:-

Occupation of the fathers in the study group. In the patients group, the majority 16 (32.0%) were civil servants, 15 (30.0%) were unskilled labourers, 8 (16.0%) were skilled labourers, 7 (14.0%) were farmer's shepherds and 4 (8.0%) were jobless. In the control group, the majority 27 (54.0%) were civil servants, 7 (14.0%) were professional, 6 (12.0%) were unskilled labourers, 3 (6.0%) were skill labourers, 3(6.0%) were unemployed and 2 (4.0%) died (P 0.00) as shown in table (3.1.7).

Table 3.1.5. Fathers' educational level (n

(n = 100)

Father's education	Case n (%)	Control n (%)	Total n (%)
Illiterate	09 (18.0%)	09 (18.0%)	18 (36.0%)
Primary	16 (32.0%)	12 (24.0%)	28 (56.0%)
Secondary	12 (24.0%)	16 (32.0%)	28 (56.0%)
Post secondary	08 (16.0%)	11 (22.0%)	19 (38.0%)
Quran school	05 (10.0%)	02 (4.0%)	07 (14.0%)
Total	50 (100.0%)	50 (100.0%)	

(P 0.566)

Table 3.1.6: Mothers' educational level

(n = 100)

Mother's education	Case n (%)	Control n (%)	Total n (%)
Illiterate	18 (36%)	10 (20.0%)	28 (56.0%)
Primary	16 (32%)	13 (26.0%)	29 (58.0%)
Secondary	11 (22%)	19 (38.0%)	30 (60.0%)
Post secondary	03 (6.0%)	07 (14.0%)	10 (20.0%)
Quran school	02 (4.0%)	01 (2.0%)	03 (6.0%)
Total	50 (100.0%)	50 (100.0%)	

(P. 0.052)

Table 3.1.7: Fathers' occupation

(n = 100)

Father's occupation	Case n (%)	Control n (%)	Total n (%)
Professional	-	07 (14%)	07 (14.0%)
Civil servant, Employee's and merchant	16 (32.0%)	27 (54.0%)	43 (86.0%)
Skill labourers	08 (16.0%)	03 (6.0%)	11 (22.0%)
Un skill labourers	15 (30.0%)	06 (12.0%)	21 (42.0%)
Farmers and shepherd	07 (14.0%)	02 (4.0%)	09 (18.0%)
Workers	04 8.0%)	03 6.0%)	07 (14.0%)
Died	0 (0.0%)	02 (4.0%)	02 (4.0%)
Total	50 (100.0%)	50 (100.0%)	

(P 0.00)

Social background of the study group:-

The type of housing, toilet and availability of electricity in the study group as shown in table (3.1.8).

Housing:-

The majority of houses, 28 (56.0%) in the patients group while 30 (60.0%) in the control were made from bricks, 17 (34.0%) compare to 14 (28.0%) were from mud, four (8.0%) compare to 1(2.0%) were from straw and 1 (2.0%) compare to 5 (10.0%) were from concrete (P 0.158).

Toilet:-

The majority of patients; 40 (80.0%) had pit latrine (private) vs 29 (58.0%) in the control group, 7 (14.0%) compare to 13 (26.0%) had siphon, 2 (4.0%) compare to 4 (8.0%) had common latrines and 1 (2.0%) compare to 4 (8.0%) were open space (P 0.490).

Electricity:-

The majority 37(74.0%) had electricity both in the patients and control group, while 13 (26.0%) of both groups had no electricity (P 0.490).

Water Supply:-

Around two third of the patients 33 (66.0%) had piped in, 8 (16.0%) had traditional well, 6 (12.0%) had deep well, 3 (6.0%) were supplied from the Nile and no one had piped out. While, in the

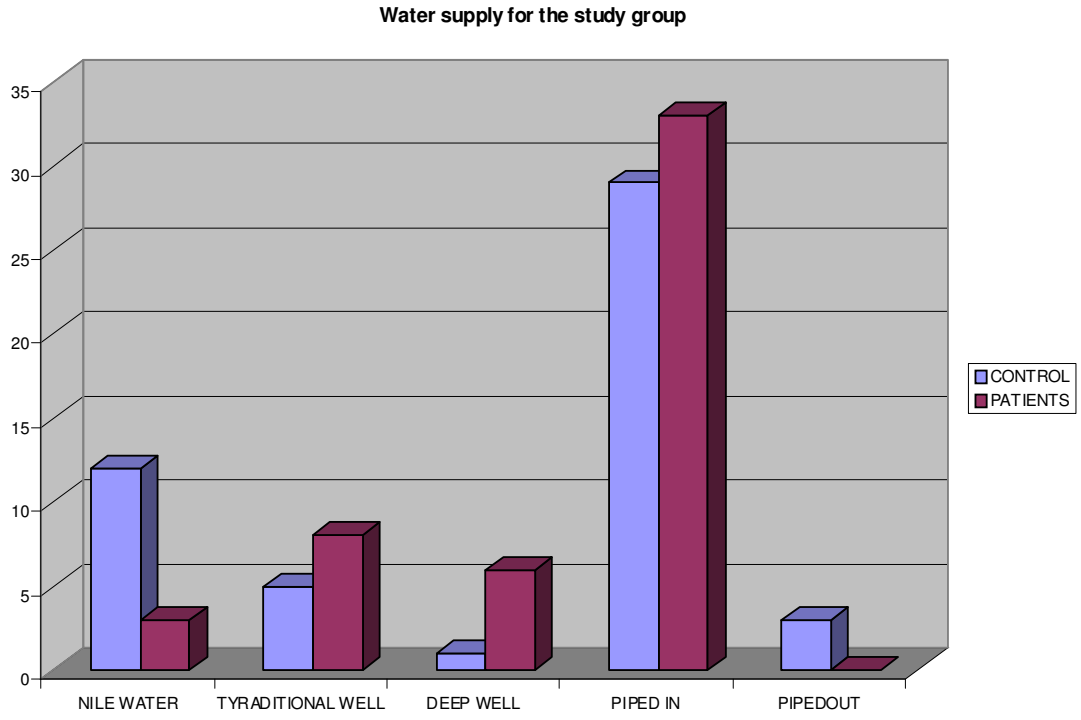
control group, 29 (58.0%) had piped in, 12 (24.0%) were supplied from the Nile, 5 (10.0%) had traditional well, 3 (6.0%) had piped out and 1 (2.0%) had deep well. (P 0.012) as shown in Fig (3.1.8).

Table 3.1.8 Social background of the study group; housing, toilet and electricity

	Case	Control	Total	p.val
	n	n	n	

	(%)	(%)	(%)
Housing			
Straw	04 (8.0%)	01 (2.0%)	05
Mud	17 (34.0%)	14 (28.0%)	31
Bricks	28 (56.0%)	30 (60.0%)	58
Concrete	01 (2.0%)	05 (10.0%)	06
Total	50 (100.0%)	50 (100.0%)	P. 0.158
Toilet			
Common latrine	02 (4.0%)	04 (8.0%)	06
Pit latrine (private)	40 (80.0%)	29 (58.0%)	69
Pit latrine		02 (4.0%)	02
Siphon	07 (14.0%)	13 (26.0%)	20
Open space	01 (2.0%)	02 (4.0%)	03
Total	50 (100.0%)	50 (100.0%)	P. 0.490
Electricity			
Yes	37 (74.0%)	37 (74.0%)	74
No	13 (26.0%)	13 (26.0%)	26
Total	50 (100.0%)	50 (100.0%)	P. 0.490

Figure 3.1.8: Water supply of the study group



3.2. Clinical pattern of the study group:-

3.2.1. Presenting complain of the study group:-

The clinical symptoms among the study group were studies

31 patients (62.0%) while 5 (10.0%) in the control group complained of malaise (P 0.00). 25 (50.0%) compare to 1 (2.0%) had vomiting, 25 (50.0%) compare to 0 (0.0%) had nausea (P 0.00) for both symptoms and 24 (48.0%) compare to 2 (4.0%) had anorexia (P 0.00). Fever was evident in 19 patients (38.0%) compare to 10 (20.0%) (P 0.038). 18 (36.0%) compared to 4 (8.0%) suffered from abdominal pain (P 0.001). 12 (24.0%) compared to 0 (0.0%) had constipation (P 0.00). 9 (18.0%) compared to 2 (4.0%) had diarrhoea (P 0.045). 5 (10.0%) compared to 0 (0.0%) had haematamesis (P 0.280) and just 4 (8.0%) compared to 0 (0.0%) had complained of yellow sclera (P 0.247) . 5 patients (10.0%) and 1 (2.0%) in the control group had dark urine (P 0.102) , 1(2.0%) compared to 0(0.0%) had impaired sensorium (P 0.500) and no one had pale stool as shown in table (3.2.1).

3.2.2. Presenting signs of the study group:-

The clinical signs among the study group were also recorded

Pallor was found in 46 patients (92.0%) and 4(8.0%) in the control group (P0.00), 48 (96.0%) had normal tempretuure, 2 (4.0%) had low temperature and none had high temperature. While in the control group, 48(96.0%) had normal temperature 2(4.0%) had high temperature and none had low temperature (p0.063)

Jaundice was detected in one patient (2.0%) in both groups (P 0.753). Hepatomegally was present in 5 patients (10.0%) compare to 1 (2.0% P0.102) while tenderness in the right hypochondrial was elicited in 2 patients (4.0%) compared to 0 (0.0% P 0.247). One patient (2.0%) compare to 3 (6.0%) had splenomegally (P 0.309). lymph node was palpable in 5 cases (10.0%) in both patients and control group (P 0.630) . 3 (6.0%) had skin rash, 2 (4.0%) had bleeding tendency, but no one in the control group had neither skin rash nor bleeding tendency(P 0.121 , 0.247) and no body had confusion, palmar erythema or spider naevi in the two groups .While 6 children (12.0%) compared to 1 (2.0%) had cattery marks (P 0.056) compare to one (2.0%) had Tribal marks in both group as shown in table (3.2.2).

Table 3.2.1: Presenting symptoms of Hepatitis in the study group (n = 100)

Symptoms	Case n (%)	Control n (%)	Total n (%)	P.value
Fever	19 (38%)	10 (20%)	29 (58.0%)	0.038
Anorexia	24 (48%)	02 (4.0%)	26 (23.0%)	0.00
Malaise	31 (62%)	05 (10%)	36 (72.0%)	0.00
Abd. Pain	18 (36%)	04 (8.0%)	22 (44.0%)	0.001
Nausea	25 (50%)	0 (0.0%)	25 (50.0%)	0.00
Vomiting	25 (50%)	01 (2.0%)	26 (52.0%)	0.00
Hematamesis	05 (10%)	0 (0.0%)	5 (10.0%)	0.280
Diarrhoea	09 (18%)	02 (4.0%)	1 1(22.0%)	0.045
Constipation	12 (24%)	0 (0.0%)	12 (24.0%)	0.00
Yellow sclera	03 (6.0%)	0 (0.0%)	03 (6.0%)	0.121
Pale stool	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.00
Dark urine	05 (10%)	01 (2.0%)	06 (12.0%)	0.102
Yellow sclera	02 (4.0%)	0 (0.0%)	02 (4.0%)	0.247
Impaired sensation	01 (2.0%)	0 (0.0%)	0 1(2.0%)	0.500

Table 3.2.2: Clinical signs of Hepatitis in the study group (n = 100)

Signs	Case	Control	Total	P. value

	n (%)	n (%)	n (%)	
Pallor	46 (92%)	04 (8%)	50 (100%)	0.00
Jaundice	01 (50.0%)	01 (2.0%)	02 (52.0%)	0.753
Temp.				
Normal	48 (96%)	48 (96%)	96 (100%)	
Low	02 (4.0%)	00 (0.0%)	02 (4.0%)	0.063
High	0 (0.0%)	02 (4.0%)	02 (4.0%)	
Hepatomegaly	05 (10.0%)	01 (2.0%)	06 (12.0%)	0.102
Rt.Hyboconderial tenderness	02 (4.0%)	00 (0.0%)	02 (4.0%)	0.247
Splenomegaly	01 (2.0%)	03 (6.0%)	04 (8.0%)	0.309
Lymphadenopathy	05 (10.0%)	05 (10.0%)	10 (20.0%)	0.630
Skin rash	03 (6.0%)	0 (0.0%)	03 (6.0%)	0.121
Bleeding tendency	02 (4.0%)	0 (0.0%)	02 (4.0%)	0.247
Tribal marks	01 (2.0%)	01 (2.0%)	02 (4.0%)	0.753
Confusion	0 (0.0%)	00 (0.0%)	0 (0.0%)	
Palmar erythema	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Spider naevi	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Cattery marks	06 (12.0%)	01 (2.0%)	07 (14.0%)	0.056

3.2.3. Significant past medical history in the study group:-

The past medical history of the study group showed that nine patients (18.0%) had past history of jaundice compare to 11 cases (22.0%) of the control ,3 (6.0%) compared to 1 (2.0 %) had jaundice after transfusion, 11 (22.0%) compared to 8 (16 .0%) had contacted jaundiced patient and 9 (18.0%) compared to 0(0.0%) had experienced hepatitis in the past . Thirty (60.0%) compared to 16 (32.0%) were hospitalized and 49 (98.0%) compared to 35 (70.0%) were operated before for different causes. Twenty three patient (46.0%) compared to 0(0.0%) received HBV vaccine, 36 (72.0%) compared to 0 (0.0%) received blood transfusion and 2 (4.0 %) compared to (0.0%) had history of reused injections as shown in table (3.2.3).

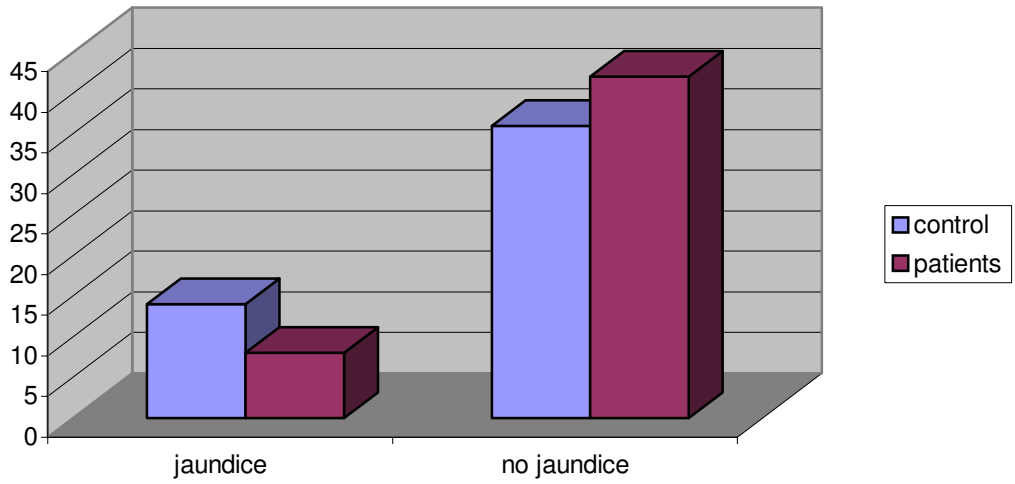
3.2.4. Significant family history in the study group:-

The family history of the study group showed that jaundice was present in 8 patients (16.0 %) with (CRF) while absent in 42 (94.0%). In Contrast, it was present in 14 (28.0%) and absent in 36(72.0%) of the control group (P0.028). History of hepatitis was found in 5 patients (10%) with (CRF) and absent in 45(90.0%), while it was not found in any case in the control group (P 0.028) as shown in (Fig3.2.4)

Table 3.2.3: Significant past medical history in the study group

Past history (P.H)		Case Frequency (%)	Control (%)	P-Value
P.H of jaundice	+ve	0 (0.0%)	0 (0.0%)	0.669
	-ve	09 (18.0%)	11 (22.0%)	
P.H of appearance of jaundice after transfusion	+ve	0 (0.0%)	0 (0.0%)	0.882
	-ve	03 (6.0%)	01 (2.0%)	
Contact with jaundice patient	+ve	0 (0.0%)	00 (0.0%)	0.605
	-ve	11 (22.0%)	80 (16.0%)	
P. H of hepatitis	+ve	0 (0.0%)	0 (0.0%)	0.669
	-ve	09 (18.0%)	0 (0.0%)	
HBV vaccine	+ve	02 (4.0%)	0 (0.0%)	0.207
	-ve	21 (42.0%)	0 (0.0%)	
P.H of hospitalization	+ve	01 (2.0%)	0 (0.0%)	0.645
	-ve	29 (58.0%)	16 (32.0%)	
P.H of operation	+ve	02 (2.0%)	0 (0.0%)	0.960
	-ve	47 (94.0%)	35 (70.0%)	
P.H of blood transfusion	+ve	01 (2.0%)	0 (0.0%)	0.486
	-ve	35 (70.0%)	0 (0.0%)	

Figure 3.2.4: Family history of jaundice among study group



3.3. Distribution of children in the study group:-

The majority of children 33 (33.0%) were on haemodialysis while 11 (11. 0%) were on intermittent peritoneal dialysis, 6 (6.0%) were on conservative and 50 (50.0%) cases were the control group as shown in Fig (3.3).

3.3.1. Patients distribution according to their dialysis center:-

The majority 16 patients (48.5%) were dialyzed in Khartoum North Hospital, 15 (45.5%) were undergone dialysis in Dr. Salma Kidney Dialysis and Transplantation Center (DS.KDTC), 6 (18.20%) in Soba University Hospital, 2 (6.1%) in Umm Dorman Military Hospital and 1 (3.0%) in Khartoum Teaching Hospital as shown in Fig (3.3.1).

3.3.2. Prevalence of anti-HCV in relation to risk factors:-

3.3.2.1. Prevalence of anti-HCV in the different study groups:-

Two patients (6.1%) were positive for anti HCV antibodies in the haemodialysis group while all the peritoneal, conservative and control group were negative (P 0.00) as shown in Fig (3.3.2.1).

3.3.2.2. Prevalence of anti HCV in relation to the duration on hemodialysis:-

The majority ,12 patients (36.0%) were on haemodialysis for Less than 6 months and all were negative, 6 (18.2%) were dailysed for a period of 6 months - < 1yr and only 1 of them (16.7.0%) was positive for anti-HCV antibodies, 3 patients (9.0%) were dialysed for

1-2 years and were negative .Eleven patients (33.0%) were on dialysis for 2- 4 yrs and only one of them(9.0%) was positive and one was dialyzed for more than four years however was negative (P 0.003) as shown in Fig (3.3.2.2).

3.3.2.3. Prevalence of anti HCV in relation to the number of dialysis centers:-

Uni-center and multi-centre dialyzed patients were also studied in relation to anti- HCV positivity. The majority of the patients;25 (75.8%) undergone dialysis in single center and 2 (8.0%) of them were positive, while 8 (24.2%) were dailyzed in multiple centers and no one was positive (P 0.00) as shown in Fig (3.3.2.3) .

Figure 3.3 :Study groups Distribution (n=100)

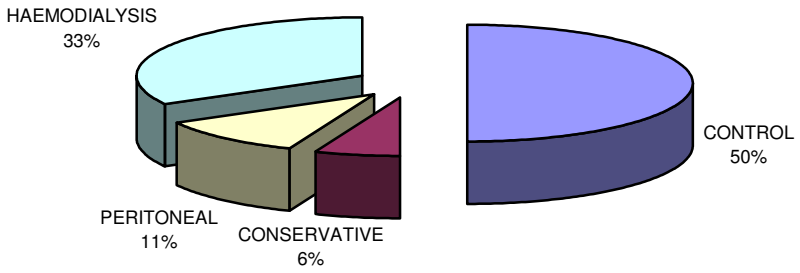

HAEMODIALYSIS
33%
PERITONEAL
11%
CONSERVATIVE
6%
CONTROL
50%

Figure 3.3.1:Patients Distribution according to their dialysis centers (n = 33)

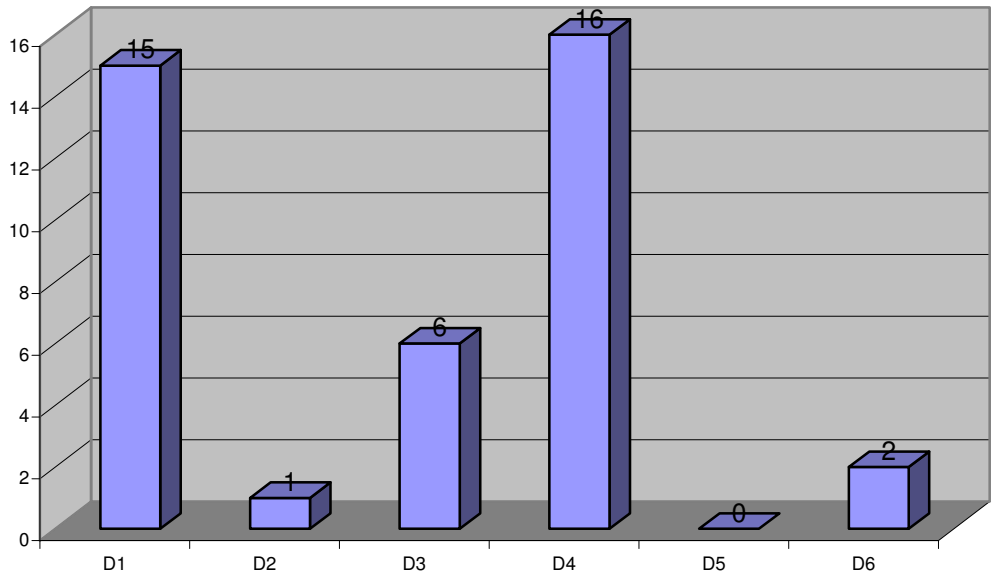


Figure 3.3.2.1: Prevalence of Anti- HCV in the different study groups

(n = 100)

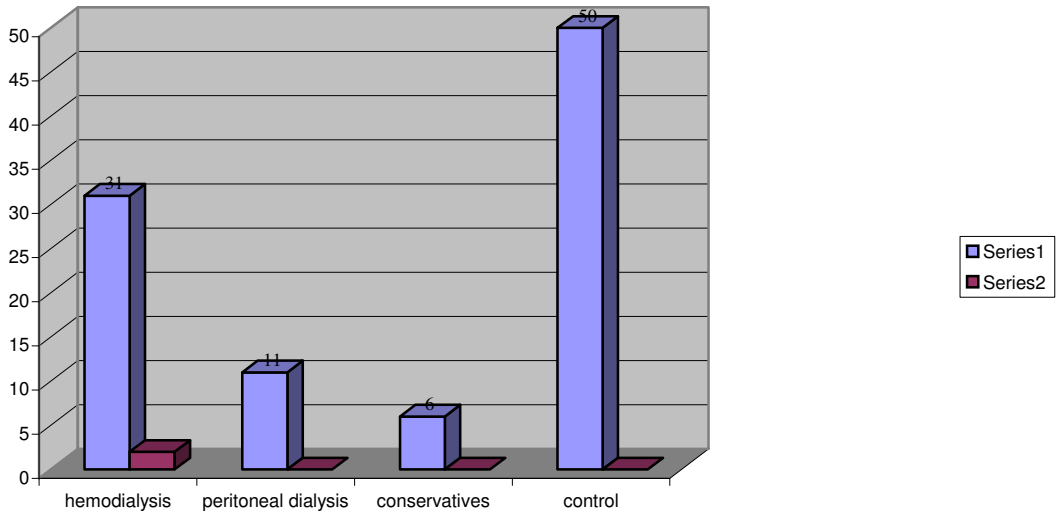


Figure 3.3.2.2: Prevalence of anti- HCV according to dialytic age groups (n=33)

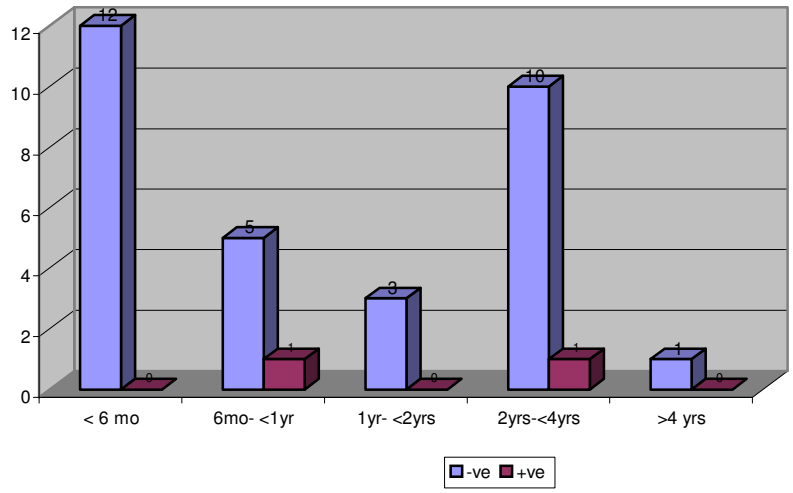
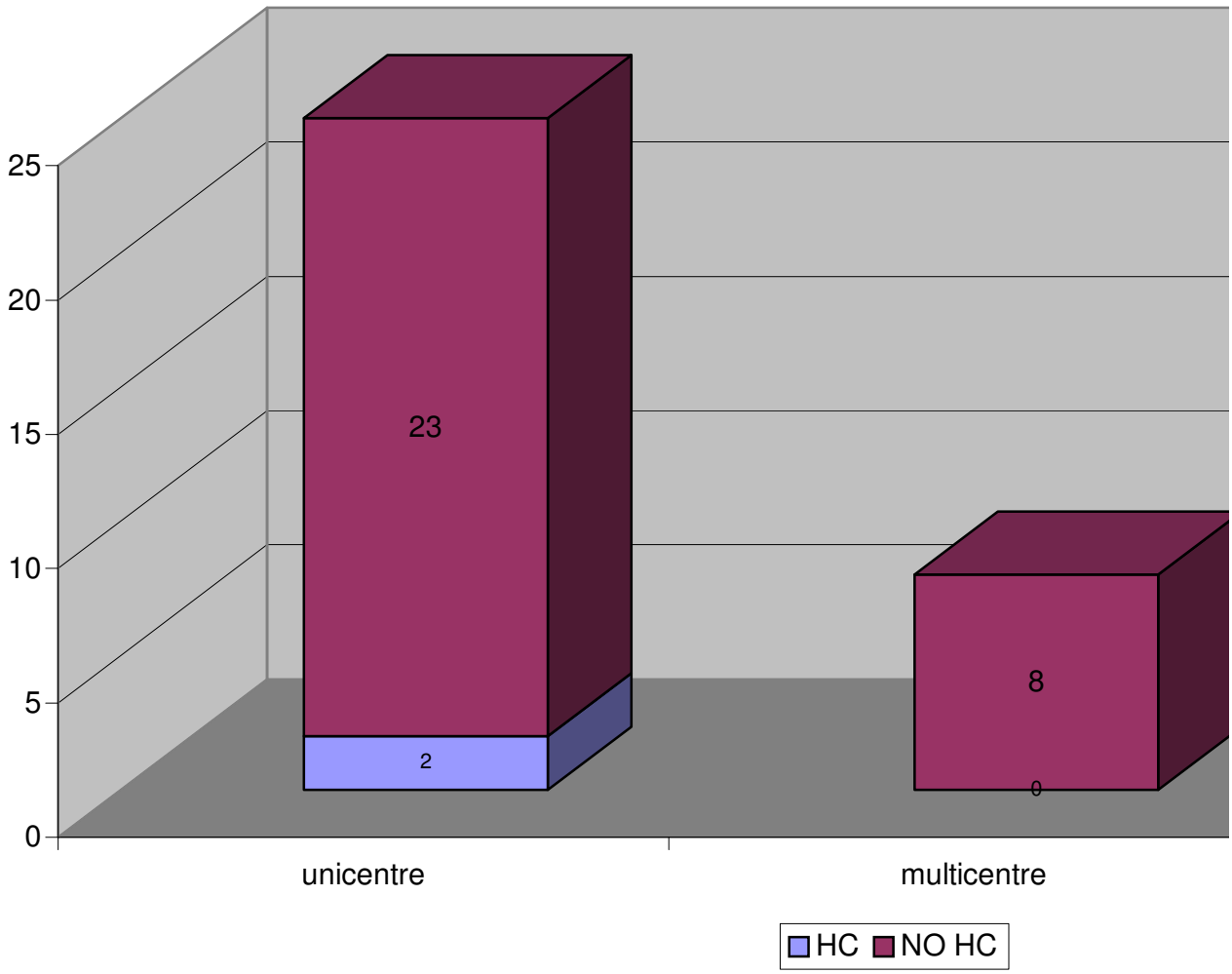


Figure 3.3.2.3: Prevalence of anti HCV according to the number of dialysis centers (n=33)


25
20
15
10
5
0
23
2
8
0
unicentre
multicentre
HC
NO HC

3.3.2.4. Prevalence of anti HCV and the blood transfusion:-

Anti- HCV positive patients in relation to their blood transfusion status was studied and it shown that; thirty nine patients (78.0%) out of 50 transfused with blood, 2 of them (5.1%) were positive. 11 patients (22.0%) neither had transfused nor anti-HCV positive (P 0.00) as shown in table(3.3.2.4) .

3.2.2.5. Prevalence of anti-HCV and the Blood Screening Status:-

Anti-HCV positive patients in relation to blood screening status showed that;

thirty six patients (92.3%) out 50 cases transfused with screened blood , 2 of them (5.6%) were positive. Three patients just (7.7%) transfused with non-screened blood and fortunately enough they were all negative for anti-HCV (P 0.001) as shown in (table 3.3.2.5).

3.3.2.6. Prevalence of anti- HCV and the units of blood:-

Anti-HCV positive patients in relation to the number of blood units was studied and it is found that;

Six patients (15.4%) received one unit, 10 (25.6%) received 2 units, 5 (12.8%) received 3 units, 3 (7.7%) received 4 units, 14 (35.9%) received 5 units, 1 (2.6%) received 8 units. all were negative apart from two patients; 1 (10.0%) from the group that

received 2 units (10.0%) and the other who received 8 units (100% P 0.001) as shown in table (3.3.2.6) .

3.3.2.7. Prevalence of anti-HCV and the Significant Past history of blood transfusion:-

Anti- HCV positive patients in relation to the past history of transfusion.

Thirty seven patients (72.0%) out of 50 were transfused in the Past, two of them (5,1%) was positive now ,while 11 patients (28.0%) were never transfused and they were all negative . (P 0.00) as shown in table (3.3.2.7).

Table 3.3.2.4: Prevalence of anti-HCV and the blood transfusion

(n = 50)

Blood transfusion	Positive n (%)	Negative n (%)	Total n (%)
Yes	02 (5.1%)	37 (94.9%)	39 (100.0%)
No	0 (0.0%)	11 (100.0%)	11 (100.0%)
Total	02 (4%)	48 (96%)	50 (100%)

(P 0.00)

Table 3.3.2.5: Prevalence of anti-HCV and the blood screening status

n = (39)

Screened blood	HCV		Total
	Positive freq. (%)	Negative freq. (%)	(%)
Yes	02 (5.5%)	34 (94.5%)	36 (100.0%)
No	0 (0.0%)	03 (100%)	03 (100.0%)
Total	02	37	39

(P 0.001)

Table 3.3.2.6: Prevalence of anti- HCV and the units of blood

Group case	1 units n (%)	2 units n (%)	3 units n (%)	4u nits n (%)	5 units n (%)	8 units n (%)	Total n (%)
HC +ve	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	01 (100.0%)	02
HC – ve	06 (100.0%)	09 (90.0%)	05 (100.0%)	03 (100.0%)	14 (100.0%)	0 (0.0%)	37
Total	06 (100.0%)	10 (100.0%)	05 (100.0%)	03 (100.0%)	14 (100.0%)	1 (100.0%)	39

(P 0.001)

Table 3.3.2.7: Prevalence of anti- HCV and the past history of blood transfusion

P. blood transfusion	HCV +ve n (%)	HCV –ve n (%)	***Total n (%)***
Yes	1 (2.8%)	35 (97.2%)	36 (100.0%)
No	1 (76.9%)	13 (23.1%)	14 (100.0%)
Total	2 (4%)	48 (96%)	50 (100.0%)

(P 0.486)

3.4.Socio-demographic characteristic of seropositive group:_

3.4.1. Age distribution of seropositive group:-

The distribution of seropositive group according to their age.

Two patients (6.9%) in the age group 12-18 were positive, while all patients in the age group 6 - < 12 yrs and 6 years or less, were negative for anti-HCV. No one was positive in all age groups in the control group (P 0.00) as shown in table (3.4.1).

3.4.2. Gender distribution of the seropositive group:-

The distribution of seropositive group according to their gende;One patient (3.0%) out of 33 (66.0%) male was positive for anti-HCV antibody. On the other hand, 1 patient (5.9%) out of 17 (34.0%) female was positive. However, both males and females in the control group were negative (P 0.00) as shown in table (3.4.2).

3.4.3. Educational level of the seropositive group:-

The distribution of seropositive group according to their educational level.

One patients (10.0%) out of 10 (20.0%) who were secondary school educated was positive, 1 (2.7%) out of 37 (74.0%) who were primary school educated was positive and zero (0.0) were positive in patients who were illiterate, post-secondary school and Quran Educated (P 0.542) as shown in table (3.4.3).

3.4.5. Residence of seropositive group:-

The distribution of seropositive group according to their residence.

One patient(5.6%) out of 18 (36.0%) who reside in rural area was positive, and 1 (1.1%) out of 9 (18.0%) was positive in the group that reside in sub-urban areas. No one from urban areas was positive (P 0.324) as shown in table (3.4.4)

3.4.6. Fathers' and mothers' educational level in the seropositive group:-

The fathers' and mothers' educational level among seropsitive group.

The two positive patients (12.5%), their father's and mother's were primary school educated (P 0.351 for both) as shown in table (3.4.5a &3.4.5b).

3.4.7. Fathers' occupation in the seropositive group:-

The two positive patients (13.3%) their father's were unskilled labourer and no positive cases among the other occupational groups (P 0.302) as shown in table (3.4.6).

Table 3.4.1: Age distribution of seropositive group

Group		6 years or less n (%)	6 - < 12 n (%)	12 – 18 n (%)	P. value
Case	+ve	0 (0.0%)	0 (0.0%)	2 (6.9%)	0.00
	-ve	6 (100.0%)	13 (100.0%)	29 (93.1%)	
Total		6 (100.0%)	13 (100.0%)	31 (100.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	3 (100.0%)	18 (100.0%)	29 (100.0%)	
Total		3 (100.0%)	18 (100.0%)	29 (100.0%)	

Table 3.4.2: Gender distribution of seropositive group

Group		Female n (%)	Male n (%)	P. value
Case	+ve	1 (5.9%)	1 (3.0%)	0.00
	-ve	16 (94.1%)	32 (97.0%)	
Total		17 (100.0%)	33 (100.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	
	-ve	17 (100.0%)	33 (100.0%)	
Total		17 (100.0%)	33 (100.0%)	

Table 3.4.3: Educational level among seropositive group

Group		Illiterate n (%)	Primary school n (%)	Secondary school n (%)	Post-secondary n (%)	Quran n (%)	P. value
Case	+ve	0 (0.0%)	1 (2.7%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	
	-ve	3 (100.0%)	36 (97.3%)	9 (90.0%)	0 (0.0%)	0 (0.0%)	0.542
Total		3 (100.0%)	37 (100.0%)	10 (100.0%)	0 (0.0%)	0 (0.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	3 (100.0%)	29 (100.0%)	16 (100.0%)	0 (0.0%)	0 (0.0%)	
Total		3 (100.0%)	29 (100.0%)	16 (100.0%)	0 (0.0%)	0 (0.0%)	

Table 3.4.4: Residence of seropositive group

Group	Urban n (%)	Rural n (%)	Sub-urban n (%)	P. value

	+ve	0	1	1	
Case		(0.0%)	(5.6%)	(1.1%)	0.324
	-ve	23	17	8	
		(100.0%)	(94.4%)	(98.9%)	
Total		23	18	9	
		(100.0%)	(100.0%)	(100.0%)	
	+ve	0	0	0	
Control		(0.0%)	(0.0%)	(0.0%)	
	-ve	21	6	23	
		(100.0%)	(100.0%)	(100.0%)	
Total		21	6	23	
		(100.0%)	(100.0%)	(100.0%)	

Table 3.4.5a: Fathers' educational level among seropositive group

Group		Illiterate	Primary school	Secondary school	Post-secondary	Quran	P. value
		n (%)	n (%)	n (%)	n (%)	n (%)	
Case	+ve	0 (0.0%)	2 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	9 (100.0%)	14 (87.5%)	12 (100.0%)	8 (100.0%)	5 (100.0%)	0.351
Total		9 (100.0%)	16 (100.0%)	12 (100.0%)	8 (100.0%)	5 (100.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	9 (100.0%)	12 (100.0%)	1 6 (100.0%)	11 (100.0%)	2 (100.0%)	
Total		9 (100.0%)	12 (100.0%)	16 (100.0%)	11 (100.0%)	2 (100.0%)	

Table 3.4.5 b: Mothers' educational level among seropositive group

Group		Illiterate	Primary school	Secondary school	Post-secondary	Quran	P. value
		n (%)	n (%)	n (%)	n (%)	n (%)	
Case	+ve	0 (0.0%)	2 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.351
	-ve	18 (100.0%)	14 (87.5%)	1 (100.0%)	3 (100.0%)	2 (100.0%)	
Total		18 (100.0%)	16 (100.0%)	11 (100.0%)	3 (100.0%)	2 (100.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	18 (100.0%)	16 (100.0%)	11 (100.0%)	3 (100.0%)	2 (100.0%)	
Total		18 (100.0%)	16 (100.0%)	11 (100.0%)	3 (100.0%)	2 (100.0%)	

Table 3.4.6: Fathers' occupation of seropositive group

Group		Professional	Civil servant	Skilled labourer	Unskilled labourer	Farmer and shepherd	Workless	P. value
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Case	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (13.0%)	0 (0.0%)	0 (0.0%)	
	-ve	0 (0.0%)	16 (100.0%)	8 (100.0%)	13 (87.0%)	7 (100.0%)	4 (100.0%)	0.302
Total		0 (0.0%)	16 (100.0%)	8 (100.0%)	15 (100.0%)	7 (100.0%)	4 (100.0%)	
Control	+ve	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	-ve	7 (100.0%)	27 (100.0%)	3 (100.0%)	6 (100.0%)	2 (100.0%)	3 (100.0%)	
Total		7 (100.0%)	27 (100.0%)	3 (100.0%)	6 (100.0%)	2 (100.0%)	3 (100.0%)	

Clinical presentation of seropositive group:-

Complains of seropositive group:-

No one of seropositive cases had fever but anorexia, malaise, nausea and vomitting were present in 1(50%). The 2 (100%) seropositive cases didn't complain of yellow discoloration . Both the two cases (100%) had pale stool. However, no one mentioned constipation, diarrhea, abdominal pain, dark urine and hematamesis as shown in table (3.5.1) .

Clinical signs of seropositive group:-

Two (100%) of seropositive cases had pallor . 1 (50%) had palpable spleen . 1 (50%) had bleeding tendency . 2 (100%) had normal or low temperature and no one had high temperature. However, jaundice, hepatomegally, right hypochondrial tenderness, lymph adenopathy, skin rash, tribal marks, confusion, palmar erythema, spider naevi and cautary marks were not clinically evident in any case as shown in table (3.5.2).

Table 3.5.1: Presenting symptoms of HCV among Seropositive group

Complaints	Seropositive		P. value
	n (%)	n (%)	
	Yes	No	
Fever	0 (0.0%)	2 (100%)	0.380
Anorexia	1 (50%)	1 (50%)	0.735
Malaise	1 (50%)	1 (50%)	0.620
Yellow sclera	0 (0.0%)	2 (100%)	0.921
Nausea	1 (50%)	1 (50%)	0.755
Vomiting	1 (50%)	1 (50%)	0.755
Diarrhea	0 (0.0%)	2 (100%)	0.633
Abdominal pain	0 (0.0%)	2 (100%)	0.405
Constipation	0 (0.0%)	2 (100%)	0.574
Pale stool	2 (100%)	0 (0.0%)	
Dark urine	0 (0.0%)	2 (100%)	0.808
Hematamesis	0 (0.0%)	2 (100%)	0.808
Impaired sensorium	0 (0.0%)	2 (100%)	0.966

Table 3.5.2: Signs of HCV infection among seropositive group

Signs	Seropositive		P. value
	n (%)	n (%)	
	Yes	No	
Pallor	2 (100%)	0 (0.0%)	0.845
Jaundice	0 (0.0%)	2 (100.0%)	0.960
High temperature	0 (0.0%)	2 (100.0%)	0.921
Hepatomegally	0 (0.0%)	2 (100.0%)	0.808
Right hypochondrial tenderness	0 (0.0%)	2 (100.0%)	0.921
Splenomegally	1 (50%)	1 (50.0%)	0.040
Lymph adenopathy	0 (0.0%)	2 (100.0%)	0.808
Skin rash	0 (0.0%)	2 (100%)	0.882
Bleeding tendency	1 (50%)	1 (50.0%)	0.079
Tribal marks	0 (0.0%)	2 (100.0%)	0.960
Confusion	0 (0.0%)	2 (100.0%)	-
Palmar erythema	0 (0.0%)	2 (100.0%)	-
Spider naevi	0 (0.0%)	2 (100.0%)	-
Cautari mark	0 (0.0%)	2 (100.0%)	0.096

Significant past medical history among serpositive group:-

The two (100%) seropositive cases had never experienced jaundice before, and neither had a history of jaundice after transfusion nor a history of contact with a jaundiced patient. They all received HBV vaccine and no one had hepatitis before.

One patient (50%) was hospitalized and 2 (100%) were undergone operation No one had history of reused injection. On the other hand, 9 (18.0%) of seronegative group had past history of jaundice, 3 (6.0%) had a history of jaundice following transfusion, 11 (22.0%) experienced hepatitis, 9 (18.0%) had contacted a jaundiced patient, 21 (42.0%) received hepatitis B vaccine, 29 (58.0%) had been hospitalized, 47 (94.0%) had history of operation and 4 (8.0%) had history of reused injection as shown in table (3.5.3)

Significant family history among seropositive group:-

No one of seropositive group had a family history of jaundice or hepatitis while 8 (16.0%) had family history of jaundice and 5 (10.0%) had history of hepatitis, but all were negative as shown in table (3.5.4).

Table 3.5.3: Significant past medical history among seropositive group

Past history (P.H)		+ve	P. value
P.H of jaundice		0 (0.0%)	
		2 (100.0%)	0. 00
P.H of appearance of jaundice after	Yes	0 (0.0%)	
transfusion	No	2 (100.0%)	0.417
Contact with jaundiced patient	Yes	0 (0.0%)	
	No	2 (100.0%)	0.00
P.H of hepatitis	Yes	0 (0.0%)	
	No	2 (100.0%)	0.827
Screened blood	Yes	2(100.0%)	
	No	0 (0.0%)	0.001
P.H of hospitalization	Yes	1 (50.0%)	
	No	1 (50.0%)	0.00
P.H of operation	Yes	2 (100.0%)	
	No	0 (0.0%)	0.00
P.H of reused injection	Yes	0 (0.0%)	
	No	2 (100.0%)	0.921
Received vaccination	Yes	2 (100.0%)	
	No	0 (0.0%)	0.00

Table 3.5.4: Family history among seropositive group

Family history (P.H) *Yes* *n* *(%)*		*+ve* *No* *n* *(%)*	*P. value*
F.H of jaundice	0 (0.0%)	2 (100.0%)	*0.607*
F.H of hepatitis	2 (100.0%)	0 (0.0%)	*0.902*
Total (100.0%)	2	2 (100.0%)	

Serology of HCV:-

Anti- HCV status before the study period:-

The control group and patients on conservative management were not screened for anti- HCV before this study. 44 patients were screened; elevenpatients (22.0%) on peritoneal dialysis and they were all negative at the beginning of the study period and they remain so and 33(66.0%) haemodialyzsis patients, one of them(3.0%) was positive for anti- HCV before the study. So one patient (2.2%) out the 44 was positive (P 0.00) as shown in table (3.6.1).

Anti- HCV Seroconversion:-

The seroconversion of anti-HCV after the study period.The haemodialyzed patient (3.0%) who was positive turned to be negative at the end of the study period. However, other 2 haemodialysis patients (6.0%) out of the 33 were negative at the beginning turned to be positive (P 0.324) as shown in table (3.6.2).

HBV status before the study:-

The same as HCV, the control group and the conservative were not screened before this study. 44 patients were screened; 11 patients (22.0%) on peritoneal dialysis and they were negative for HBV infection and 33 patients (66.0%) on haemodialysis, 4 of them

(12.1%) were positive. So 4 patients(9.1%) out of the 44 were positive (P 0.00) as shown in table (3.6.3).

HBV seroconversion:-

The seroconversion of HBV after the study period .

The 4 haemodialyzed patients (12.1%) which were positive, 2 of them became negative and 2 stiII positive while other 4 patients on haemodialysis were negative at the start became positive now. So a total of 6 haemodialysis patients (18.2%) out of the 33 were positive .

The 11 patients (22.0%) on peritoneal dialysis continued to show the same negative result as shown in table (3.6.4).

Table 3.6.1: Anti- HCV status before the study period (n = 100)

Group / HCV	Conservativ n (%)e	Peritoneal n (%)	Haemoialysis n (%)	Control n (%)
Positive	-	-	1 (3.0%)	-
Negative	-	11 (100%)	32 (97.0%)	-
Not screened	6 (100%)	-		50 (100.0%)
Total	6 (100%)	11 (100%)	33 (100%)	50 (100%)

(P 0.00)

Table 3.6.2: Anti- HCV Seroconversion

(n = 100)

HCV before the study	HCV during the study	
	+ ve n (%)	- ve - n (%)
Positive	-	1 (1.0)
Negative	2 (2.0%)	41 (41.0%)
Not screened	-	6 (6.0%)
Control	-	50 (50.0%)
Total	2	98

(P 0.324)

Table 3.6.3: HBV status before the study

(n = 100)

Group / HBV	Conservative n (%)	Peritoneal n (%)	Haemoialysis n (%)	Control n (%)
Positive	-	-	4 (12.1%)	-
Negative	-	11 (100.0%)	29 (87.9%)	-
Not done	6 (100.0%)	-	-	50 (100.0)
Total	6 (100.0%)	11 (100.0%)	33 (100.0%)	50 (100.0%)

(P 0.00)

Table 3.6.4: HBV seroconversion

(n = 100)

HBV before the study	HBV during the study	
	+ ve n (%)	- ve - n (%)
Positive	2 (2.0%)	2 (2.0%)
Negative	4 (4.0%)	36 (36.0%)
Not done	-	6 (6.0%)
Control	-	50 (50.0%)
Total	6 (6.0%)	94 (94.0%)

(P 0.00)

Correlation of ALT level to Anti -HCV status:-

The ALT level in relation to Anti- HCV status .One patient(2.0%) out of the 50 patients was positive for Anti -HCV and had high ALT level and 1(2.0%) was positive for Anti HCV and had normal ALT Level. 48 (96.0%) had normal ALT level and were negative for anti- HCV .

One case (2.0%) in the control group had high level of ALT but it was negative for anti- HCV and 49 (98.0%) were normal for ALT and negative foranti- HCV infection (P 0.00) as shown in table (3.7).

Table 3.7: Correlation of ALT level to Anti- HCV status (n = 100)

ALT	*Case* *n* *(%)*	*Control* *n* *(%)*	*P.V*
High (+ve)	1 (2.0%)	0 (0.0%)	(0.000)
(-ve)	0 (0.0%)	1 (2.0%)	
Normal(+ve)	1 (2.0%)	0 (0.0%)	
(-ve)	48 (96.0%)	49 (98.0%)	
Total	50 (100.0%)	50 (100.0%)	

(P 0.00)

HCV Co-infection:-

Hepatitis C & B co-infection:-

HCV&HBV co-infection:-

None of the patients was positive for both C & B .2 patients (4.0%) were positive for anti- HCV but negative for B. 6 patients (12.0%) were positive for HBV antigen but negative to C . 42 (84.0%) were negative for both and all the control group were negative for B and C as shown in table (3.8.1) .

HCV & HIV Co- infection:-

HCV and HIV co-infection:-

None of the patients was positive for HCV and HIV, nor positive for HIV and negative for the HCV . 2 patients (4.0%) were positive for HCV but negative for HIV. All the control group were negative for both as shown in table (3.8.2) .

Table 3.8.1: HCV&HBV Co-infection

(n = 100)

	Hepatitis B		
Hepatitis C	Positive	Negative	Total
Positive	0	2	2
Negative	6	92	98
Total	6	94	100

(P 0.158)

Table 3.8.2: HCV& HIV Co-infection

(n = 100)

	HIV		
Hepatitis C	Positive n	Negative N	Total n
Positive	0	2	2
Negative	0	98	98
Total	0	100	100

Medical management of Anaemia in relation to Anti-HCV status:-

Anti- HCV status in patients receiving oral iron therapy and/or blood transfusion:-

The oral iron therapy and blood transfusion in relation to HCV status

The majority of the patients 45 (90.0%) were receiving iron while 5 (10.0%) were not. 27 patients (60.0%) out of 45 were transfused while18 (40.0%) were not transfused and all those who were not taken oral iron 5 (100.0%) were not transfused (P0.032) .

Two (4.4%) out of the 45 who received oral iron were anti-HCV positive vs. 0 (0.0%) out of 5 (P 0.120) as shown in table (3.9.1) .

Anti-HCV status in patients receiving parental iron and/or blood transfusion:-

The parental iron and\or blood transfusion in relation to anti-HCV status.

Thirty (60%) were taken parental iron vs 20 (40%) were not taken.

Twenty three (76.7%) out of the 30 (60.0%) vs. 12 (60.0%) out of the 20 (40.0%) were transfused while 7(23.3%) vs. 8(40.0%) (P 0.019) .Two (6.7%) out of the 30 were positive vs. 0(0.0%) out of 20 (P 0.012) as shown in table (3.9.2).

Anti-HCV status in patient receiving erythropoietin and/or blood transfusion:-

The erythropoietin and blood transfusion in relation to anti-HCV status.

Twenty-eight (56.0%) were taken EPO vs 22 (44.0%) were not taken Epo.

Twenty two (78.6%) out of the 28 vs. 5 (22.7%) out of the 22 were transfused and 6 (21.4%) vs. 17(77.3%) were not transfused (P 0.006).

Tow (7.1%) out of 28 of those who were taken EPO were positive vs 0 (0.0%) in those who were not taken EPO (P 0.005) as shown in table (3.9.3).

Table 3.9.1: Oral iron therapy and blood transfusion in relation to anti- HCV status

(n= 50)

Blood translation	Oral iron yes		Oral iron No	
	+ve	-ve	+ve	-ve
Yes	2	25	0	0
No	0	18	0	5
Total	2	43	0	5

Table 3.9.2: Parental iron and blood transfusion in relation to anti-HCV status

(n = 50)

Blood translation	Oral iron yes		Oral iron No	
	+ve	-ve	+ve	-ve
Yes	2	21	0	4
No	0	7	0	16
Total	2	28	0	20

Table 3.9.3: Erythropoietin and blood transfusion in relation to anti-HCV status

(n = 50)

Blood translation	EPO Yes		EPO No	
	+ve	-ve	+ve	-ve
Yes	2	20	0	5
No	0	6	0	17
Total	2	26	0	22

DISCUSSION

General Consideration:-

Parentally transmitted hepatitis virus infection has always been a major health problem in patients with CRF, specially those on haemodialysis [17].

The potential importance of HCV infection in Sudanese children has been recently noted with the rate of anti-HCV about 16.4% in the polytransfused and 20% in the jaundiced children vs. 13% in adult [5].

Despite these results, few studies were conducted in this field.

Thus, this study was targeted specifically for CRF patients as they are high-risk group, so as to identify the incidence of HCV seropositivity among them.

Characteristics of Anti-HCV positive cases:-

The total number of anti- HCV positive cases during the study period were two cases (4.0%). The study showed that this prevalence was in the haemodialysis group 2(6.0%) only while no positive cases in the peritoneal, conservative or control group. This result was significant (p 0.000).

Higher results were reported from Singapore; (45.0%) [54], Brazil (50%) [55], Germany (10.1%) [56], USA (12.0) [57] and Italy 17.3% [58].

The prevalence was in the eldest age group; 12 – 18 years, most probably longer duration of ill health, adherence and exposure to dialysis, blood transfusion, Bilharzias and other risk factors were the explanation . This was showed statistical significance (P 0.00) .It was similar to what was reported by A. Wahab in Egypt [59], and studies conducted in Jeddah [60,61].

Female to male ratio was 5.9: 3 equal to 1.9. This trend of gender was statistically significant (P 0.00) and it was similar to Haren Kumar study [17], but it was different from studies conducted abroad.[62,63,64]

The possible explanation might be the normally lower hemoglobin level in female and physiological anaemia in the pubertal age that may be aggravated by (CRF), so necessitating blood transfusion at lower hemoglobin level compared to the male in the same age group.

So there was age and sex difference which were opposite to studies reported from India and China[65,66].

The seroprevalence of HCV were higher among the secondary school educated patients than the primary one, (10.0%) vs (2.7%) respectively, but this difference was statistically insignificant statistically P 0.542). However, this result could be explained by the fact that patients with ESRD are living longer with increased facilities

and improved techniques of haemodialysis, so they live until they enter the school, but they lost there after due to complication of ESRD. It was found in this study that the seroprevalence of HCV infection was highest (5.6%) in rural than Subarban area, in which it was (1.3%) and urban area (0.0%). Despite this, no statistical difference was shown (P 0.324). This could be attributed to non-adherence to screening program in rural blood bank. However, this result was evident in the study conducted by Dimetri as the majority of cases were from El Gezira.[25)]

It was evident in this study that the seroprevalence was confined to children of un-skilled labourers fathers (13.3%), although the relation to the father's occupation did not show any statistical significance, it might be explained by the fact that, those children live in poor conditions, thus became more susceptible to HCV infection, also the un-skilled laborers are more subjected to trauma. This was in contrast to what was shown by Ngatchu in his study where a significant trend was seen.[(67)] It was also shown that (14.0%) of the seropositive cases were among primary school educated fathers and mothers, but no statistical significance was shown (P 0.351) for both. This result was similar to what was found by Dimitri.[(25)] It was justified by the use of traditional treatment like cauterization , among the lower educated parents.

Clinical patterns of HCV:-

Regarding presentation among those who showed HCV positivity, it was similar to what was stated in the literature, all HCV positive were asymptomatic and a febrile, no one had complained of yellow sclera, the most evident complain was pale stool, I thought it was over prescribed. Anorexia, malaise, nausea and vomiting were mentioned in 50%. No one had clinical jaundice, hepatomegally, right hypochondrial tenderness, Cautery marks or any signs of chronic hepatitis or chronic liver disease. Pallor was evident in all patients; which is most probably is due to their CRF. Bleeding tendency and splenomegaly were evident in some of seropositive patients. This asymptomatic presentation was reported by Tong in USA.[68] However, Roberts reported that approximately 20% of HCV infections were symptomatic [69]. Another study[70] showed that the onset of HCV infection is often un-recognized, and the early course of the disease is often indolent and acute hepatitis with an icteric phase was rare and occurs only in (15%-20%) of infections. However, the infection leads to chronicity. Clinical diagnosis based on signs and symptoms was very difficult to attain, since in most cases, the infection was asymptomatic.

Risk factors of HCV in CRF:-

The study revealed that, prevalence confined to the haemodialysis population which was (6.1%) (P 0.00). Although it was lower compared to (70%) for KSA [71] and (75%) for Egypt [72]. But it was nearer to those results seen in Spain, Germany and the UK where the prevalence of anti-HCV was (20%), (5.5%) and 1% respectively.[73]

This lower prevalence could be attributed to possibly good application of universal precaution in these centers. In this study the prevalence was (8.7%) in single center dialysis while (0.0%) in muti-center dialysis. Although the trend toward single-centre dialysis was significant statistically (P 0.00) ,it was in contra distinction to what has being reported in Abu El-Gasim study's [74]; where the trend was toward multi-center dialysis.

The study done by Abdulla Mohammed[75] revealed that (78%) of those who utilized more than one center acquired HCV infection, compared to (64.3%) in those who were exclusively treated at single center and the same conclusion was drawn out from a study done in UAE.[76]

Another study carried out in the KSA[77], also showed this positive relationship between multi center dialysis and acquisition of HCV infection even among patients who were not transfused.

The study also, revealed increased prevalence which was (10%)-(20%) with increased duration on haemodialysis. Statistically it was a very significant result (P 0.003) and it was compatible with the result of others studies.[75] Multi varate analysis[74] has revealed that seropositivity of HCV infection increases with longer dialytic age. Our figure were nearer to those reported from Germany (14%)[56] , Japan 14%[78] and Italy (26%).[79]

Various factors implicated for this high frequency are the cross infection through the use of common equipment, extra corporeal Haemocirculation ,immunocompromised state, contact with an infected person and contamination of environmental surfaces, gloves, clamps and dressing.[62,80,81]

So duration on HD is considered one of the important risk factors for acquiring HCV infection, the mean age on HD among anti-HCV antibodies positive cases was 15 months in this study which was higher than HCV negative patients (6 months).This result in agreement with a study conducted in Elmadina Almunawara [82] where they found that the duration on HD was longer in Anti -HCV positive group than in the negative group ,the same result was in Taiwan and Qatar.[83,84,85]

However, in a study conducted in Spain[86], the mean age on HD didn't showed statistical significance differences between sero converter and non – sero convertes;36 vs 35months respectively .

The study revealed that Blood transfusion was another risk factor for acquiring HCV infection as it showed 5.1%seropositivity among blood transfused patients vs. (0.0%) among non-transfused.

So (100%) of seropositive group were transfused, (p 0.00) statistically significant **.**

This finding was in agreement with studies done in Kuwait[60], UAE[76] and Netherlands[87] where the prevalence of anti- HCV antibodies was higher in patients who received blood transfusion It is also supported by another study conducted in 102 hospital in KSA[71] where they found a positive correlation between annual incidence of anti-HCV seroconversion and history of blood transfusion but no correlation with the number or frequency of blood transfusion was found.

However, in studies carried out in Jeddah[61] and the western province of Saudi Arabia[88] no association between anti –HCV positivity and blood transfusion was found. This study showed that , the trend of seropositivity was towards frequent blood transfused patients; (10 %)of seropositivity among those who were received 2units while reaching (100%) among those who received 8 units, (P

0.00) highly significant and similar result had been reported by many other investigator. [89,90,91,92]

On the other hand, our study showed no single case with positive anti- HCV anti bodies received non screened blood and the 4.3% positive cases all were received screened blood transfusion, (P 0.001) was significant.

However this lower prevalence (5.1%)among blood transfused could be explained by application of screening program for the blood and it is products for anti-HCV anti bodies in the blood bank [93]. Nevertheless, another study[84] showed that 65 of 97 patient on HD (67%) who had not received previous blood transfusion had positive anti-HCV antibodies, a finding which indicates that factors other than blood transfusion was contributing to the transmission of HCV infection.

Other investigators[61,84,94] also found no correlation between blood transfusion and positive anti-HCV antibodies and they had suggested that the association between dialysis - associated hepatitis and transfusion was not causal but it was rather related to duration on HD.

The study showed that seropositivity was the same among patients who had past history of transfusion and those who had not, (P 0.486) which was significant.

Significant past medical and family history:-

The study showed no history of transfusion hepatitis in sero-positive cases as they never experienced jaundice, (P 0.00) was significant nor jaundice following transfusion, (P 0.417) was not significant statistically .This points was mentioned by Juneja in his study[95] where HCV positivity was 57% in this group of patients.

More over, the study showed that none of the HCV positive cases had contacted jaundiced patients and (P 0.00) statistically significant .

This finding was not corresponding to what was found by El Faleh and Khalifa in their study [96,97] where the prevalence was about 15% among those who had positive history of contact.

In addition, the study showed that past history of hepatitis was not existed in seropositive cases, (p.0.827) was insignificant.

This was in contradistinction to what was reported in other study[5], but the explanation could be the small sample size .

Also, history of hospitalization was present in (50%) of seropositive cases (p0.00), which was statistically significant.

It is clear that hospital admission is a risk factor for nasocomial infection. History of operation was present in 100%of seropositive cases and the (p 0.00), very significant statistically and it was similar to Alfaleh and Khalifa studies's [96,97,98] . Specifically

speaking history of cauterization as minor operation was not found in seropositive cases, however, it was present in 52 of seronegative and the (P 0.096) .

The result also showed that family history of jaundice and hepatitis were not significant statistically (P 0.607) & (P 0.902) respectively .

Liver enzyme(ALT) &anti- HCV seropositivity:-

ALT level was found to be high in 50% of seropositive (P 0.00), highly significant, so our result in agreement to what mentioned in numerous reports regarding correlation between serum ALT level and anti-HCV positivity [83,89]. However more recent report did not find any such correlation and elevated ALT levels were found in (24%) - (67%) of dialysis patients with positive anti-HCV antibodies[99,100] and even when HCV-RNA studied , elevated ALT was found in only (31%) of those patients and in (30%) of those who had biopsy proven hepatitis.[111]

Postulated reasons for this correlation are depressed baseline ALT level in patients on haemodialysis[102], some of anti-HCV positive patients may have cleared the infection and seropositiviy may be the remnant evidence of past infection [103] and the positivity may also reflect viral replication occurring at extra hepatic sites [104] or infection caused by none virulent HCV strains. Other studies

showed that serum ALT levels are poor predictors of liver disease.[101,104,105] However, it had been shown that the greater elevation in liver enzymes the higher the probability of histological evidence of liver disease.[105]

Serum ALT, the most reliable of the liver test is associated with fluctuation during the chronic stage of HCV infection .As high as (30%) of chronic HCV patients may fall within the normal range of serum ALT despite significant liver disease.[106,107] Another study[108] concluded that HCV-related liver disease is more benign in HD patients, suggesting that Hepatocyte growth factor (HGF) serum level attained during dialysis would attenuate the liver damage caused by HCV.[109,110] Previous study showed that HD is a potent stimulus to HGF which accelerates liver repair and it suppresses HCV-induced apoptosis, so they came out with the possible future therapeutic use of HGF in chronic hepatitis C.[111] Rampnio et al[112] observed that milder histological lesion in patients receiving HD in comparison to patients with normal renal function.

Prevalence of HBs -Ag in CRF patients in our study was 6 patients(12%) which is higher than HCV which was 2 patients (4.0%).It was in accordance with the result of other studies [113]. This fact is expected for many reasons, first, the prevalence of HBV is higher than the prevalence of HCV. Second, the viraemia of HBV is

higher than that of HCV, so the transmission of HBV is easier and more effective than that in the case of HCV transmission from patients to health people. However, the prevalence was just (3%) in study done in Bahrian.[114]

HCV Co- infections:-

The result showed no one of seropositive cases had existing HBV co-infection nor HIV (P. 0.158) ,although insignificant it was similar to study done in Syria.[115]

Drug management and/or blood transfusion and it is relation to HCV seropositivity:-

The study showed that 40% of patients who were taken oral iron were not transfused. In additional to this, non-transfused patients were seronegative, so oral iron therapy is important in reducing blood transfusion which is one of the risk factor for HCV infection. While 23.3% of patients who were taken parental iron were not transfused and 22% of patients who received EPO were not transfused, there was no similar study done in this aspect .

Our study showed that blood transfusion was still higher 60% among those who were taken oral compare to 0.0%among those who were not taken iron (P 0.032), also 76.7 % of those who were taken parentral iron were transfused vs 60% among those who were never receive parentral iron (P 0.019) was significant. Furthermore,

it account for 78% of patients who received Epo vs 29% of those who did not received Epo (P 0.006), it was significant. In both groups, the non-transfused patients were negative for Anti-HCV.

So still medical treatment did not replace blood transfusion in management of anaemia in CRF patients who were at risk .

CONCLUSION

- The prevalence of anti –HCV antibody among CRF patients on haemodialysis was 6.1%.
- No co-existing HIV or HBs antigen anti-HCV positive children with CRF.

- The main risk factors are; haemodialysis, its duration, and frequent history of blood transfusion.
- Socio demographic factors didn't reveal any difference between the study groups.
- History of jaundice, hepatitis and post transfusion jaundice were not significant.
- However, history of surgical operation was significant.
- Seropositive group were clinically a symptomatic.
- Liver enzyme (ALT) was a predictor of infection in half of sero positive patients.
- The prevalence of HBV antigen was 12.0% in the Haemo dialysis patients.

RECOMMENDATIONS

- Screening for children who were transfused with blood before 1992, and those who received clotting factors before 1987.
- Use of EPO in mangment of anemia due chronic renal disease.

- Confirmatory assay like recombinant immunoblot assay (RIBA) and polymerase chain reactions (PCR) should be made available.
- Estimation of transaminase levels in all dialysis patients should be done routinely.
- Patients showing persistently raised levels of ALTs and are anti- HCV antibodies positive must be dialyzed separately.
- Adaptation of strict disinfection protocols and universal precautions in every dialysis unit, will reduce the cost effectiveness in stead of discontinuing reuse of dialyzer.
- Automation in dialyzer reprocessing can go along way in limiting the spread of hepatitis C viral infection.
- Conduction of further studies in high-risk group and blood donors so that true incidence is established.
- Prospective studies in the issue of the pathogenicity of the different genotypes and subtypes are required to determine the epidemiology of HCV genotype.
- Evidence based strategy for the management of HCV liver diseases.

REFERENCES

1) Huhta JCL. Chronic renal failure. In: McMillan IA, De Agelis CD, Feigin RD, Warshaw JB (editors). Oski's Pediatrics: Pediatrics Principal and Practice, 3rd Ed. Philadelphia; Lippincot Williams and Wilkins**:** 1999**.** P. 1726.

2) Levey AS, Coresh J, Balk E: National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003 Jul 15; 139(2): 137-47[Medline].

3) Scharer K. Incidence and courses of chronic renal failure in childhood. Proc Europ Dialysis Transplant Assoc 1971; 7: 211.

4) Purcell RH, Alter HJ. Pattern and pathogenesis of hepatitis C virus. 37th Annul meeting of the infectious disease society of America. Philadelphia; 1999. Session 70: S 110.

5) Sakran MH. Prevalence of Hepatitis C Virus in high risk Sudanese children in Khartoum state**.** MD Thesis. University of Khartoum; Sudan: 2000.

6) Riyad AS, Yousef YH, Nabil SM, Mohammed SR. Hepatitis C virus infection in hemodialysis patients in Jordan**.** *Saudi Med J* 2003; 2(24): S137.

7) Mohammed AD, Mohamed AE, Aisha MD, Mansour M, Werfalli AA et al. Prevalence of Hepatitis C virus antibodies among

different populations of relative and attributable risk**.** *Saudi Med J* 2003; 2 (24): 137.

8) Yassin IE, Shakunthala V, Bari MZ, et al. Hepatitis C virus infection among dialysis patients in the United Arab Emirates**.** *Saudi Med J* 2003; 2 (24): S134.

9) Aboud O, Rashid A, Al-Kaabi S. Hepatitis C virus infection in hemodialysis patients in Qatar**.** *Saudi Med J* 2003; 2 (24): 135.

10) WHO**.** Hepatitis C virus**.** *Saudi Med J* 2003; 2 (24): 102.

11) Bakir TM. Age specific prevalence of antibody to Hepatitis C virus among the Saudi population**.** *Saudi Med J* 2003; 2 (24): S120.

12) Omar MN, Mohammed AT, El-Tonsy A. Prevalence of hepatitis C virus antibody. *Saudi Med J* 2003; 2(24): S122.

13) Jonas MM, Zilleruelo GE, Larve SI. Hepatitis C infection in paediatric dialysis population. *J Pediatr* 1993; 89: 707-9.

14) Kleter GE, Brouwer JT, Heijtink RA, Schalm SW. Detection of hepatitis C virus RNA in patient with chronic hepatitis C virus infection. *Anti Microbiol Agents Chemother* 1993; 37: 595-97.

15) Megmar AS, Martins RM, Sheila AT, Simonne AS, Carmen LL et al. Hepatitis c prevalence and risk factors in haemodialysis patients. File://a:/HIND9.HTM

16) Oliva JA, Maymo RM, Carrio J, Oelgard D, Mall JM. Late sero conversion of c virus markers in haemodialysis patient. *Kidney Intern* 1993; 43: 5.

17) Haren K, Naqui SA, Ahmed A, Hamid S. Hepatitis c virus antibodies (Anti HCV) in haemodialysis vs non-dialysis patients. *Kidney Int* 1994; 2 (44): 35-6.

18) Snyder DJ , Pickering KL . Hepatitis A & E. In: Behrman RE, Kliegman RM, Arvin AM, (editors). Nelson Textbook of Pediatrics, 15th ed. Philadelphia; WB Saunders: 1996. P. 1609-1611.

19) Betts PR, Mc Grath G. Growth pattern and dietary intake in children with chronic Renal Insufficiency. *Br Med* J 1972; 2:189.

20) Cameron S, Jean AD, David PG, Ritz E. Haemodialysis, complication during haemodialysis and adequacy of haemodialysis. In: Cameron S, Jean AD, David PG, Ritz E (editors) Oxford Text Book of Clinical Nephrology, 2nd Ed. New York; Oxford University Press: 1992: 1418-1439.

21) Henryh HS, Stephn M, Hoofnagle J. Acute viral hepatitis. In: Henryh HS, Stephn M, Hoofnagle J (Editorials) Oxford Clinical Textbook of Infectious Diseases. Principal and Practice, 1st Ed. New York:; Churchill Livingstone**:** 1995. P.1184-1186.

22) A-Kader HH, Balistreri WF. Hepatitis C virus: implications to pediatric practice. *Infect Dis J* 1993; 12:853-67.

23) Choo QL, Kuo G, Weiner A. Isolation of CDNA clone derived from blood borne-non-A, non-B viral hepatitis genome. *Science* 1989; 244: 359-62.

24) Houghton M, Weiner A, Han J, Kuo G, Choo QL. Molecular biology of the hepatitis C viruses: Implications for diagnosis development and control of viral disease. *Hepatol* 1991; 14: 381-88.

25) Dimitri ME, Kadaru AG El-Tigani A. Prevalence of hepatitis C virus antibody and associated B virus markers among Sudanese patients with acute viral hepatitis in Khartoum. MD thesis. University of Khartoum, Sudan 1996.

26) Nowicki MJ, Balistreri WF. The hepatitis C virus: Identification, epidemiology and clinical controversies. *J Pediatr Gastroenterol Nutr* 1995; 20:248-74.

27) Garson JA, Tedder RS. The detection of hepatitis C infection. *Rev Med Virol* 1993; 3: 75-83 .

28) Esteban JI, Genesca J, Alter HJ. Hepatitis C molecular biology, pathogenesis, epidemiology clinical features and prevention. *Progress Liver Dis* 1992; 10: 253–82.

29) Simmonds P, Alberti A, Alter HJ. A proposed nomenclature of hepatitis C viral genotypes. *Hepatol* 1994; 19: 1321-323.

30) Kumar U, Monjardino J, Thomas HC Hypervariable region of hepatitis C virus envelope glycoprotein (E2/NS1) in a gammaglobulinemic patients. *Gastroenterology* 1994; 106:1072-75.

31) Mahaney K, DiBisceglie AM, Hoofnagle JM, Sallie R. Genomic variability of the hepatitis C virus development of mutations during antiviral therapy. *Hepatology* 1993;18: 92.

32) Kao JH, Chen PJ, Lai MY, Chen DS. Super infection of heterologus hepatitis C virus in patients with chronic type C hepatitis. *Gastroenterology* 1993; 105: 583-87.

33) Hayashi N, Hagiwara H. Viral factors affecting outcome of hepatitis C virus infection. *Viral Hepatitis* 1996; 2:187-98.

34) Barrakat S, Fedail SS, El- Tigani A . Hepatitis B and C in hepatocellular carcinoma. MD Thesis, University of Khartoum, Sudan 1998.

35) Takada N, Takase S. HCV genotypes in different countries. *J Hepatol* 1993;17: 277-83.

36) Lefkowitch JH, Schiff ER, Davis GL, Perrillo RP, Lindsay K, Bodenheimer HC et al. Pathological diagnosis of chronic

hepatitis C: a multi center comparative study with chronic hepatitis B. *Gastoenterology* 1993; 104: 595-603.

37) Scheuer PJ, Ashrafzadeh P, Sherlock S. The pathology of hepatitis C. *Hepatology* 1992; 15: 567-71.

38) Hess G, Massing A, Rossol S. Hepatitis V virus and sexual transmission. *Lancet* 1989; 2: 987.

39) Bhandari BN, Wright TL. Viral hepatitis. Current diagnosis and treatment. *California: Appleton and Lange* 1996: 484-94.

40) Martin P, Bernstein D, Alter M. The natural history of hepatitis C: an evolving story, prognostic factors, disease progression and long–term burden. *Digest Dis* 2000; (13): 63-5.

41) Thaler MM. Hepatitis C in infants and children. *Curr Opin Pediatr* 1997: 508-12.

42) Neal AH, Jon SA. Hepatitis C virus infection. *J Pediatr* 1998; 101(3): 481-85.

43) Wang JT, Wange TH, Shev JC, Lin JT, Chen DS. Hepatitis C virus transmission. *J Med Virol* 1992; 36: 28-31.

44) Lott JA, Notte FS, Gretch R, Kott RS, Seett LB. Laboratory guide lines for screening, diagnosis, and monitoring hepatic injury. In: DuFour DR (Editor). Laboratory Medicine Practice

Guidelines. Washington (DC): National Academy of Clinical Biochemistry 2000: 21-23.

45) Pawlotsky JM, Lonjon I, Hezode C, et al. Serological determination of hepatitis C virus genotype: comparison with a standardized genotyping assay. *J Clin Microbiol* 1997; 35: 654-59.

46) Clue P, Fang JW, Rouzier PR, et al. Pegylated interferon alpha and preliminary efficacy, pharmacodynamics, safety and preliminary efficacy data. Hepatitis C intervention therapy group. *Clin Pharmacol Ther* 2000; 68: 556-67.

47) Hoofnagle JH, Mullen KD, Jones DB, et al. Treatment of chronic non-A, non-B hepatitis with recombinant human alpha interferon: a preliminary report. N *Engl J Med* 1986; 315: 1575-578.

48) DiBiscglie AM, Martin P, Kassianides J. Recombinant interferon alpha a therapy for chronic hepatitis C: a randomized, double-blind, placebo controlled trial. *N Engl J Med* 1989; 321: 1506-510.

49) Cameron S, Jean AD, David PG, et al. Hepatitis B & C screening. In: Cameron S, Jean AD, David PG, et al (editors) Oxford Textbook of Clinical Nephrology, 1st ed. New York; Oxford University Press: 1992. P. 1285-1290.

50) Sulkowski MS. HIV and hepatitis C virus. 37th Annual Meeting of the Infectious Diseases Society of America, Philadelphia 1999; Session 70: S 113.

51) Sulkowski MS, Mast EE, Seeff LB. HCV infection as an opportunistic disease in persons with HIV. *Clin Infect Dis* 2000; 30: 557-84.

52) McIntyre NE, Benhamou JP, Birche J, et al. Infection of the liver. In: McIntyre NE, Benhamou JP, Birche J, et al (editors) Clinical Textbook of Hepatology. 2nd ed. Philadelphia; Churchill Livingstone: 1993: 1184-1186.

53) Yuonne E. Hepatitis in renal unit. In: Yuonne E (editor) Hepatitis and its Control, 1st ed. London; Bailliere Tindall: 1977: 183.

54) Choong HL, Koh L, Woo KT. Anti -HCV seropositivity in long term haemodialysis patients. *Nephrol J* 1992; 4: 91.

55) Yoshida S, Takahashi C, Gaspar AM. Hepatitis C Virus in chronic haemodialysis patients with Non-A Non-B hepatitis. *Nephron J* 1992; 60: 150 – 53 .

56) Schlipkoter U, Roggendor FM, Ernst G. Hepatitis C virus antibodies in haemodialysis patients. *Lancet* 1990; 336: 243-44.

57) Zeldis JB, Depner TA, Kuramoto IK. The Prevalence of hepatitis C virus antibodies among haemodialysis patients. *Ann Intern Med* 1990; 112: 958 – 60 .

58) Gilli P, Morethetti M, Sor ftritti S. Anti- HCV positive patients in dialysis units. *Lancet* 1990; 336: 243 – 44 .

59) Abdel Wahab MF, Karias Za, Kamel M, Abdel Khaliq MK, Mabrouk MA et al. High sero prevalence of hepatitis C infection among risk group in Egypt. *Am J Trop Med Hyg* 1994; 51(5): 563 –67.

60) El-Reshaid K , Kapoor M, Sugathan T, Al-Mufti S, Al-Hilali N. Hepatitis C virus infection in patients on maintenance dialysis in Kuwait: epidemiological profile and efficacy of prophylaxis. *Saudi Kidney Dis Transplant* 1995; 6(2):144– 50.

61) Al- Shohaib SS, Abdelaal MA, Zawawi TH, Abbass FM, Shaheen FM. The prevalence of Hepatitis C virus antibodies among hemodialysis patients in Jeddah area, Saudi Arabia. *Saudi J Kidney Dis Transplant* 1995; 6(2):128 – 31.

62) Machida J , Yamaguchi K, Ueda S. High incidence of hepatitis C virus antibodies in haemodialysis patients. *Nephron* 1992; 60:117-18.

63) Consolo F, Freni MA. Nosography and immunopathogenesis of viral hepatitis. *Nephron* 1992; 61: 251– 54 .

64) Dentico P, Volpe A, Buongiorno R. Hepatitis C virus in haemodialysis patients. *Nephron* 1992; 61: 307 – 8.

65) June ja M, Dubey AP, Kumari S, Pra Kash C, Mittal SK. Hepatitis B & C in multi transfused children. *Trop Gastroenterol* 1998; 19:34 –6 .

66) Niy H, Chang MH, Lue HC, HSU HY, Wang MJ et al Post transfusion hepatitis C virus infection in children. *J pediatr* 1994; 124 (5): 709 – 13.

67) Nagatchu T, Stroffolini T, Rapicetta M, Chionne P, Lantum D et al. Sero prevalence of anti – HCV in an urban child population : A pilot Survey in developing area, Cameroon. J *Trop Med Hyg* 1992; 95: 57–61.

68) Tong MJ, El Farra NS, Rei Kes AR, Corl S. Chronic viral hepatitis C & B. *N Eng J Med* 1995 ; 332: 1463 – 465 .

69) Roberts EA. Chronic hepatitis B and C in children. *Saudi J Gastrol* 1995; 1: 157 – 62 .

70) Laver GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001; 345 : 41- 52 .

71) Souqiyyeh MZ, Shaheen FM, Huraib SO, Al Khadet AA. The annual incidence of seroconversion of antibodies to the hepatitis C virus in haemodialysis population in Saudi Arabia. *Saudi J kidney Dis Transplant* 1995; 6(2): 167–73 .

72) Rashad B. Renal replacement therapy in Egypt. *Saudi J Kidney Dis Transplant* 1997; 8(2): 152- 54.

73) Fa Kunle Y, Al- Mo Farren M, El- Karaman YW, Ezzat H, El-Edreees et al. A prevalence of antibodies to hepatitis C virus in haemodialysis patients in Riyadh. *Ann Saudi Med* 1991; 11(5): 504 – 6.

74) Abul Kashem M, Nuairat I, Mohamed M, Ramzy M, Nemma J. Hepatitis C virus Among haemodialysis patients in Najran: prevalence is more among multi centre visitors. *Saudi J Kidney Dis Transplant* 2003; 14 (2): 206 –11.

75) Abdulla MY, Al Jiffri S, Fadag RB, TawfiK M, Ghabrah F, Ibrahim A. Hepatitis C virus infection among patients on haemodialysis in Jedddah: a single center experience. *Saudi J Kidney Dis Transplant* 2003; 14(1): 84 –9 .

76) ElShalhat YI, Varma S , Bari MZ , Nawaz MS, Abdulrahman S et al. Hepatitis virus infection among dialysis patient, United Arab Emirates. *Saudi J Kidney Dis Transplant* 1995 ; 6(2): 157-62.

77) Saeed MG , Al Harbi AS. Hepatitis C virus sero -status in haemodialysis patients returning from holiday: another risk factor for HCV Transmission. *Saudi J Kidney Dis Transplant* 2001; 12(1):14–20.

78) Yamguchi K , Nishimura Y, Fu Kvo ka N. Hepatitis C virus antibodies in haemodialysis patients. *Lancet* 1990; 335: 1409-410.

79) Mosconi G, Desanctis LB, Ste Foni S. Epidemiology of hepatitis C in a population of haemodialysis patients. *Nephron* 1992 ; 61: 298 –99.

80) Alter JI, Coleman PJ, Alexander WJ. Importance of heterosexual activity in transmission of hepatitis B and non- A non-B Hepatitis. *JAMA* 1989; 262:1201–205 .

81) Esteban J, Esteban R, Viladomiu L. Hepatitis C virus antibodies among risk group in Spain .Lancet 1989; 2: 294-96.

82) Bernioh B , Allam M, Halepota A , Mohammed AO, PorKar J et al. Prevalence of hepatitis C virus antibodies in haemodialysis patients in Madina AL Munawarah . *Saudi J Kidney Dis Transplant* 1995; 6(2): 132 – 35.

83) Lin DY, Lin HH, Hunag CC, Liaw VF. High incidence of hepatitis C virus infection in Haemodialysis patients in Taiwan. *Am J Kidney Dis* 1993; 21(3): 288 – 91.

84) Hardy NH, Sandronis Y, DnieIson T, Wilson WJ. Antibody to hepatitis C virus increases with time on haemodialysis. *Clin Nephrol* 1992; 38:44 –8.

85) Abboud O, Rashid A, Al Kaabi S. Hepatitis C virus infection in haemodialysis patients in Qatar. *Saudi J Kidney Dis Transplant* 1995; 6(2): 151 – 53.

86) Oliva JA, Maymo RM, Carrio J, Gado DEI, Mallatare JM. Late sero conversion of C virus markers in haemodialysis patients. *Kidney Int* 1993; 43: S153-56.

87) Keur I , Schneeberger PM , Vander Graa FY , Vos J, Dij KWC, et al . Risk factor for HCV infection in two Haemodialysis units in the Netherlands. *Neth J Med* 1997; 50(3): 97–101.

88) Shaheen FAM, Huraib So, Al-Rashed R. Prevalence of hepatitis C antibodies among haemodialysis in Western province of Saudi Arabia. *Saudi J Kidney Dis Transplant* 1995; 6(2): 136-36.

89) Muller GY, Zabaleta ME, Arminio A. Risk factor for dialysis - associated hepatitis C in Venezuela. *Kidney Int* 1992; 41:1055 – 58.

90) Ayoala EA, Huraibs, Ari FM. Prevalence and significant of antibodies to hepatitis C virus among Saudi hemodialysis patients. *J Med Virol* 1991; 35: 155 – 59 .

91) Saeed AA, Fairclough D, Al- Addmawi AM. Hepatitis C virus in Saudi Arabia: a preliminary survey. *Saudi Med J* 1990; 11: 331 –32 .

92) Mitwalli A, Al- Mohya S, Al -WaKeel J. Hepatitis C in chronic renal failure patients. *Am J Nephrol* 1992; 12: 288 – 91.

93) Donahre JG, Munzo A, Ness PM. The declining risk of post transfusion hepatitis C virus infection. *N Eng I J Med* 1992; 884 –92.

94) Berneih B, Allam M, Halepota A. Prevalence of hepatitis C virus antibodies in hemodialysis patients in Medina Al Munawarah. *Saudi Kidney Dis Tranplant Bull* 1993; 4:573.

95) Juneja M, Dubey AP, Kumaris, Prakash C, Mittal SK. Hepatitis B & C in multitransfused children. *Trop Gastroenterol* 1998; 19:34 -6

96) Al-Faleh FZ, Ayoola EA, Al-Jeffry M. Prevalence of Antibody to hepatitis C virus among Saudi Arabian children. A community based study. *Hepatolo*gy 1991; 14(2): 215–18.

97) Khalifa AS, Mitchell BS, Watts DM, El -Samahy MH, El Sayed MH et al. Prevalence of hepatitis C virus antibody in transfused Egyptian children. *AM J Trop Med Hyg* 1993; 49: 316- 21.

98) Angyo IA, Ya Kub UAM. Lack of association between some risk factors and hepatitis B surface antigenaemia in children with sickle cell anaemia. *West Afr J Med* 2001; 20(3): 214-18.

99) Oguchi H, Miyasa Ka M, To Kunaga S. Hepatitis virus Infection and HCV in eleven Japanese hemodialysis units. *Clin Nephrol* 1992; 38: 36 – 43.

100) Vasile A, Allegran V, Canciani D Forchi G, Mengozzi G. Prospective and retrospective assessment of clinical and laboratory parameters in maintenance haemodialysis patients with and without HCV antibodies. *Nephron* 1992; 61: 318-19.

101) Pols Romeo R, Zins B. Hepatitis C virus RNA in Anti-HCV positive hemodialyzed patients: significance and therapeutic implications. *Kidney Int* 1993; 44:1097-100 .

102) Ross EA. Abnormal Liver function test-1. *Semin Dial* 1993; 6:355 –58 .

103) Alberti A, Morsica, Chemellol. Hepatitis C viraemia and liver disease in symptom-free individual with anti-HCV. *Lancet* 1992; 340: 697 – 98.

104) Brillanti S, Foli M, Goiani S, Masci C, Miglioli M. Persistent Hepatitis C viraemia without liver Disease. *Lancet* 1993; 341:464 –65.

105) Van Ness MM, Diehl AM. Is liver biopsy useful in the evaluation of patients with chronically elevated liver enzymes? *Ann Intern Med* 1989; 11: 473 – 78.

106) Prieto M, Olaso V, Verdu C, Cordoba J, Gisbert C. Does the healthy hepatitis C virus carrier state really exist? An analysis using polymerase chain reaction. *Hepatology* 1995; 22 : 413–17.

107) Shaki Ao, Cnry-Catilena C, Alter HJ, Haya Ship, Kleiner DE et al. Volunteer blood donors with antibody to Hepatitis C virus: clinical ,biochemical, virologic and histologic features. *Ann Intern Med* 1995; 123: 330-37.

108) Carameio C, Ortiz A, Aguikera B, Porresj C, Navas S et al. Liver disease patterns in haemodialysis patients with antibodies to hepatitis C virus. *Am J Kidney Dis* 1993; 22: 822-28.

109) Pereira BJ, Natov SN, Bouthot BA, Murthx BV, Ruthazer R et al. Effects of hepatitis C infection and renal transplantation on survival in end-stage renal disease. The New England Organ Bank Hepatitis C study group. *Kidney Int* 1998; 53:1374-381.

110) Seeff LB, Buskell-Bales Z, Wright EC, Durako SJ, Knddell RG et al. Long-term mortality after transfusion-associated non-A, non–B, hepatitis. The National Heat, Lung and Blood Institute Study Group. *N Eng I J Med* 1992; 327:1906-11.

111) Matsumoto K, Nakamura T. Heparin functions as a hepatotrophic factors by inducing production of hepatocyte

growth factor. *Biochem Biophys Res Commun* 1996; 227: 455-61 .

112) Rampino T, Arbustini E, Gregorini M, Guallini P, Libetta C et al. Hemodialysis prevents liver disease caused by hepatitis C virus: role of hepatocyte growth factor. *Kidney Int* 1999; 56: 2286 –291.

113) Gibas A, Blewett DR, Schoen Feld DA, Dien Stag JL. Prevalence of viral Hepatitis in health workers in the pre-hepatitis B vaccination era. *Am J Epidemiol* 1992; 136: 603 - 10.

114) Al-Arrayed S. Renal replacement therapy in Bahrain. *Saudi J Kidney Dis Transplant* 1998; 9(4): 457 –58.

115) Basem M, Othman M, Fawza S, Monem A. Prevalence of hepatitis C virus antibodies among health care workers in Damascus, Syria. *Saudi Med J* 2001; 22(7): 603 –5.

University of Khartoum

Postgraduate Medical Studies Board

Department of Paediatrics and Child Health

PREVALENCE OF HEPATITIS C VIRUS ANTIBODIES AMONG CHILDREN WITH CHRONIC RENAL FAILURE IN KHARTOUM STATE

Date of interview:…….. Serial No……

1- Personal data:

Name…… **Age**:…….

Gender: 1) Male 2) Female ☐

Residence

1) Urban 2) Rural 3) Suburban ☐

School grade

1) Illiterate 2) Primary 3) Secondary ☐

4) Post Secondary 5) Quran school (*Khalwa*)

A-**Father's Occupation**

1-Professionals 2-Civil servants ,Employees ,Merchants ☐

3-Skilled labourers 4-Uskilled labourers

5-farmer's,Shepherds 6-Unemployed

Father's Education

1-Illiterate 2-Primary 3-Secondary ☐

4-Post Secondary 5-Quran School

Mother's Education:

1-Illiterate 2-Primary 3-Secondary ☐

4-Post secondary 5-Quran school

2-Presenting compliant

Fever	*1) Yes*	*2) No*	
Anorexia	1) Yes	2) No	
Malaise	1) Yes	2) No	
Abdominal pain	1) Yes	2) No	
Nausia	1) Yes	2) No	
Vomiting	1) Yes	2) No	
Haematemsis	1) Yes	2) No	
Diarrhea	1) Yes	2) No	
Constipation	1) Yes	2) No	
Pale stool	1) Yes	2) No	
Dark urine	1) Yes	2) No	
Yellow sclera	1) Yes	2) No	
Impaired sensorium	1) Yes	2) No	

3- Past history:

P.H of bilharsiasis	1) Yes	2) No	
P.H of jaundice	1) Yes	2) No	

If yes, when:

1) Before dialysis 2) After dialysis

Appearance of jaundice after transfusion 1) Yes 2) No

P.H of contact with jaundice pt 1) Yes 2) No

Does the child has hepatitis 1) Yes 2) No

If Yes what is the type ……..

Hepatitis 1) A 2) B 3) C 4) HIV 5) Others

When

1) Before dialysis 2) After dialysis 3) before transfusion

Does the diagnosis of hepatitis confirm?

1) Yes 2) No

1) By history 2) Examination 3) Investigation

Does the child received hepatitis B vaccine: 1) Yes 2) No

Does the child treated for hepatitis 1) Yes 2) No ☐

Does the child have a result of ALT, AST 1) Yes 2) No ☐

1. ALT …….

2. AST …….

P.H of hospitalization 1) Yes 2) No ☐

If Yes how frequent 1) Once 2) Twice 3) More

P.H of operation or procedure? 1) Yes 2) No ☐

Type of operation

1) Abdominal 2) Cardiothoracic 3) Tonsillectomy ☐

4)Abscess drainage 5) Cautary marks

6) Tattooing marks 7) Circumcision 8) Uvulectomy

9) Tooth removal 10) Others

P.H of blood transfusion 1) Yes 2) No ☐

If Yes, how many before dialysis

1) Once 2) Twice 3) Trice 4) More ☐

How many after dialysis?

1) Once 2) Twice 3) Trice 4) More ☐

Is it screened blood? 1) Yes 2) No ☐

PH of reuse of injections 1) Yes 2) No

4- Family history: ☐

F.H jaundice 1) Yes 2) No ☐

Hepatitis 1) Yes 2) No ☐

5-Social history

Housing 1) straw 2) mud 3) Bricks 4) Concrete ☐

Toilets:

1) Communal latrine 2) Pit latrine (private) ☐

3) Pit latrine (shared) 4) Siphon

5) Open space 6) Others

Electricity 1) Yes 2) No ☐

Water supply

1) Nile 2) Traditional wells 3) Deep wells ☐

4) Piped in 5) Piped out

6- Examination:

Weight …… kg Height……..

Pallor	**1) Yes**	**2) No**		☐ ☐
Jaundice	1) Yes	2) No		
Temp.	1) Normal	2) Low	3) High	☐
Hepatomegaly	1) Yes	2) No		☐
Rt. Hypochnodrium tenderness	1) Yes	2) No		☐
Splenomegaly	1) Yes	2) No		☐
Lymph Node	1) Yes	2) No		☐
Skin rash	1) Yes	2) No		☐
Bleeding Tendency	1) Yes	2) No		☐
Tribal marks	1) Yes	2) No		☐
Confusion	1) Yes	2) No		☐
Palmar Erythema	1) Yes	2) No		☐
Spider Naevi	1) Yes	2) No		☐
Cautry marks	1) Yes	2) No		☐

7- Investigations:

Liver enzymes	ALT……		
Hepatitis C by 3rd generation ELISA	1) +ve	2) -ve	☐
Hepatitis B	1) +ve	2) –ve	☐
HIV	1) +ve	2) –ve	☐