Republic of Iraq
Ministry of Higher Education
And Scientific Research
University of Diyala
College of Medicine

Rate of HDV Infection among HBsAg Positive Blood Donors and Patients with Chronic Hepatitis B Virus Infection In Diyala Province

A Thesis

Submitted to Council College of Medicine - University of Diyala in Partial Fulfillment of the Requirements for the Master Degree of Science in Medical Microbiology

By

Linda Munjed Hadi

BSc. Biology - University of Diyala

Supervised by

Assistant Professor
Dr. Areej Atiyah Hussein
(Ph.D. in Medical Microbiolgy)

Assistant Professor
Dr. Ali Musa Ja'afer
(F.I.C.M.S)

2018 A.D./ January

1439 A.H./ Rabi Al-Thani

إِنَّمَا يَخْشَى اللَّهَ مِنْ عِبَادِهِ الْعُلَمَاءُ

صدق الله العظيم

سورة فاطر، الآية (٢٨)

Summary

Hepatitis B virus is the most important causative agent of blood borne hepatitis in humans. Hepatitis D virus infection occurs either as a co-infection or super infection in HBV carriers.

The present study is designed to determine the infection rate of hepatitis D virus in two groups of individuals infected with the hepatitis B, the first one includes blood donor and the second include chronic hepatitis B patients also to look for the relationship between HDV infection and sociodemographic and clinical characteristics as well as studying the association between the risk factors and the HDV infection.

All of them are subjected to different tests such as HBsAg, HBcIgM, HBcIgG, HDVIgM and HDVIgG using separate ELISA kits and full information are collected from each participant by using a questioner sheet which includes the sociodemographic and clinical characteristics such as age, gender, educational level, marital status, occupation, family history, blood transfusion, surgical operation, dental history, endoscope, any medical problem, tattoo and cupping also are recorded.

Serum samples are collected from 132 HBsAg positive blood donors (107 males and 25 females, age range 19-67 years) from blood bank in Baqubah teaching hospital and 132 serum sample of hepatitis B patients (74 male and 58 female, age range 19-67 years) from Baqubah Teaching Hospital, during the period from 11thAugust 2016 till 25th April 2017.

The data from this study shows that

1. Minimum age was 19 years and maximum was 68 years. The highest age-specific frequency in studied groups is in the age group of 19-34 years.

2. Three cases (2.3%) of blood donors and 7 cases of chronic hepatitis B patients (5.3%) are anti-HBcIgM positive; while all of the participants in this study are anti-HBcIgG positive.

3. Among blood donors group 6 cases (4.5%) are positive to HDV IgG and they were all males, while in the chronic hepatitis B patients group only one case is positive to HDV IgG and is females.

4. The HDV infection in patients lived in the urban places is more than in rural areas in blood donors is 5cases and only one case among chronic hepatitis B lived in rural areas.

5. All HDV positive cases [6 blood donors and 1chronic hepatitis B] are recorded in married patients.

6. Among blood donors with positive HDV infection 2(33.3%) are recorded in patients with primary school, secondary school and high education for each one, while one case with illiterate within chronic hepatitis B patients.

7. The results of the blood donors and chronic hepatitis B patients are mainly belong to the un-employed 3cases and 1case respectively.

8. There are no significant differences between HDV infection and different risk factors.

Table of Contents

Table of Tables

Table of Figures

Table of Abbreviations

Abbreviate	Key
Abs	antibodies
ALT	Alanine aminotransferase
Anti-HBc	Antibodies to the HBV core antigen
Anti-HBs	Antibodies to the HBV surface antigen
Anti-HD	Anti-hepatitis delta
AST	Aspartate aminotransferase
Au-Ag	Australian antigen
CccDNA	Covalently closed circular DNA
CD4+	Cluster of differentiation 4
CD8+	Cluster of differentiation 8
DNA	Deoxribonucleic acid
DS	Double-stranded
ELISA	Enzyme-linked immunosorbent assay
ESCRT	Endosomal sorting complex required for transport
GGT	Gamma-glutamyl transpeptidase
HBcAb	Hepatitis B core antibody
HBcAg	Hepatitis B core antigen
HBeAg	Hepatitis B virus e antigen
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B virus surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCWs	Health care workers
HDAg	Hepatitis delta antigen
HDV	Hepatitis delta virus
HeLa	Henrietta Lacks (uterine cell variety; named for deceased patient)
HepG2	Hepatoblastoma G2
HIV	Human immunodeficiency virus
HNF1α	Hepatocyte nuclear factor 1α
HNF4α	Hepatocyte nuclear factor 4α
IFN	Interferons
Ig	Immunoglobulin
IRF	Interferon regulatory factor

ISGs	Interferon stimulated genes
JNK	c-Jun N-terminal kinase
L	Large surface antigen
L-HDAg	Large delta antigens
M	Middle surface antigen
MAPK	Mitogen-activated protein kinase
MHC	Major histocompatibility complex
mRNA	Messenger RNA
MVB	Multivescular bodies
NC, NCs	Nucleocapsid
NF-κB	Nuclear factor-kappa B
NIH	National institute of health
NK	Natural killer
NLRs	Neutrophil-lymphocyte ratio
NOD	Nucleotide oligomerization domain
NTCP	Na+-taurocholate cotransporting polypeptide
ORFs	Open reading frames
PAMPS	Pathogen associated molecular pattern
PCR	Polymerase chain reaction
PEGIFNa	Pegylated IFNa
PgRNA	Pregenomic RNA
PRRs	pattern recognition receptors
RcDNA	Relaxed circular DNA
Rig	Retinoic acid-inducible gene
RLRs	RIG-I like receptors
RNA	Ribonucleic acid
RT	Reverse transcriptase
S	Small surface antigen
S-HDAg	Small HDAg
SS	Single-stranded
TLR,TLRs	Toll-like-receptors
WHO	World health organization

1. Introduction

Hepatitis, a general expression referring to inflammation of liver, may result from various causes, both infection (ie, viral, bacterial, fungal and parasitic organisms) and non-infectious eg, alcohol, drug, auto immune disease and metabolic disease (Buggs *et al*., 2014).

Hepatitis D virus (HDV) is associated with hepatitis; it is a small spherical RNA enveloped viroid. This is one of five known hepatitis viruses: A, B, C, D, and E. Hepatitis D virus is considered to be a subviral satellite because it can propagate only in the presence of the hepatitis B virus (HBV) (Cunha *et al*., 2015). Hepatitis D virus is a deficient RNA virus that requires the help of hepatitis B virus for its replication and assembly of new virions (Abbas and Afzal, 2013).

Hepatitis delta viruse is transmitted through the same routes of hepatitis B viruse, including blood-borne, sexual, percutaneous and vertical (perinatal) transmission (Fonseca, 2002).

The sexual transmission seems to be less efficient mode of transmission as there is a lower incidence of delta infection in homosexuals compared to intravenous drug abusers. "Clustering" happen within families; the spread within families is not vertical but seems to be horizontal. In spite of vertical transmission can occur, it does not appear to be an important means of transmission. The infection is observed particularly among drug addicts, who are reputably exposed to inoculation with HBV infected blood (Su *et al*., 2006).

Hepatitis delta virus reproduces only in an individual who has coexisting HBV, due either to co-infection of the two viruses or super-infection of a chronic HBV carrier (Lin *et al.*, 2015). Hepatitis delta virus affects an estimated 15 to 250 million individuals worldwide, and the clinical significance of HDV infection is more sever forms of viral hepatitis, acute or chronic, and a higher risk of developing cirrhosis, hepatocellular carcinoma (HCC) in comparison to HBV mono-infection (Surea and Negro, 2016).

The infection is endemic in the Middle East, Africa, Southern Europe and, probably, Latin America. Delta exists in most of the countries of the world where it has been looked for, and the only possible exception being Japan and China. Except of Taiwan, most of the countries of the Far East at the moment appear to have quite a low incidence of delta (Heidrich *et al*., 2009).

In Iraq the studies about HDV are very limited such as a study performed by Ali and Yassen (2001) who studied the prevalence of hepatitis B and D viral infections among hospital personnel in Mosul-Iraq. Another study done by Al-hilli and Yassen (2002) who determined the prevalence of hepatitis delta virus super infection in chronic HBV infection in Baghdad city. Another study done by Al-Jewari *et al.,* (2011) who focused on seroprevalence of hepatitis Delta virus in a sample of Iraqi patients with hepatitis B virus-related liver diseases. Recently in Duhok city another study detected that the infection rate of hepatitis delta was 6.6% in patients with chronic hepatitis B virus (Hussein *et al.*, 2015). Depending our information there is no Iraqi study done in Diyala province about hepatitis delta infection rate, so the preset study designed to assess this point.

1.2 Aims of study.

1. To determine the infection rate of hepatitis D virus in two groups of individuals infected with the hepatitis B, the first one includes blood donors with positive HBsAg and the second includes patients with chronic hepatitis B in Diyala province.

2. To look for the relationship between HDV infection and sociodemographic and clinical characteristic in the study groups such as gender, age, residence, marital status, educational level and occupation,

3. To study the association between HDV infection and risk factors such as family, surgical and dental history, blood transfusion, smoking habit, arkilaih smoking habit, drinking alcohol, endoscopic procedure, tattoo and cupping.