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Risk factors of Hepatitis B Transmission in North West Bank: A Case-Control study

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DEDICATION

إلى روح والدي – رحمه الله– الذي زرع في قلبي الدين و العلم

إلى والدتي – حفظها الله – التي لازمني دعاؤها

إلى زوجي العزيز الذي ساندني دائما

إلى أولادي الأحباء و أختي الغالية نجوى

إلى قريتي الصغيرة– الريحانية– التي لا تزال تنتظر عودتنا على مشارف حيفا

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Risk factors of Hepatitis B Transmission in North West Bank: A Case-Control study

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Declaration

The work provided in this thesis, unless otherwise referenced, is the research's own work, and has not been submitted elsewhere for any other degree or qualification.

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List of Abbreviations

ALT	*Alanine aminotransferase*
Anti-HBc	*Hepatitis B core Antibody*
Anti-HBs	*Hepatitis B surface Antibody*
NNU	*An-Najah National University*
CHB	*Chronic Hepatitis B*
CDC	*Communicable Disease Prevention and Control*
CSWs	*Commercial sex workers*
HAV	*Hepatitis A virus*
HB	*Hepatitis B*
HBc Ag	*Hepatitis B core Antigen*
HBeAg	*Hepatitis B envelop Antigen*
HBIG	*Hepatitis B immunoglobulin*
Anti-HBs	*Hepatitis B surface Antibody*
HBV	*Hepatitis B virus*
HCC	*Hepatocellular carcinoma*
HCV	*Hepatitis C virus*
HCW	*Health care worker*
HIV	*Human Immunodeficiency Virus*
IDU	*Injecting drug users*
IRB	*Institutional Review Broad*
IU	*International Unit*
MOH	*Ministry of Health*
NHANES	*National Health and Nutrition Examination Survey*
NIS	*New Israel Shekel*
NGOs	*Nongovernmental organizations*
OR	*Odds Ratio*
PCR	*Polymerase-chain-reaction*
PHC	*Primary Health Care*
SPSS	*Statistical Package of Social Sciences*
STDs	*Sexually transmitted diseases*
UK	*United Kingdom*
WHO	*World Health Organization*

Risk factors of Hepatitis B Transmission in North West Bank: A Case-Control study

By
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Abstract

Background: Hepatitis B virus (HBV) infection is a significant health problem in Palestine where the risk factors for the disease transmission and their relative contributions are not well studied.

Objectives: The main objective of the study is to find out the risk factors of hepatitis B transmission among the household contact in the north areas of the West Bank; in order to prevent and control this prevalent health problem.

Methods: A prospective case-control study was implemented; 100 hepatitis B virus seropositive cases and another 100 seronegative controls. Univariate analysis and logistic regression model were performed to examine probable risk factors of acquisition of hepatitis B infections.

Results: Univariate analysis showed HBV case-patients were more likely to report having history of blood transfusion, dental visits, hospitalization, Hejamat, sharing shaving equipments, intravenous drug use, and living abroad. The logistic regression model revealed history of dental visits to be the most significant risk factor, (P value <0.001, OR 5.6; 95% CI 2.8-11.1).

***Conclusion*:** The presence of these risk factors emphasizes the need for both increasing the use of hepatitis B vaccines and risk-targeted public health education. Development and enforcement of appropriate infection control guidelines for dental care services are important to prevent HBV transmission. Further research with more sample size is recommended to further explore the rare risk factors.

Chapter One

Introduction and Literature Review

1.1 Background:

Communicable diseases remain a significant public health problem despite the progress in diagnosis, treatment, and prevention, the widespread use of antibiotics and vaccination. Nowadays, sexually transmitted diseases (STDs); food borne diseases; emergence of antimicrobial resistant bacteria; vector borne diseases and vaccine preventable diseases are still considered of high concern at both national and international levels[(1)].

Hepatitis B virus (HBV) infection is widely present worldwide, approximately one third of the world's population has been exposed to the virus and an estimated 400 million people are chronically infected [(2)]. Approximately 25% of them may be exposed to death due to chronic liver disease or hepatocellular carcinoma (HCC) [(3).]

HBV infection is the leading cause of acute and chronic hepatitis. Whereas acute infection may last for several months, chronic infection is often lifelong and can lead to liver failure, cirrhosis and HCC [(4).] The high HBV related morbidity and mortality create global substantial burden of the disease.

1.1.1 Biological characteristics of the infectious agent

HBV is an enveloped DNA virus from the Hepadenaviridae family, structurally it consists of partially double stranded DNA, and neocleocapsid core antigen (HBc Ag) that encloses the viral DNA, The viral envelope encoded by the *S* gene that represents hepatitis B surface antigen (HBsAg). See Figure 1.

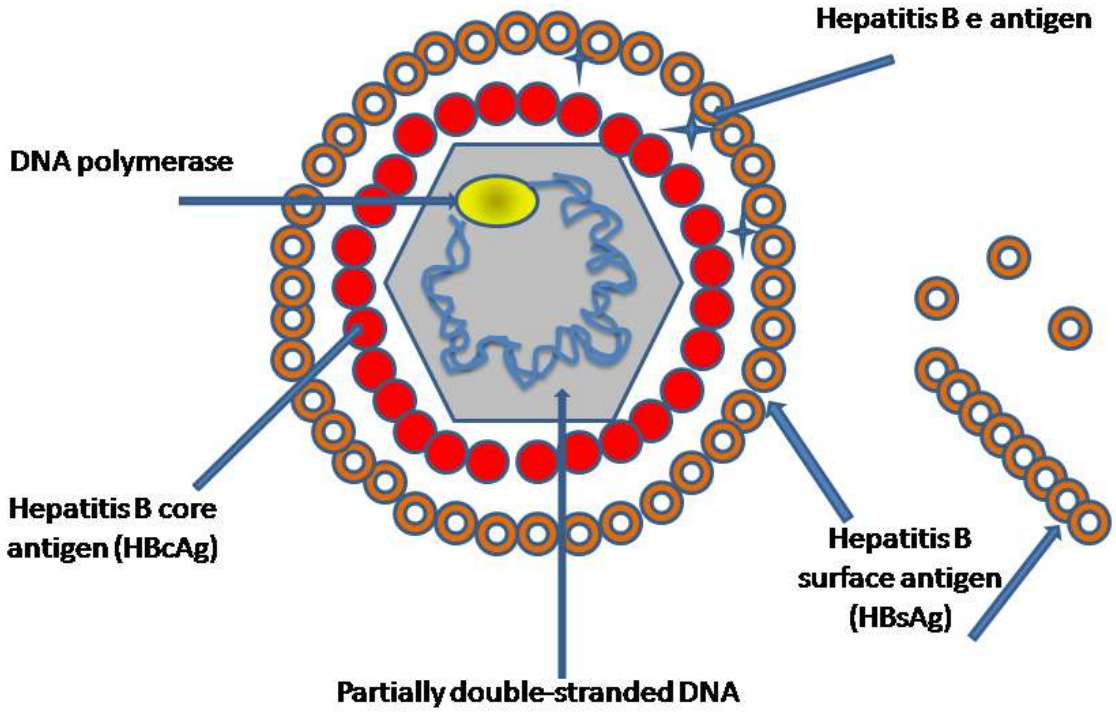

Figure 1: Structure of the Hepatitis B virus

Hepatitis B envelop antigen (HBeAg) is a circulating peptide, Which is derived from the core gene, and then it is modified and exported from liver cells, serving as a marker of active viral replication as it is substantially related to its infectivity [(4)].

The immunogenicity and antigenicity of the virus' envelop can be retained after the exposure to either ether, acid (PH=2.4 for 6 hours) or heat (98^0C for 1 minute or 60^0C for 10 hours). However these conditions can't be used for the virus inactivation because of incomplete destruction of the virus if its concentration is high, while the antigenicity of the HBsAg can be destroyed by exposure to 0.25% of sodium hypochlorite for 3 minutes, and the virus infectivity can be completed by boiling of the serum for 2 minutes, autoclaving (121^0C for 20 minutes) or dry heat at 160^0C for 1 hour. These facts are important in infection prevention and control being used as significant step (with the vaccination) toward HBV eradication [(5)] .

1.1.2 Pathology

The clinical manifestation of the liver disease ranges from acute (including fulminent hepatic failure) to chronic hepatitis B (CHB), cirrhosis and HCC.

Acute HB diagnosis in adults is based on clinical features that vary from mild to fulminent form and may last from 6 weeks to 6 months, as jaundice (yellowing of skin and eyes), dark urine, fatigue, nausea, and vomiting with abdominal pain. While in infants it is mostly asymptomatic, just 5-15% of children from 1-5 years old may produce typical illness. The laboratory criteria of acute HB are anti-HB core antibodies (anti HBc- IgM) positive or hepatitis B surface antigen (HBs Ag) positive [(6)].

No symptoms are associated with CHB, but its diagnosis depends on laboratory investigations of the virus serological markers; specifically when HBs Ag test is positive for at least 6 months, or Anti- HBc (IgM) negative with positive result of one of the following tests: HBsAg, HBeAg, HBV DNA[6,]. The inflammatory destruction of the hepatocytes accompanied by progressive fibrosis, and the extent of fibrosis determine the prognosis and the severity of the disease, and continuous destruction lead to liver chirrhosis which can be defined as a diffuse destruction of the hepatocytes which is the end stage of the liver disease, characterized by high morbidity and mortality [3].

1.1.3 Natural History:

The patient with HBV infection may develop acute icteric infection (30-50% of them) that may lead to complete clearance of the disease and life-long immunity, but alternatively the host may develop chronic infection [7].

Based on viral-host interaction, the HBV infection has three stages: immune tolerant phase, immune clearance phase, inactive carrier phase with or without viral reactivation.

- Immune tolerant phase: the patients remain HBeAg positive after the acute infection, with high level of serum HBV DNA, normal ALT with little or no symptoms, and minimal histological activity in the liver. This phase may last for 2-4 weeks mostly among

children or young adults but may last much more (perhaps for years) among adults. In this phase the patient is highly contagious and can transmit the disease easily [8].

- Immune-clearance phase: the patients lose toleregenic effect, and the immune- mediated lyses of the infected hypatocytes become active with increasing levels of ALT and decrease in serum HBV DNA. This may last for several months to years, and then it is followed by the carrier phase [9].

- Carrier phase: in which sero-conversion of the HBeAg to HBeAb, and low level of HBV DNA or even undetectable reflecting no or low replication effect of the virus, normal ALT, and no to mild hepatic injury. The inactive carrier may last for several years or life-long, then the patients can spontaneously resolve from the disease and develop HBsAb. However, reactivation of the chronic infection, spontaneously or by immuno-suppresion induction, could occur with high level of ALT and HBV DNA, and moderate to severe liver histological damage [10].

1.1.4 Epidemiology

The prevalence of HBV carrier varies worldwide according to the region, and categorized by WHO into low, intermediate and highly endemic areas [2, 11]. See Fig 2.

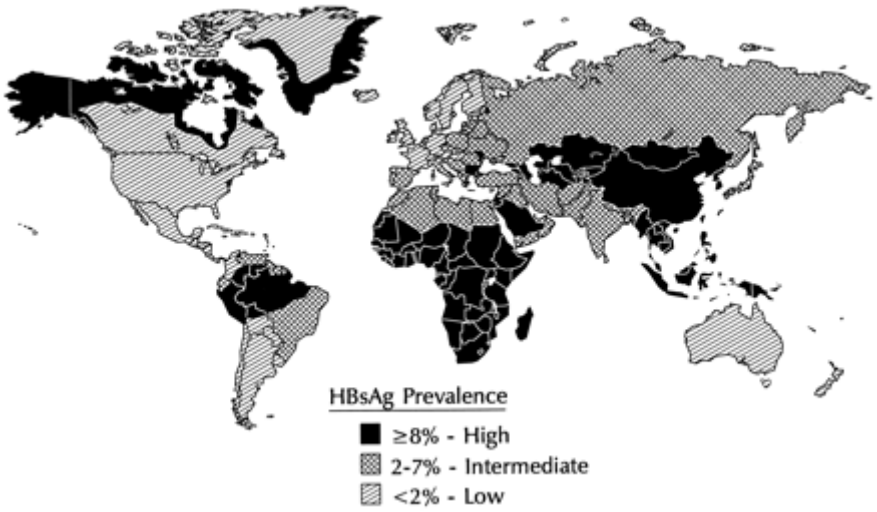

Figure 2: Geographic distribution of chronic HBV infection[4].

- HBV High endemic areas: mainly in developing countries, such as Sub-Saharan Africa, South East Asia, China and Amazon Basin regions, where more than 8% of the population is HBV carrier and 70-95% have past or present HBV infection. This indicates high asymptomatic infection during infancy and childhood, and chronic liver disease and hepatic carcinoma [11].

- HBV moderate endemic areas: parts of Eastern and Southern Europe, Middle East region, Japan, and part of South America, whereas 10-60% of the population has evidence of hepatitis infection, and 2-7% are chronic carriers. In these areas mixed

patterns of transmission exists during infancy and early childhood and adulthood [11].

- HBV low endemic areas: mainly in developed countries as in North America, Northern and Western Europe and Australia where 5-7% of the population have HBV infection and 0.5-2% of them are chronic carriers. In this category, the infection occurs during the adolescence and adulthood specially in high- risk groups; injection drug users (IDU), homosexual males, health care workers (HCW), and patients on blood transfusion or hemodialysis [2, 11].

In the Middle East region, the prevalence of HBV carrier among adults varies from low (<2%), to intermediate (2-5%), to high (>5%). For example, Bahrain is among the low endemic area with a prevalence of 0.9-1.25%, while Libya and Emirates are with intermediate prevalence, but Republic of Yemen is highly endemic of HBV (18.5% of the population). In Palestine, the prevalence of HBV carrier is 5-6% (this number is before 1997), while it is 1%in Israel [12].

Palestine has been categorized as HB moderate endemic area. The incidence rate decreased from 0.98 per 100,000 in 2008 to 0.5 in 2009, then increases to 1.1 per 100,000 population in 2010, to decrease to 0.9 in 2011, while the incidence rate of the carriers was 39.37 per 100,000 population in 2008 decreased to 35.1 in 2009 and increased to 36 per 100,000 population in 2010, then decreased to 29.3 per 100,000 in 2011[13]. These numbers are

expected to shift to the left in the future after the adoption of the universal infant vaccination in 1992 into the Palestinian Expanded Program of Immunization, and the strong surveillance policy that is being implemented by the ministry of health (MoH).

1.1.5 Mode of transmission:

Hepatitis B virus is transmitted through percutaneous or mucosal contact with infected blood or body fluids. Infection can occur perinatal, i.e. from mother to child during childbirth, through household and sexual contact, sharing of infected needles and through occupational or medical exposure [14].

In countries with high hepatitis B prevalence, transmission occurs mainly perinatally and horizontally during early childhood, while in low endemic countries, transmission is largely limited to groups with risk behavior such as high risk sexual behavior and intravenous drug use [11].

The transmission of HBV from infected mothers to their babies is the most important determinant of the prevalence of HB, especially in high endemic areas. The peri-natal mode of transmission can be occurred through three possible routes: trans-placental (in utero), natal (during delivery), post-natal (during baby care) making the babies of infected mothers at high risk of getting HB infection [11, 14]. The risk of perinatal transmission from a positive mother to her child during childbirth is high

and varies from 10-30% for HBe Ag negative mothers to 70-90% for HBe Ag positive mothers[4].

The sexual mode of transmission make homosexual , bisexual male, female sex trade workers and sexual partners of infected persons a high risk group, emphasizing on a fact that HB is a STD, and can be transmitted by infected semen and vaginal secretions [15] . Hepatitis B virus can also be transmitted by saliva ,but it is rare, which was proved in a study after examination of the parotid tissue of infected patients [16] .

Hepatitis BV can survive more than 7 days on inanimate surfaces [17], causing transmission via contaminated equipments as in injections, and other health-care procedures, by percutaneous mode of transmission, which includes also the transfusion of contaminated blood and its products, as well as needle sticks (including tattooing) or other sharp equipments, making HCWs a high risk group, as well as patients with frequent blood transfusion (e.g. hemodialysis patients) and injected drug users [9] .

Person-to-person transmission with house-hold contacts is another route of HBV transmission, the exact mechanism of which is unclear, but may be explained by contamination of body fluids and secretions on the surfaces at home (e.g. saliva), and frequent contact of the skin and mucosal membrane with these secretions[18] .

1.1.6 Prevention and Control of Hepatitis B

1.1.6.1 Primary Prevention:

Primary prevention aims to prevent a disease from occurring. For hepatitis B, primary prevention is possible through vaccination, implementation of universal blood and body fluids precautions, screening of blood donors and health education of the public regarding patterns of transmission. A safe and effective vaccine has been available since the early 1980s. Different approaches to vaccination exist from selective vaccination of high risk groups to universal childhood vaccination [(11)].

Hepatitis B Vaccine

Discovering the molecular biology and the consequences of the genetic material of the virus led to the successful development of vaccine in 1982. This has increased the capability of eradication of the chronic HBV infection, until the hepatitis neonatal vaccination is accepted globally[(7).]

The usual immunization schedule recommended for prevention of Hepatitis B consisting of three doses of the vaccine, the first two priming are one month apart, while the third dose is given after 5 months of the second dose, infants born to infected mothers may be given HB immunoglobulin(HBIG) as an additional protection[(4).]

The duration of immunity after HB vaccination was studied by measuring the decline of Anti-HBs level finding that there is rapid decline in the first year after the third dose of vaccination among adults, then gradual decrease continue after 5 years the concentration becomes < 10 mIU/ml in 7-50 % of the vaccines. (4)

Universal blood and body fluids precautions:

They are recommendations used to prevent blood – borne pathogens transmission in health-care settings, because the infectious potential of human blood and other body fluids is not always known. The use of gloves and other protective barriers to prevent hands contamination when handling blood and other body fluids. While frequent hand washing immediately after contact with blood and other body fluids, and after use of gloves. In addition needle stick prevention including no recapping, and proper disposal of used needles and other sharp instruments (waste management), as well as disinfection and sterilization of contaminated equipments. (19)

1.1.6.2 Secondary prevention:

It is aimed at early disease detection to allow interventions to prevent progression of the disease and its complication.

Screening of high-risk groups of HBV infection is an effective secondary preventive measure. These groups include intravenous-drug users, homosexual men, persons who have heterosexual contact with multiple

partners, household contacts of persons with chronic HBV infection, hemophiliacs, hemodialysis patients and staff, inmates of long-term correctional facilities, persons with occupational exposure to blood and infectious body fluids (HCWs), and institutionalized persons with developmental disabilities [4].

No specific management for acute hepatitis, but just supportive and symptomatic treatment is indicated. In terms of for chronic infection, many antiviral drugs were studied and proved to reduce the HBV replication, and normalize the liver enzymes including alpha-2b interferon and nucleotide analogues such as lamivudine.[4]

1.1.7 Surveillance:

Public health surveillance is of the important public health tools to prevent and control infectious diseases and to identify changes in disease occurrence.[1]. Information collected through surveillance is necessary to evaluate and adjust control policies. In Palestine a disease notification system is well established, in which the Public Health Law requires that all newly diagnosed hepatitis B infection cases, both acute and chronic, are to be reported to the preventive medicine clinic at the regional health directorates. Subsequently, the preventive medicine clinic in-charge physician contacts the patients and their families and invited them to the clinic, where epidemiological data such as sex, age, occupation, marital

status, and most likely transmission routes are reported and detailed through laboratory examinations.[47]

1.2 Significance of the Study:

Although HBV infection is preventable through safe and effective vaccination and health education, it is highly associated with high morbidity and mortality, high economic burden and the development of HCC.[4]

The identification of the demographic and behavioral determinants of the disease transmission is important to highlight the risk factors responsible for its spread, improve the knowledge of people in general and specifically the house-hold contact specifically, and to define the target population in order to conduct appropriate measures to prevent and control HBV .

1.3 Aim and Objectives

1.3.1 Aim

The aim of this study is to find out the risk factors of hepatitis B transmission in the northern area of West Bank; in order to get appropriate recommendations to limit its means of transmission and to decrease its morbidity and mortality.

1.3.2 Specific Objectives

The study will try to achieve the following objectives:

- To determine the risk factors of hepatitis B mode of transmission among the household contact, which can be categorized into:
  - Exposure to health-care services: blood transfusion, invasive surgery, hemodialysis, dental visit, and hospitalization.
  - Personal and community-based practices: Hejamat (phlebotomy), sharing toothbrush or shaving equipments, barber visit for shaving, jaundice, piercing, tattoos, history of Haj and Omra, intravenous drug use, living board including stay in Israel for at least one year, history of jail for more than 3 months, and history of STDs.
- To identify the relationship between the hepatitis B transmission and the demographic and personal characteristics as gender, occupation, family size, socioeconomic status, and residency

1.3.3 Hypothesis:

- There is no difference between the HB patients and the controls in relation to health-care services exposures.
- There is no difference between the HB patients and the controls in relation to personal and community-based practices

- There is no difference between the HB patients and the controls in relation to demographic and personal characteristics

1.4 Literature review:

1.4.1 Prevalence of HBV:

Worldwide, many studies tried to investigate and assess the prevalence of HBV, and the results of these studies varied in developing countries than that in the developed ones. In the USA, a study conducted to assess the trend of the prevalence of HB infection after the wide spread of its vaccination. It was done among the National Health and

Nutrition Examination Survey's (NHANES 1999-2006) participants aged ≥ 6 years, and the results showed that the prevalence of HBsAg and Anti-HBc were 0.3% and 5% respectively [(20)]. In Canada the prevalence of HB carriers was 0.5%- 1% among population in 1998\1999 with an incidence rate of 2.3\100,000 population, according to an epidemiological review of studies and surveillance reports in that year [(21)] .

In Egypt, a cross-sectional study targeting the blood donors aimed to assess the prevalence of HBs Ag and Anti-HCV, found that the HBsAg is positive among 1.4% of blood donors [(22).] It showed as well demographic determinants as male aged > 29 years, urban areas residency, and occupation as manual workers are most predominant risk factors. In Egypt, another community – based study targeting the endemic area with

Schistosoma mansoni found that the prevalence of HB (HBsAg and\or Anti-HBc) and hepatitis C virus (HCV) (Anti – HCV) were 19.6% and 10.3% respectively and 5% were positive for both[23].

In Palestine, a national survey conducted in 2000 by MoH showed the prevalence of HB among students as 3.4%, which is lower than that reported in the MoH reports; this variation could be due to difference in target population and sample size [24].

1.4.2 Risk factors of HBV

Many studies were conducted to assess different risk factors of HB transmission that vary according to the social and behavioral determinants in every corresponding community, and to the target population used in the study (Table 1).

In Nigeria a case-control study design was performed among patients admitted to the hospital to find out the risk factors of HB transmission, it showed that several high risk behaviors and practices as the use of unsterile medical equipments, multiple sexual partners and scarification in that community lead to HB transmission[25]. Across-sectional study in Brazil among tattoo individuals found an increasing number of tattoos, and non-professional tattoo makers which have significant associations with HB transmission [26].In Italy a cross-sectional study was conducted among prisoners in order to find out the determinants of HB, HCV and HIV co-

infection showed that the educational level, intravenous drug users and sharing needles are the most common risk factors of this diseases [27].

But in Bosnia and Herzegovina, a prospective case-control study conducted on the family members of the HB chronic carriers to identify the interfamilial transmission of HB risk factors, emphasized that the vertical mode of transmission (from the mother) within the family is the main risk factor, and the family members contact with index case with HBeAg positive had higher proportion of HBs Ag positive than those contact with HBe Ag negative index cases [28]. In Singapore a population study conducted to identify the risk factors of HB transmission among the house-hold contact of acute HB patients, found that contact with a symptomatic interfamilial HBs Ag positive carrier is the main one, while sharing personal and house-hold objects as razors and toothbrushes is associated with its transmission[29].

In Moldova two case-control studies, targeting acute cases among adults and children; were conducted to identify the mode of transmission of acute HB. Results showed that injection during dental visit and hospitalization were the most significant in adults, while among children was only during hospitalization [30]. The sexual mode of transmission of HB was unproven in some studies, as in a prospective cohort study done in Jamaica targeting the STDs patients to determine the prevalence of HIV, HCV and HBV and their risk factors[31], as well as in a case-control study conducted in the UK among heterosexual patients attending the

genitourinary medicine clinics to examine whether the heterosexual activity is a risk factor for acquiring HB infection by measuring the HB markers among the heterosexual patients[32]. On the other hand another study in Uroguay proved this association, this study tried to evaluate the sexual transmission of HIV, HCV and HBV by measuring the prevalence of these viruses among males transvestite commercial sex workers (CSWs). The results showed high prevalence of HB among them, making prostitution a risky behavior with HB transmission [33]. Another case-control study done in South Africa took the black patients with a history of syphilis as a case and blood donors free of syphilis as a control and measuring HB markers in their serum, the study proved a significant higher incidence of HB among females with a history of syphilis than males which may support an assumption that HB can be transmitted easier from infected male to the female than vice versa [34]. A cross-sectional study in Brazil among viral hepatitis patients showed that the prevalence of HB was higher among multiple sexual partners, and injecting drug users (IDU), emphasizing that sexual mode of transmission plays a major role in HB transmission [35]. Another cross-sectional population survey in Brazil to assess the prevalence of HB among population and the risk factors of its transmission showed that health-care jobs and previous hospitalization are the major risk factors [36].

A history of contact with HB, extramarital sexual activity, and IV-drug use, were the major risk factors of chronic HB transmission among the

population in a case-control study done in Iran [37], while others found that unqualified dental care, un-sterile injection, sharing sharp instruments (as blades), and sharing tooth brush are the major risk factors in HB mode of transmission in developing countries as in Pakistan[38]. Those were the results of a case-control study done among blood donors, to asses the prevalence of HBV infection and it's transmission risk factors [38], and in Pakistan also a case-control study done among patients admitted to a hospital to find out the risk factors of HB and HC transmission and assess their knowledge about mode of transmission of these two diseases; emphasized the previous results as well as exposure to medical procedures and tattooing [39]. Injection in health – care settings was found to be the major source of HB infection in a case-control study done in Pakistan targeting the acute HB cases while minimizing other mode of transmission as during dental care or hospitalization even blood transfusion [40].

In Turkey, a case-control study design among acute cases and population controls, aimed to identify HB risk factors, found that living with HB positive parents (house-hold transmission), spouse (sexual transmission), and hemodialysis were strongly associated with HBV transmission and minimizing the other risky behavior mode of transmission[41].

In Egypt a case-control study to define the risk factors of HB transmission among acute HB patients, found that providing injections, injected drug use, being in military, house-hold contact to carriers, and

exposure to invasive medical procedures are the most significant [42] . In Jordan, a similar study design among population admitted to a hospital, showed that the most dominant risk factors are: sharing toothbrushes, unhygienic dental care and living abroad for at least 1 year are the most significant risk factors [43].

In Palestine, several studies were implemented to assess the prevalence of HBV infection among various population groups. A cross sectional study was done to detect the prevalence of HBV and HCV and its associated risk factors among hemodialysis patients in Gaza [44]. The results showed that the prevalence of HBV among hemodialysis patients was 8.1%, and its transmission was found to be associated with the age of the patients, educational level, duration of dialysis, number of blood transfusion units, and a history of being treated abroad and place where the patient was treated.

A cross sectional study conducted at north area of the West Bank in Palestine to assess the prevalence of Anti-HBc Ab among blood donors and the prevalence of HBV DNA among the Anti-HBcAb positive donors, showed high prevalence of HBV DNA (92%)among positive Anti-HBcAb donors, indicating the high prevalence of occult HBV among Palestinian blood donors[45].

Moreover, Jadallah et .al[46] showed that the prevalence of HBsAg among high risk group as hemodialysis, kidney transplant and blood

dependent patients; and non-vaccinated HCWs was 29.4%, 17%, 22.5% and 9.6% respectively, while the hemodialysis and kidney transplant patients are the highest contagious

Table 1: Summary of the studies included in the literature review

Risk factors	***Type of study***	***Place and year of study***
Use of unsterile medical equipments, multiple sexual partners, and scarification	Case - control	Nigeria\ 2010
Increase number of tattoos and non professional tattoo	Cross sectional	Brazil\2002
Educational level, IDU, and sharing needles.	Cross sectional	Italy\2007
Vertical transmission and contact with HBe Ag positive carrier	Case - control	Bosnia\2009
House-hold contact HBV carrier and sharing their objects.	Cross sectional	Singapore\1985
Dental visit and hospitalization among adults, and hospitalization among children.	Case - control	Moldova\1999
Sexual transmission	Cross sectional	Uroguay\2003
Sexual transmission	Case - control	South Africa\ 1984
Sexual transmission and IDU	Cross sectional	Brazil\2002
HCW and hospitalization	Cross sectional	Brazil\2010
Sexual transmission , IDU and contact with HB	Case - control	Iran\2005
Dental visit, sharing sharp instruments and toothbrushes, and unsterile injection	Case - control	Pakistan\2005
Dental visit, sharing sharp instruments and toothbrushes, unsterile injection, history of medical procedure, and tattooing	Case - control	Pakistan\2009

Risk factors	***Type of study***	***Place and year of study***
Injection in health-care settings	Case - control	Pakistan\2003
House-hold and sexual transmission and hemodialysis	Case - control	Turkey\2011
Providing injection, IDU, military, house-hold contact of HB carrier, and history of invasive medical procedure.	Case - control	Egypt\2010
Sharing toothbrush, dental care and living abroad> 1 year	Case - control	Jordan\2010
Residency, family size, tattoo, house-hold contact	Cross sectional	Palestine\2011

Chapter Two

Methodology

2.1 Study Design:

A case-control study was conducted to evaluate the potential risk factors of HB transmission among HB patients. All incident cases of HB infection during the period from Dec 2011 to Dec 2012 and who meet the inclusion criteria were enrolled in the study.

2.2 Study setting:

The study was conducted at the preventive medicine clinic in the primary health care (PHC) departments in north area of the West Bank (Tubas, Jenin, Nablus, Tulkarim, and Qalqelia).

These clinics were selected for the study because all newly discovered HB cases in any health sector (including private or public clinics, the NGOs and blood banks) should be notified to the preventive medicine clinic in the primary health care departments.

2.3 Study Population:

The study population consisted of all new diagnosed hepatitis B patients, within the past six months, attending the preventive medicine clinic in the PHC centers in north areas of the West Bank depending on the diagnosis policy that is followed by the MOH in Palestine. The controls are

the house-hold contact of these cases with HBsAg negative, within 5- years age categories.

2.3.1 Eligibility for the study

Inclusion criteria: All newly diagnosed (within six months) hepatitis B positive cases (acute or chronic) and living in north area of the West Bank was included in the study. The controls were selected from the hepatitis B negative house-hold contact of the cases.

Exclusion criteria:

1. Old diagnosed HB patients, for more than six months.
2. Less than 20 years old (because they had already vaccinated during infancy; HB vaccination started at 1992 in Palestine).

2.3.2 Defining cases and controls

A Hepatitis B case was defined as any person with a confirmed diagnosis of hepatitis B infection according to MOH policy.

Based on the MOH policy; diagnosis of acute HB is based on onset of symptoms and jaundice or elevated serum alanine aminotransferase levels (ALT>200), and confirmed by laboratory tests (Anti- HBc IgM positive, or HBsAg positive, IgM anti- HAV negative and not known to have chronic HB, while the chronic case can be diagnosed as probable case if has a single HBsAg positive or HBV DNA positive, or HBeAg positive

but not meeting the case-definition of acute HB, and confirmed if it meets either of laboratory criteria for it's diagnosis Anti HBc-IgM negative and positive result of one of the following: HBsAg, HBeAg, or HBV DNA, or positive result of HBsAg or HBV DNA or HBeAg two times at least 6 months apart(any combination of these tests performed 6 months apart are acceptable) [47] .

The control group consisted of cases' house-hold subjects with no laboratory evidence of old or active Hepatitis B infection (seronegative).

2.3.3 Identification of case patients and control subjects

Case patients were identified through voluntary reports to national or regional systems for surveillance of infectious diseases in Palestine during a one-year period from 1 January 2012 through 31 December 2012. At each preventive medicine clinic, nurses in charge were required to identify a control subject from the case relatives.

The surveillance policy of the Palestinian ministry of health (MOH) for all health sectors (private, nongovernmental organizations (NGOs), and blood banks); is to notify the preventive medicine clinic in the PHC centers about any new hepatitis B cases; in order to give the appropriate health care to the patients, and to screen the house-hold contacts then vaccinate the hepatitis B negative ones.

2.4 Sample size and sampling method:

2.4.1. Sampling method:

All cases attended the preventive medicine clinic in the PHC centers in the area of the north area West Bank who were diagnosed with hepatitis B infection during the study period were included, and one of their house-hold contact that confirmed free of HB as controls (convenient sampling).

2.4.2. Sample size:

During the time period of the study (one year) 100 cases and 100 controls were enrolled.

2.5 Data Collection Tool:

An interviewer administered questionnaire was used to achieve the study objective. It was constructed by the researcher depending on the literature [30, 37-43]

The questionnaire (annex 1) consisted of 36 questions, mainly covers the following areas: demographic characteristics of the participants, the source of HB detection and vaccination status and Hepatitis B transmission determinants.

In order to explore more on the mode of transmission, the Hepatitis B transmission determinants part was categorized into three parts

- The first is about health-care services related determinants, such as receiving blood, invasive surgery (including endoscopy procedure), hemodialysis, dental visit, and hospitalization

- The second is about the family source of infection, such as house-hold contact with HB carrier or jaundiced patient, family history of HB

- The third division is about personal and community-based practices as Hejamat (phlebotomy, a procedure in traditional medicine of Palestine that seems similar to bloodletting), intravenous drug use, sharing shaving instruments, sharing toothbrush, shaving at barber, piercing, tattoos, history of Haj and Omra, jail history (for more than three months), STDs history, and living abroad for at least one year (including working in Israel).

Prior to data collection, the questionnaire was pre-tested with a convenient sample of 10 candidates of the study population to ensure the clarity, time, and ease of administration. Refinements were made on the basis of feedback from the pre test. Those who participated in the pre-testing were excluded from the study sample.

Both cases and controls were interviewed by the preventive medicine nurse. All nurses were provided with a standard training on how to interview the participants and clarifying the questionnaire; emphasizing

that each factor happened during the last six months before detecting the HB infection.

2.6 Study Variables:

2.6.1 Dependant variables: The hepatitis B infection.

2.6.2 Independent variables:

The hepatitis B transmission determinants: the exposure to the following risk factors within past 6 months of their infection.

A. Demographic variables*:*

1. Age: 20-30, 31-40,41-50,>50.
2. Gender: male, female.
3. Residency: camp, village, city.
4. Level of the education: elementary, secondary, high education, illiterate.
5. Occupation: office employee, HCW, soldier, self-employee, housewife, businessman, student, manual work, non-employee, others.
6. Marital status: single, married, divorced, and widow.
7. Family size: less than3, 3-5, 5-8, more than 8.

8. Socioeconomic status: less than3000 (NIS), equal or more than 3000.[48]

B.1.Source of HB detection:

After blood donation, pregnancy profile tests, pre-employment exam, post symptoms diagnosis or after screening of contacts.

B.2. ***Vaccination****:*

1. History of vaccination of HB: Yes, No.

C. Hepatitis B transmission determinants:

The exposure to health-care:

1. History of blood transfusion: Yes, No.
2. If Yes; frequency of transfusion: 1, 2, 3, >3.
3. History of invasive surgical operation (including endoscopy): Yes, No.
4. If Yes; frequency of operation: 1, 2, 3, >3.
5. History of hemodialysis: Yes, No.
6. If Yes, frequency of dialysis per a week : 1, 2, 3.
7. History of pre-used needle stick: Yes, No.
8. History of dental visit: Yes, No.

9. If Yes; frequency of visit: 1, 2, 3, >3.

10. History of hospitalization: Yes, No.

Source of family member infection:

11. Direct contact with HB carrier or jaundiced patient: Yes, No.

12. Family history of HB: Yes, No.

13. If yes, the relative is: son/daughter, mother, father, husband/wife, and brother/sister.

Personal and community-based practices:

14. History of Hejamat (phlebotomy). Yes, No.

16. History of sharing shaving istruments: Yes, No.

17. History of pre-used toothbrush (sharing): Yes, No.

18. History of barber visit (for shaving): Yes, No.

19. Piercing: Yes, No.

20. Tattoos: Yes, No.

21. History of Haj and/or Omra: Yes, No.

22. Intravenous drug use: Yes, No.

23. Living aboard for one year at least (including Israel): Yes, No.

24. History of jail (more than 3 months) : Yes, No.

25. History of STDs: Yes, No.

2.7 Data analysis Plan:

The Statistical Package of Social Sciences (SPSS) version 17 was used for data entry and statistical analysis.

- Descriptive statistics were computed for the demographic factors of the cases and the controls, and to assess the personal characteristics of the participants.
- Univariate analysis was performed with odds ratio (OR) calculated for risk factors with Chi-square test
- Characteristics that were found, through univariate analysis, to be significantly associated with HB infection were entered into a multivariate logistic regression model, to rule out the confounding factors and to determine which characteristics were independent predictors of HB infection status of the participant O.R. was calculated for the all variables simultaneously.
- Confidence interval was set at 95%. *P*-value of less than 0.05 was considered to indicate statistical significance.

2.8 Ethical Consideration:

The study was approved by the Institutional Review Broad (I.R.B.) of An-Najah National University (ANU) (annex 2) and approvals were obtained from the Palestinian MoH.

Every participant in the study received an explanation about the purpose, confidentiality of the study and participation in the study was voluntary and based on the patient's ability to give an informed consent. A signed consent form was obtained from all participants.

All data and information gathered were treated with confidentiality and used exclusively for the objectives of the study.

Chapter Three

Results

The study included 200 participants ;(100 hepatitis B cases and 100 controls), who agreed to participate in the study and filled the questionnaire. The cases and the controls were matched for age; within 5 years age categories.

3.1 Socio-demographic characteristics

Table 2 shows social and demographic characteristics of participants. Nearly half of them (57%) were male, and 43% were female. The majority live in villages (58.5%) and 20% of them live in camps. Sixty eight percent (68%)of the participants claimed to have primary or secondary education and 3% of them were illiterate. The majority of study participants (77%) were in the age group 20-40 years. About 31% of the participants have family size of 5 or more, and 73% of them were married. Regarding the occupation and income, the majority of the participants were students or employee and 11.5% and 8% were manual laborers (not office employee) in Israel and soldiers, respectively. Sixty eight (68.5%) of the participants lived with income less than 3,000 NIS. We observed no significant difference between the two groups for all the socio-demographic characteristics, except for the gender and occupation. Males were predominant in the case group, and females were more in the control group (Table 2).

Table 2: Distribution of socio-demographic characteristics of the cases and controls

Variable	*Case (n=100)* *Frequency (%)*	*Control (n=100)* *Frequency (%)*	*P value*[$]	*Total (n=200)* *Frequency (%)*
Age:				
▪ 20-30	34(34)	41(41)	0.394	75 (37.5)
▪ 31-40	38(38)	41(41)		79 (39.5)
▪ 41-50	21(21)	14(14)		35 (17.5)
▪ > 50	07(07)	04(04)		11 (05.5)
Gender:				
▪ Male	69(69)	45(45)	0.001	114 (57.0)
▪ female	31(31)	55(55)		86 (43.5)
Residency*:*				
▪ City	22(22)	21(21)	0.984	43 (21.5)
▪ Village	58(58)	59(59)		117 (58.5)
▪ Camp	20(20)	20(20)		40 (20.0)
Level of education:				
▪ Illiterate	04(04)	02(02)	0.615	06 (03.0)
▪ Elementary & Secondary	69(69)	67(67)		136 (68.0)
▪ University	27(27)	31(31)		58 (29.0)
Occupation:				
▪ Manual	14 (14)	09 (09)	0.005	23 (11.5)
▪ HCW	06(06)	04 (04)		10 (05.0)
▪ Military	14(14)	02 (02)		16 (08.0)
▪ Others*	66(66)	85 (85)		151 (75.5)
Marital status:				
▪ Married	75(75)	71 (71)	0.524	146 (73.0)
▪ Unmarried	25(25)	29 (29)		54 (27.5)
Family size:				
▪ <5	66(66)	71(71)	0.447	137 (68.5)
▪ ≥5	34(34)	29 (29)		63 (31.5)
Socioeconomic status:				
▪ <3000NIS	68(68)	69 (69)	0.87	137 (68.5)
▪ ≥3000NIS	32(32)	31(31)		63 (31.5)

*Others: students, employee, …etc, [$] Chi Squared test

For vaccination, only 10 of the participants (5%) claimed to be vaccinated for hepatitis B (Figure 3); 3 of them were cases, while the other 7 were controls.

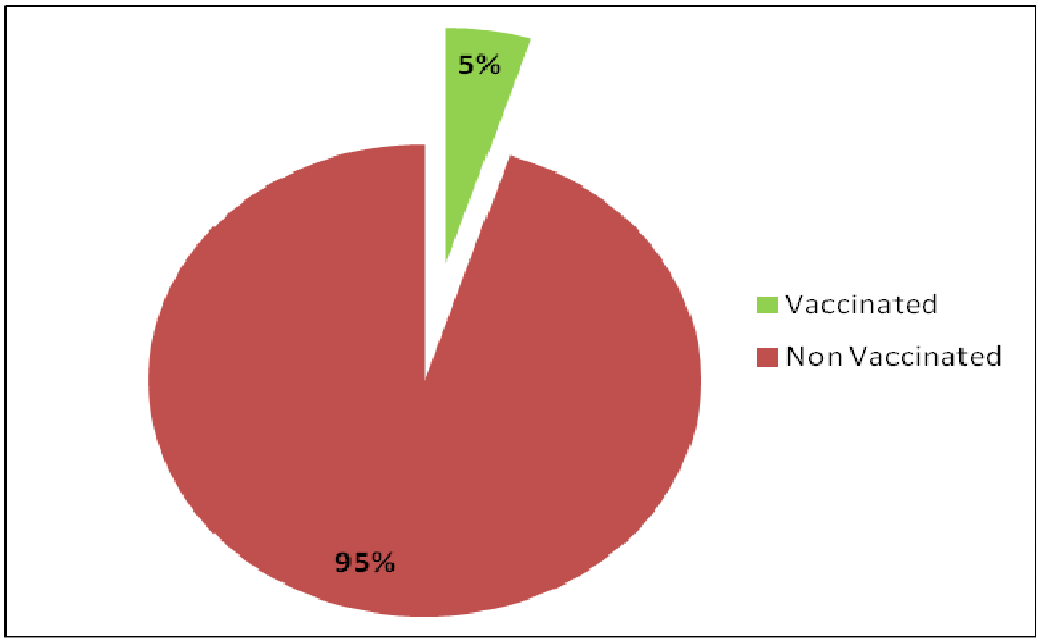

Figure 3: Distribution of participants regarding the vaccination status

For the family history, 47% of the HB cases had a family member with history of HB infection. Perinatal transmission (from mother) constitute the most frequent family member with history of HB infection among the HB cases, (Figure 4)

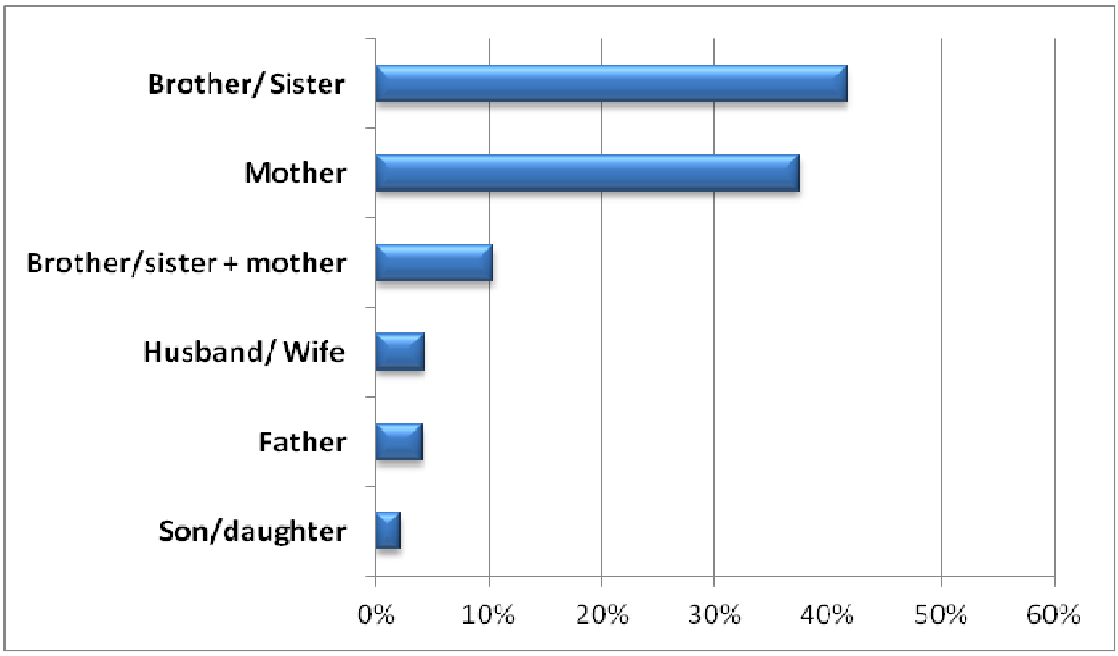

Figure 4: Distribution of HB cases by family members with history of HB infection (n=47)

3.2 Mode of HB detection

Evaluating the manner and how the cases were detected, we found that 29% of the cases were discovered after blood donation. This constitutes the main source of detection of HB in the study, where a pre-screening test of the HBsAg is being done for the donors before blood transfusion of the blood unit (or any of its products). Pre-employment examination comes second; then the pregnancy profile tests discovered 22% of the female cases. Other sources are post symptoms diagnosis and screening of contact discovered (13%) and (11%) of the cases respectively (Figure 5).

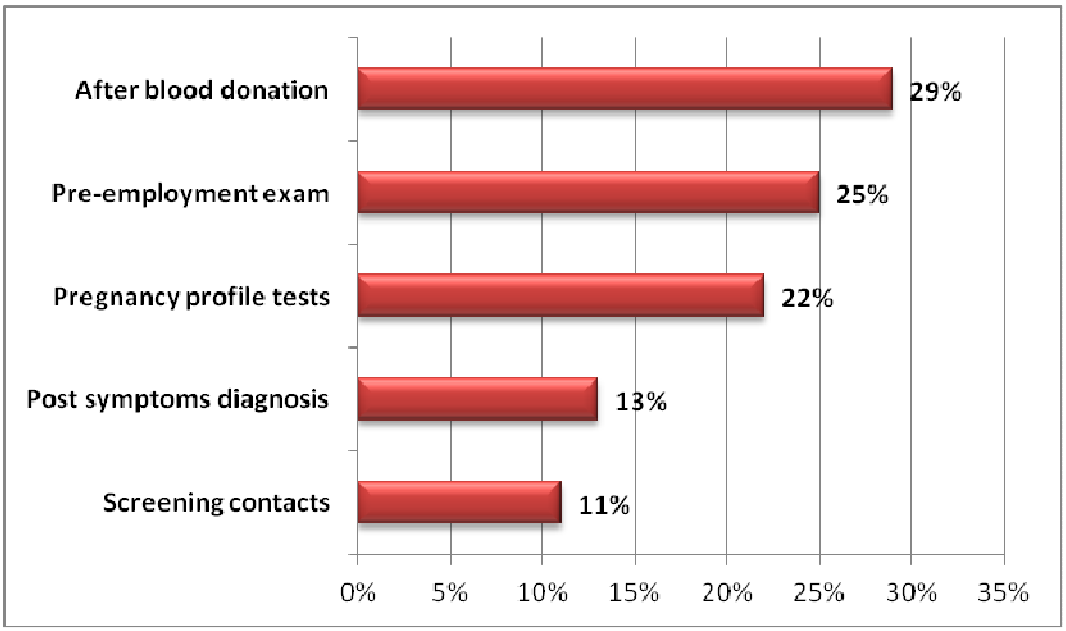

Figure 5: Distribution of HB cases by mode of detection

3.3 Healthcare services exposure risk factors:

To explore the risk factors between cases and controls, many health care services exposure factors were studied, such as; dialysis, blood transfusion, needle stick, operations, dental visits and hospitalization.

Only three of the participants (3%) were hemodialysed patients and all were cases, however, this difference did not reach statistical significance. As well, a significant relation was found between blood transfusion or any of its products and HB infection; 24% of the cases received blood (or any of its products) compared to 9% of the controls. This difference in proportions was found to be statistically significant, (P value 0.004, OR= 3.2). 46% the cases received blood transfusion more than once compared to only 11.1% of the controls (p value = 0.065). Nine of the participants

(4.5%) reported being exposed to preused needle stick; seven of them were among the case.

Of the various health-related risk factors, the history of dental visit was the strongest independent risk factor for HB seropositivity; 75% of the cases had history of dental visit compared to 29% of the control group, (P value <0.001, OR=7.3). In addition to that, it was clear that the probability to be infected increases with the increased frequency of visiting a dentist; 61.4% of the cases who reported they were visiting dentists more than twice, compared to 44.8% of the control group. This difference was found to be statistically significant, p value = 0.013. In addition hospitalization was a significant risk factor; 45% of the cases had history of hospitalization compared to 28% of the control group, (P value = 0.013, OR= 2.1) (Table 3).

The univariate analysis did not show significant differences between cases and controls with regard to the other health care services related factors such as history of invasive operation, history of needle stick injury and history of dialysis (Table 3).

Table 3: Univariate analysis for the health-care exposure risk factors of HB

Variable	*Case Frequency (%)*	*Control Frequency (%)*	*P value*	*OR$ (95% CI^)*
History of dialysis:				
▪ Yes	3 (3)	0 (0)	0.346@	2.0 (0.76-5.34)
▪ No	97 (97)	100 (100)		
History of blood transfusion:				
▪ Yes	24 (24)	9 (9)	0.004*	3.2 (1.4-7.28)
▪ No	76 (76)	91 (91)		
Frequency of transfusion:				
▪ Once	13(54.2)	8(88.9)	0.065*	0.14 (0.016-1.37)
▪ More than once	11(45.8)	1(11.1)		
History of needle stick:				
▪ Yes	7 (7)	2 (2)	0.170@	3.7 (0.75-18.2)
▪ No	93 (93)	98 (98)		
History of surgical operation:				
▪ Yes	35 (35)	23 (23)	0.061*	1.8 (0.97-3.3)
▪ No	65 (65)	77 (77)		
Frequency of operation:				
▪ Once	28 (80)	19 (83)	0.800*	0.8 (0.2-3.2)
▪ More than once	7 (20)	4 (17)		
History of dental visits:				
▪ Yes	75 (75)	29 (29)	<0.001	7.4 (3.9-13.7)
▪ No	25 (25)	71 (71)	*	
Frequency of dental visit:				
▪ Once[1]	10 (13.3)	12 (41.4)	0.670*	1
▪ Twice	19 (25.3)	4 (13.8)	0.006*	5.7 (1.5-22.3)
▪ More than twice	46 (61.4)	13 (44.8)	0.013*	4.2 (1.5-12.0)
History of hospitalization:				
▪ Yes	45 (45)	28 (28)	0.013*	2.1(1.17-3.78)
▪ No	55(55)	72 (72)		

*Chi Squared test, @Fisher exact test, $OR= Odds Ratio, ^CI: Confidence Interval [1] Reference Group

3.4 Personal behavior risk factors:

Behavioral risk factors are among the important determinates of HB infection. To assess its relation with HB cases in Palestine, many of them were evaluated in our study, such as; Hejamat, Tatoos, piercing, sharing shaving equipment, intravenous drug use, barber visit, living abroad, etc.

Univariate analysis revealed significant relation between HB infection and some behavioral risk factors such as Hejamat, IV drug use, barber visit and living abroad. Eleven percent of HB cases had history of Hejamat compared to 2% of the controls (*P* value 0.01, OR=6.1). On the other hand, 5% of HB cases had history of IV drug use compared to none of the controls (*P* value 0.024, OR=2.05). For the barber visit, 29% of HB cases had history of barber visit compared to 10% of the controls (*P* value 0.032, OR=2.5). Living abroad was also found to significantly related to HB infection; 21% of HB cases had history of living abroad compared to 8% of the controls (*P* value 0.009, OR=3) (Table 4).

On the other hand, other personal behavioral risk factors didn't show significant relation with HB transmission as tattoos, piercing, sharing pre-used tooth brush, history of Haj and Omra, history of jail more than three months, and history of STDs. (Table 4)

Table 4: Univariate analysis of the personal behavior risk factors of HB

Variable	***Case*** *Frequency (%)*	***Control*** *Frequency (%)*	***P value***	***OR$^{\$}$ (95% CI^)***
History of Hejamat				
• Yes	11 (11)	2 (2)	0.010*	6.1 (1.3-28.07)
• No	89 (89)	98 (98)		
Tattoos				
• Yes	5 (5)	1 (1)	0.097*	5.2 (0.59-45.4)
• No.	95 (95)	99 (99)		
Piercing				
• Yes	4 (4)	3 (3)	0.700*	1.36 (0.25-6.18)
• No	96 (96)	97 (97)		
Sharing shaving equipment$^{\alpha}$				
• Yes	29 (42.20	11(24.4)	0.049*	3.3(1.02-7.07)
• No	40 (58)	34 (75.5)		
History of sharing toothbrush				
• Yes	15 (15)	8 (8)	0.121*	2.0 (0.82-5.03)
• No	85 (85)	92 (92)		
Intravenous drug use				
• Yes	5 (5)	0 (0)	0.024$^{@}$	2.05 (1.8-2.3)
• No	95 (95)	100 (100)		
History of barber visit$^{\alpha}$				
• Yes	29 (42.0)	10 (22.2)	0.032*	2.5 (1.1-5.9)
• No	40 (58.0)	35 (77.8)		
History of Haj and/or Omra				
• Yes	12 (12)	7 (7)	0.228*	1.8 (0.68-4.81)
• No	88 (88)	93 (93)		
Living abroad (> one year)				
• Yes	21 (21)	8 (8)	0.009*	3.0 (1.28-7.280)
• No	79 (79)	92 (92)		
History of jail:				
• Yes	9 (9)	3 (3)	0.074*	3.1 (0.84-12.2)
• No	91 (91)	97 (97)		
History of STDs:				
• Yes	1 (1)	0 (0)	0.316$^{@}$	2.0 (1.75-2.31)
• No	99 (99)	100 (100)		

* Chi-square Test, $^{@}$ Fisher exact test, $^{\$}$OR= Odds Ratio, ^CI: Confidence Interval
$^{\alpha}$ For male participant only

3.5 Logistic-Regression Model

The multivariate logistic regression model included all variables found to be significant in the univariate analysis; gender, occupation, blood transfusion, dental visit, hospitalization, Hejamat, sharing shaving equipment, intravenous drug use, barber visit and living abroad.

Controlling for all above mentioned variable, Logistic-Regression Model identified only the dental visit to be associated with acquisition of HB infection (*P* value<0.001, OR= 5.6). (Table 5)

Table 5: Multivariate analysis for the Hepatitis B risk factors

Variable	Case *n (%)*	Control *n (%)*	*P* value	*OR*[$] *(95% CI^)*
Occupation:				
▪ *HCW*	4(4)	6(6)	0.66	1.4 (0.2-6.8)
▪ *Solider*	2(2)	14(14)	0.09	4.6 (0.8-28.2)
▪ *Manual*	9 (9)	14 (14)	0.50	1.5 (0.5- 4.8)
▪ *Others*[1]	85(85)	66(66)	0.38	1
History of blood transfusion	24 (24)	9 (9)	0.33	1.6 (0.6-4.6)
History of dental visits	75 (75)	29 (29)	<0.001	5.6 (2.8-11.1)
History of hospitalization	45 (45)	28 (28)	0.43	1.4 (0.6 – 3.0)
History of Hejamat	11 (11)	2 (2)	0.20	3.5 (0.6 - 20.2)
Sharing shaving equipment	29 (42.2)	11(24.4)	0.48	1.4 (0.5 – 3.9)
Intravenous drug use	5 (5)	0 (0)	0.48	1.1 (0.2-4.2)
History of barber visit	29 (42.0)	10 (22.2)	0.33	1.6 (0,6 - 4.37)
Living abroad (> one year)	21 (21)	8 (8)	0.19	2.0 (0.71-6.1)

[$]OR= Odds Ratio, ^CI: Confidence Interval, [1] Reference group

Chapter Four

Discussion

Hepatitis B is a major public health problem that incorporates high economic and social burden. However, it is often neglected because of its largely asymptomatic course with long-term complications. Since the infection has serious consequences, there is still a continuous need to examine its epidemiology so that we can formulate some prevention and control measures.

The case group showed male predominance and control group showed the female predominance. It has been shown in the literature that males are at higher risk to develop HB infection. Several studies conducted in Egypt, Turkey and Brazil, showed that male was considered as a risk factor for HBV infection [36, 42, 43].

The majority of study population was young adults, aged 20 to 40 years. This result may be due to the rising incidence of risk factors for hepatitis B infection toward the end of adolescence. As well, this is consistent with the allowed age range of blood donation and employment and child bearing age of the females; the three most common source of HB cases detection, as noticed in Figure 5.

Routine screening and vaccination of the HCWs as well as the military forces and other risky groups is one of the most important

preventative measures adopted to prevent and control HB infection at the community level. Our study revealed that only 5% of the study population reported being vaccinated against Hepatitis B; 3% of the cases and 7% of the controls (Figure 3). This is consistent with what have been shown in a study conducted in Egypt by Talaat M and colleagues [42]. Actually, this low proportion of vaccinated participants alarmed us to spend more efforts to vaccinate adults born before 1992.

The findings in this study, using the Univariant analysis, identified blood transfusion, dental visit, and hospitalization as significant health-related risk factors. On the other hand, the significant personal behavior risk factors were history of Hejamat, sharing of shaving equipments, barber visit, intravenous drug use, and living abroad.

4.1 Personal behavior risk factors:

The unsafe and unhygienic personal and community practices are risk factors of HB transmission. Nearly tenth of the HB cases gave history of having practiced Hejamat whereas only 2% of the control subjects had similar history. This relation was found to be statistically significant in univariate analysis. This is inconsistent with what have been shown in other communities as in Iran [37]. This result may be due to the fact that Hejamet is usually being conducted in our country by nonprofessionals, and there are neither rules nor guidelines to regulate and supervise this practice. Similarly, sharing of shaving equipments was found to be more

prevalent among the cases compared to the controls. This risk factor was also significant in several studies done in developing countries [25, 38, 39].

History of barber visit (for shaving) was also found to be significantly related to HB infection in univariate analysis. This is consistent with what have been found by Afzal and colleagues [40]. This can be explained by the fact that most of the barbers use the same blades and scissor for every customer that increases the transmission of Hepatitis to both customers and barbers. A study among barbers in China had shown the prevalence of HBsAg as 16.8% that was higher than found in subjects of other professions such as employees of departmental store. Thus barbers shops are leading to occupational hazards and potential source of transmission of infection to the customers [50].

HB virus is stable on environmental surfaces for at least 7 days; indirect inoculation of HBV can occur via inanimate objects such as shaving equipments, blades and scissor. Using such unsterile instruments, that is contaminated with blood of the HB patient, emphasizing the fact that sharing such objects is a risk of acquiring HB infection.

4.2 Healthcare services exposure risk factors:

Our univarient analysis of the data identified hospitalization as a risk factor for HB infection. This is consistent with what have been shown in different places; as in Moldova [31], in Brazil [37] and in KSA [51]. In KSA, Bani I., conducted a cross sectional study among pregnant women to asses

the prevalence of HB and its associated factors. They showed that hospitalization is a significant risk factor for hepatitis B infection**.** This result could indicate deficiencies in HCWs' knowledge and practice of the standard infection prevention and control precautions in health care settings. A study done in India [52], to assess the knowledge and the practice of the nurses and doctors toward the infection and prevention measures, showed the lack of both the knowledge and practice, exposing the patients and themselves to nosocomial infection.

Blood transfusion as a significant risk factor for HB infection, by univerient analysis, is consistent with other studies**.** A recent study conducted in Nigeria among pregnant women showed that the history of blood transfusion is a significant risk factor [53]. As well, a cross sectional study done among HCWs in Uganda showed same results [54].

This finding support the conclusion by Al-Hindi and colleagues [46] that the routine tests screening of blood units and its products to detect HB infection by HBsAg test alone is not enough in Palestine, and there is a need to consider introducing Anti-HBc test and HBV DNA in order to discover the occult HBV, to minimize the risk of HBV transmission by blood and its products.

Hemodialysis was insignificant risk factor in this study; inconsistent with what have been shown in other communities as in Turkey [42]. This may occur due to the fact that hemodailysis in the West Bank is done in

three MoH hospitals in which there is a prophylactic vaccination of all patients of chronic renal failure , and the use of HB positive labeled machine for the HB positive patients that aren't used for HB negative patients, while in Turkey this condition is applied only in the large centers but not in the private health centers with small hemodialysis units, as well the few devices that are available for large number of patients[42]. This explanation should be taken with caution; taking in mind the limited number of hemodailysis cases among the participants that could make the study unable to highlight this relation.

The insignificant association with sexual transmitted diseases may reflect difficulties in eliciting information from the participants, and the sociocultural context of Palestinian society.

After use of the logistic regression of these risk factors; to control for confounding factors, just the dental care remained a risk factor for HB transmission. The majority of the HB cases gave history of dental visits (75%), where as only 29% of the control subjects had similar history. This difference between the two groups was found to be highly statistically significant. Unhygienic dental care is a significant risk factor and plays a crucial role in HB transmission. Dental procedures have been shown to be associated with HB infection in many studies in countries such as in Jordan [44] Iran[38] , Pakistan[39, 40] and in Moldova[31]. This has been attributed to the lack of sufficient knowledge and practice in clinical infection control, which indicates the need to implement the standards of infection

prevention, which will limit the transmission of other blood borne pathogens for both the dental staff and the clients.

This finding goes with the results of a cross sectional study conducted in the West Bank in 2004 by Mosleh S. and colleagues [55], about Medical Waste Disposal and Occupational Health Hazards in Dental Clinics in Nablus Districts. The study showed that only 54.6% of the participants wear gloves during treatment of patients, 53.6% use the 70% alcohol solutions as a disinfectant agent and 83.2% of them use dry heat as sterilization method which is judged to be inefficient.

In Jordan, another study was conducted to assess the compliance of dentists in the private dental clinics with infection control measures[56], found that only 41.8% of the dentists change the hand pieces between patients, 81.8% wear gloves in treatment and change them between patients, and approximately 60% use autoclave for sterilization. The authors concluded that these findings reflect the great opportunity to transmit the blood borne pathogens as HBV by dental care. All these results indicate the lack of knowledge and/or ignorance by working clinics**.**

In South Africa, Mehtar and his colleagues [57] did a study to assess the knowledge of infection control measures and compare it with the practices, found a significant difference between the knowledge and the practices, making unhygienic dental care a potential hazard for both dental staff and clients.

A Japanese study done to examine the viral hepatitis in dental staff (HBV and HCV), finding out that immunized workers with HBV vaccine more protected than non-immunized ones, suggesting the HBV vaccine as the first protective line, which is an effective protective measure for the dental staff as a high risk group [58].

The HBV can be transmitted in dental care clinic either through direct contact with blood and oral fluids, or through indirect contact with contaminated objects; instruments, equipments, and surfaces. These routes can transmit the disease from the dental staff to the patient, or vice versa, and from one patient to another [59].

4.3 Study Limitation

Our findings should nevertheless be interpreted with caution. The first limitation of our study is recall bias; one of the common sources of bias in case control studies that is more prominent when prevalent cases are used.

To minimize it, incident cases of HB were used in our study and a standard method of data collection was conducted; the same nurse and the same standardized questionnaire were used to ask cases and controls. As well, all nurses participated in data collection were trained, by the main researcher, on a standard method of asking all participants. Since most episodes of hepatitis B are symptom free, cases were likely as controls to recall exposures potentially associated with HBV infection.

The second limitation was the small sample size, especially to assess the rare risk factors such as IUD and STDs that have been published in other studies. This may affect the power of the study to detect the true association with these factors. Few patients reported these exposures, restricting the power to detect the relation with the outcome.

Other possible limitation is that we couldn't study the house - hold effect as an important risk factor, since the controls were the house- hold contacts of the cases. This is because we wanted to explore more the behavioral and health-care exposure risk factors for HB infection.

4.4 Conclusion and Recommendations

This case-control study was an effort to highlight the main risk factors that lead to HBV infection. It revealed that several high risk behaviors and practices for the transmission of this infection are significantly more prevalent among the patients compared to the controls. Specifically, it identified the unhygienic dental care risk factor as the main source of HB transmission; it was already identified in other studies done among other communities. The adoption of infection prevention standards as strategy will be the key of HB prevention and other blood borne pathogens, while health education for the personal hygiene will protect the public, emphasizing on the vaccination of the risky behavior groups as a first protective line.

4.4.1 Recommendation:

HB infection still a public health problem despite the availability of the HB vaccine since 1992, which is largely attributed to its asymptomatic course and carrier patients. Identification of HB risk factors and development of prevention strategies based on epidemiological studies can form the basis for developing a comprehensive prevention strategy to prevent blood borne pathogen transmission, such as HCV and HIV, in Palestine.

Based on the study findings, the researcher managed to present the following recommendations:

1. Instituting routine HB vaccination for high-risk adults in settings such as dentists and other HCWs, prisons and jails, STD clinics seems to be necessary

2. Adoption of infection prevention and control standards as a national strategy through the MoH, that aims to align evidence based practice with monitoring, assurance, quality improvement and scrutiny.

3. Recurrent supervision visits by infection prevention and control committee should be conducted to dental clinics to assess standards of infection prevention and control and should be empowered to prohibit patient care by dentists who are not compliant.

4. Provide formal and obligatory infection control courses and guidelines for dentists by MoH and disseminating standard infection prevention and control manuals that incorporate all published updated recommendations.

5. Raising the public awareness about the determinants of Hepatitis B, its spread and transmission, developing info kit for professions at risk containing basic information on the disease, preventive measures, immunization, screening of blood products, sterilization of instruments, disposable syringes, gloves and instruments to reduce disease transmission in the communities

6. All individuals who receive blood or blood products and surgical and dental treatment should be screened for HB infection.

7. Carriers and patients with chronic HBV infections should be properly counseled regarding lifestyle modifications and prevention of transmission.

8. Further studies to assess the dental staff awareness toward the infection prevention and control standards and its implementation, and to evaluate the prevalence of HBV among the dentists.

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Annex 1: Questionnaire

بسم الله الرحمن الرحيم

أخي المواطن/ أختي المواطنة ،،

تحية وبعد،،

دراسة إحصائية/ صحية. الموضوع:

تهدف هذه الدراسة الى معرفة "**محددات انتشار مرض إلتهاب الكبدي الوبائي "ب" في شمال الضفة الغربية** "،من اجل التعرف على العوامل المؤدية الى انتشار هذا المرض ، للوصول الى التوصيات الممكنة للحد من انتشاره، وقد تم إختياركم لتكونوا جزءاً من عينة الدراسة، لذى نأمل منكم الإجابة بموضوعية على أسئلة الإستبيان، بوضع إشارة على الإجابة التي ترونها مناسبة في المكان المخصص لها.

مؤكدين إقتصار إستخدام المعلومات الواردة في هذه الإستبيان على أغراض البحث العلمي، ومراعاة السرية التامة والحرية الكاملة بعدم الاجابة عن اي سؤال،حيث سيبقى إسمك طي الكتمان و لن يكون لأي شخص- ما لم ينص القانون على ذلك- حق الإطلاع على الاستمارة بعد تعبئتها، مع إمكانية الانسحاب من المشاركة في الدراسة دون ان يؤثر ذلك على العناية الطبية المقدمة .

و بناءا على ما سبق ارجو التوقيع اشعارا بالموافقة على الاشتراك، علما بأن ممرضة الطب الوقائي ستقوم بالشرح وايضاح أي سؤال في الاستبيان.

(شاكرين لكم حسن تعاونكم)

الباحث / انعام محمد صبح

جامعة النجاح الوطنية

توقيع المشترك :.....

الجزء الأول:- معلومات شخصية:

1	**الجنس**	ذكر	أنثى

2	**العمر**	(30-20)	(40-31)	(50-41)	أكثر من خمسون

3	**مكان الإقامة**	مدينة	قرية	مخيم

4	**المستوى التعليمي**	أمي	أساسي	ثانوي	بكالوريوس و دراسات عليا

5	**طبيعة العمل**	عامل في المجال الصحي **- حدد المهنة -**	عمل مكتبي (عام – خاص)	عسكري	عامل داخل الخط الأخضر	غير ذلك حدد

6	**الحالة الإجتماعية**	متزوج	أعزب	أرمل	مطلق

7	**عدد أفراد الأسرة**	أقل من (3) افراد	3 -5	(8-5)	أكثر من (8) أفراد

8	**الدخل الشهري / شيقل**	أقل من (3000) شيقل	(3000 وأكثر)شيقل

الجزء الثاني:- الإستبيان:

اكتشفت أنني حامل لفيروس التهاب الكبد الوبائي بعد (خاص بالمصابين) ضع اشارة عند رمز الاجابة:			
أ	التبرع بالدم		
ب	الفحص في بداية الحمل		
ج	أجري لي الفحص بعد شعوري بأعراض المرض		
د	قيامي بالفحص المطلوب لأغراض العمل		
ه	فحص المخالطين		
	أجيب/ي بـ (نعم) أو (لا):	**نعم**	**لا**
2	**تلقيت التطعيم الخاص بالتهاب الكبد الفيروسي نوع ب سابقا**		
3	**أقوم بإجراء غسيل كلوي**		
أ	إذا كان الجواب (نعم) – حدد عدد المرات		
4	**أتلقى أو تلقيت سابقا نقل دم أو احد مشتقاته**		
5	إذا كان الجواب (نعم) – كم عدد المرات ؟: أ.مرة واحدة ب. مرتان ج.ثلاث مرات د.أكثر من ثلاث مرات		
6	**تعرضت لوخز الإبر(الطبية) المستعملة سابقا**		
7	**أجريت لي عملية جراحية (يشمل ذلك عمليات المنظار)**		
8	إذا كان الجواب (نعم) – كم عدد المرات ؟: أ.مرة واحدة ب. مرتان ج.ثلاث مرات د.أكثر من ثلاث مرات		
9	**قمت بزيارة لطبيب الأسنان سابقا**		
10	إذا كان الجواب (نعم) – كم عدد المرات ؟: أ.مرة واحدة ب. مرتان ج.ثلاث مرات د.أكثر من ثلاث مرات		
11	**أقمت في المشفى كمريض (المبيت)**		
12	**أعيش مع شخص مصاب بمرض (التهاب الكبد الوبائي "ب") في منزل واحد**		
13	**يوجد قريب درجة أولى يحمل المرض**		
14	إذا كان الجواب (نعم) – (صلة القرابة) أ. أب ب. أم ج. أخ/ت د. ابن/ة ه. زوج/ة		
15	**قمت سابقا بإجراء الحجامة**		
16	**قمت سابقا بإجراء الوشم**		
17	**قمت سابقا بإجراء ثقب الأذن، الأنف**		
18	**اضطر أحيانا أن أشارك احد ما في أدوات الحلاقة**		
19	**اضطر أحيانا أن أشارك احد ما في فرشاة الأسنان**		
21	**استخدم الحقن(الابر) بشكل مستمر**		
22	**زرت الحلاق سابقا بهدف حلاقة وجهي**		
23	**ذهبت إلى الحج أو العمرة خلال الست أشهر الماضية**		
24	**سكنت خارج البلاد لمدة سنة (بما فيها – داخل الخط الأخضر)**		
25	**سجنت لمدة تزيد عن ثلاث أشهر متواصلة**		
26	**عانيت من احد الأمراض الجنسية**		

Annex 2: IRB

An-Najah
National University
Faculty of Medicine

بسم الله الرحمن الرحيم

جامعة
النجاح الوطنية
كلية الطب

IRB Approval letter

Study title:
The risk factors of hepatitis B transmission in the North of West Bank .

Submitted by:
Inam Mohmmad Sobuh

Date Reviewed:
Dec 18, 2011

Date approved:
Feb 8, 2012

Your study titled" The risk factors of hepatitis B transmission in the North of West Bank". Was reviewed by An-Najah National University IRB committee & approved on Feb 8, 2012

Samar Musmar,MD, FAAFP
IRB Committee Chairman,
An-Najah National University

IRB

نابلس - ص.ب ٧٠٧,٧ هاتف: ٠٩)٢٣٤٢٩٠٢/٤/٧/٨/١٤)(٩٧٢)، فاكسميل ٠٩)٢٣٤٩٧٣٩(٩٧٢)(

جامعة النجاح الوطنية
كلية الدراسات العليا

عوامل اختطار انتقال العدوى لمرض التهاب الكبد الوبائي نوع "ب" دراسة الحالة والشاهد

إعداد
أنعام محمد وراد صبح

اشراف
د. زاهر نزال

قدمت هذه الأطروحة استكمالاً لمتطلبات درجة الماجستير في الصحة العامة بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.
2013

عوامل اختطار انتقال العدوى لمرض التهاب الكبد الوبائي نوع "ب"
دراسة الحالة والشاهد

إعداد
أنعام محمد وراد صبح
اشراف
د. زاهر نزال

الملخص

مدخل الى الدراسة: ان مرض التهاب الكبد الوبائي نوع "ب" يمثل مشكلة صحية رئيسية في فلسطين, ولكن عوامل اختطار المرض غير مدروسة بشكل جيد.

هدف الدراسة: الهدف الرئيس من الدراسة هو تحديد عوامل اختطار انتشار مرض التهاب الكبد الوبائي نوع "ب" بين المخالطين, في شمال الضفة الغربية، من اجل الوقاية و مكافحة المرض.

طريقة البحث: تم اجراء البحث عن طريق دراسة الحالة (الحامل للمرض) والشاهد (الخالي من المرض)، و ذلك بأخذ عينة حجمها (مئة حالة) وعينة مماثلة (مئة شاهد)، و باستعمال التحليل الاحصائي احادي المتغير ومتعدد المتغيرات، بهدف الحصول على عوامل اختطار انتشار المرض.

النتائج: من خلال التحليل الاحصائي احادي المتغير وجد ان عوامل الاختطار التالية هي الاكثر ارتباطا بانتشار المرض : (نقل الدم او احد مشتقاته، زيارة عيادة الاسنان للكشف, المبيت في المستشفى, الحجامة، المشاركة في ادوات الحلاقة، الادمان عن طريق الحقن, السفر للخارج لاكثرمن سنة)، لكن بالتحليل الاحصائي المتعدد المتغيرات تبين ان زيارة عيادة الاسنان للكشف هو الاكثر ارتباطا مع انتشار المرض (قيمة احتمالية <0.001 و نسبة ارجحية = 5.6 و فترات الثقة 2.8–11.1).

الاستنتاج: ان التوصل الى النتائج السابقة يؤكد ضرورة التطعيم للفئات المعرضة للمرض بشكل كبير, اضافة الى التثقيف الصحي لهم، و كذلك رفع وعي العاملين في المجال الصـــحي حـــول قواعد مكافحة العدوى و الالتزام بتطبيقها في العمل خاصة في عيادات الاسنان .

يفضل اجراء دراسات اخرى حول نفس الموضوع و لكن بحجم عينة اكبر حتى تستوضح فيـــه بعض العوامل القليلة الحدوث.