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Prevalence of SEN Virus and Pegivirus (GBV-C) among Patients on Maintenance Hemodialysis in Al-Kindy Dialysis Center in Baghdad

A Thesis

Submitted to Council College of Medicine - University of Diyala as Partial Fulfillment of the Requirements for the master's degree of Sciences in Medical Microbiology

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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صدق الله العظيم

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Supervisor Certification

We, certify that this thesis entitled **(Prevalence of SEN Virus and Pegivirus (GBV-C) among Patients on Maintenance Hemodialysis in Al-Kindy Dialysis Center in Baghdad)** has been conducted under my supervision at the College of Medicine, University of Diyala, as partial fulfilment of the requirements for the Master Degree of Science in Medical Microbiology.

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Given the available recommendation, I forward this thesis for debate by the examining committee.

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We, as the examining committee, certify that we have read this thesis and examined the student (**Hayder Ahmed Kadhim**) in and its contents, found it adequate as a thesis for the Master Degree of Science in Medical Microbiology.

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Dedication

I dedicate the current study ...

To my dear and lovely mother for her encouragement and support. To my father who taught me the first letter.

To my lovely wife and lovely children

Yosef, Dawood, and Ibrahim

Acknowledgment

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Hayder

Abstract

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List of Abbreviations

Abbreviation	Meaning
AASLD	American Association for the study of liver diseases
ALP	Al□aline phosphate
ALT	Alanine aminotransferase
AST	Aspartate amino transferase
β	Beta
cDNA	Complementary □NA
CKD	Chronic □idney diseases
DNA	□eoxyribonucleic acid
dNTPs	□eoxynucleotide triphosphates
E1	Envelope protein- 1
E2	Envelope protein- 2
EDTA	Ethylenediaminetetraacetic acid
EIA	En□yme Immunoassay
ELISA	En□yme lin□ed immunosorbent assay
ESRD	End stage renal diseases
FDA	Food and drugs administration
GTs	Genotypes
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HCWs	Health care wor□ers
HD	Hemodialysis
HIV	Human immune deficiency virus
ICTV	International committee on taxonomy of viruses
IFN I	Interferon type one
IgG	Immunoglobulin G

IL	Interleu□in
ISGs	Interferon stimulating genes
IV	Intravenous
KT	□idney transplantation
NANB	Non-A non B hepatitis
NAT	Nucleic Acid Testing
NK	Natural □iller cell
NNIs	Non-nucleotide inhibitors
NS	Nonstructural
NS2	Nonstructural region 2
NS3	Nonstructural region 3
NS4	Nonstructural region 4
NS5	Nonstructural region 5
ORF	□pen reading frame
PBMC	Peripheral blood mononuclear cell
PCR	Polymerase chain reaction
PH	Power of hydrogen
RdRp	RNA dependent RNA polymerase
RNA	Ribonucleic acid
RRT	Renal replacement therapy
RT-PCR	Real-time Polymerase chain reaction
SPSS	Statistically pac□age for social science
TRAIL	Tumor necrosis factor related apoptosis inducing ligand
Treg	T- regulatory cell
USA	□nited States of America
WHO	□ orld health organi□ation

Chapter One

Introduction

1. 1 Introduction

It is well □nown that patients underlying dialysis treatment, and in particular hemodialysis (H□), are more susceptible ris□ for viral infections. This is due to their underlying low cellular immunity, which increases their susceptibility to infection. In addition, the process of hemodialysis need blood, that causes to exposure to infectious materials through the extracorporeal circulation for a prolonged period. Moreover, H□ patients may re□uire a blood transfusion, fre□uent hospitali□ations, and surgery, which increase opportunities for nosocomial infection exposure (Bernieh, 2□15). Approximately 1□□ of transfusion-associated hepatitis and 2□□ of community-ac□uired hepatitis cases do not have a defined etiology, suggesting the existence of an additional causative agent (Al-□u□aili, 2□1□). Patients on long-term hemodialysis are especially susceptible to parenterally transmitted agents and therefore represent an important population for analysis of the clinical and epidemiological implications of newly identified agents (Forns et al., 1999). Perhaps one of the most common viral infections are caused by hepatotropic or other hepatitis-associated viruses, including hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis G virus (GBV-C) (□□darendeli et al., 2□□5), and SEN Virus (Abd El-Hady et al., 2□□6).

In 1995-1996, GBV-C was described as putative agents that accounted for the unexplained non-A to non-E hepatitis. The virus□s genome is consisting of single-stranded RNA with positive polarity., and belongs to the flaviviruses family. It only has one open reading frame, which encodes the viral polyprotein. There is contrary information as to whether or not GBV-C replicates in the liver. The clinical significance of GBV-C infection in humans it is still to be establish and few data in patients on H□ are available (□□darendeli *et al.*, 2□□5□Bernieh, 2□15). A high rate of GBV-C infection has been extensively reported in several countries in the last stage of renal failure and in chronic H□ patients, ranging from 6 to 44 percent. Analysis of the 5-untranslated region (□TR) suggests

that GBV-C variations may be split into five genotypes. Genotype 1 is common in the western and central African countries genotype 2 is widespread in Europe, North and East Africa, Pa istan and apan genotype 3 occurs across Asia genotype 4 occurs in South East Asia genotype 5 in South African countries is prevalent (darendeli et al., 2 5).

SEN virus (SENV), was discovered in 1999, the name for the SENV was derived from the initials of the first identified patient (Abbasi et al., 2 16 Abd El-Hady et al., 2 6). SENV is a small, single-stranded, non-enveloped circular NA virus (Abd El-Hady et al., 2 6) and belongs to the Ciconiidae family (Abbasi et al., 2 16) It is probably accounting for many cases of non-A-E hepatitis. This virus is parenterally transmitted, and therefore, appropriate screening of blood and blood products could control its spread. In addition, this virus appears capable of co-infecting patients who have other types of viral disease raising the possibility that it may aggravate their clinical course and or their response to treatment. Phylogenetic analysis of SENV isolates had demonstrated the existence of eight highly divergent genotypes (A-H). Genotypes SENV- and SENV-H are more prevalent in patients with transfusion-associated non A-E hepatitis (Al- u aili, 2 1). The high prevalence of SENV observed among patients with HIV, HBV, HCV infections indicate a shared route of transmission (Abbasi et al., 2 16). The association of SENV infection with hepatocyte damage or serum levels of aminotransferase remains uncertain. The role of SENV infection in patients on maintenance hemodialysis is also far from clear (ai et al., 2 5) therefore, the present study try to determine the prevalence of SENV (SENV- and SENV-H strains) and GBV-C among hemodialysis patients and some of their clinical significance in Al- indy center for dialysis Baghdad.

1.2 Aims of the study:

The aims of this study as is formulated to:

1. □etermine the prevalence of SEN-V infection in hemodialysis patients by nested PCR.
2. □etermine the prevalence of GBV-C infection in hemodialysis patients by reverse nested PCR.
3. Evaluate any possible association between SEN-V and GBV-C with HCV and their clinical importance in hemodialysis patients by biochemical test (ALT and AST).
4. The association of SENV and GBV-C with □emographic, clinical characteristics and some ris□factors.