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Evaluation of Hepatitis B Immunization Program for Children in Gaza Governorates, Palestine, 2007

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Evaluation of Hepatitis B Immunization Program for Children in Gaza Governorates, Palestine, 2007

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إهداء

أهدى هذا العمل إلى روح والدي الطاهرة وإلى والدتي العزيزة وإخواني وأخواتي الأعزاء

وزوجتي الحبيبة و أبنائي وبناتي الأحباء، ولا أنسى أصدقائي الأوفياء.

شحدة برهوم

Dedication

I dedicate this work to the spirit of my father

To my mother

To my wife

To my children

To my brothers and sisters

To my friends

Shehda k. A. Barhoum

Declaration

I certify that this thesis submitted for the degree of Master is the Level of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution**.**

Signed

Shehda Khalil Ali Barhoum

Date: 29.12.2007

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Abstract

Hepatitis B virus (HBV) is one of the major diseases of mankind, a silent, unnoticed killer destroying or stimulating development of liver cancer in someone who thinks he is completely well. Vaccination is the most successful tool for HBV prevention, over 90% of susceptible children develop Anti-HBs (≥10 mIu/ml) following three doses of vaccine, approximately 5 to 15% of infants fail to produce protective levels of anti-HBs (<10 mIu/ml).

This study is based on a sero-survey for Measles Rubella and HBV conducted in year 2003, carried out among Palestinian children aged 18-30 months old. HBV Level shows that, the non-respondent to HB vaccination child numbers were, 66 in West Bank and 63 in Gaza Governorates. The purpose is to evaluate HB immunization program for children in Gaza governorates, Palestine, 2007 and to study the associated factors lead to a poor response for HB vaccination among vaccinated children in year 2001 in Gaza Governorates, Palestine. The study population includes all (63) identified as non-respondents to HB vaccine and (126) respondents as controls, carried on Governmental and UNRWA public health centers in Gaza Governorates.

The study is a quantitative, case-control, retrospective. The vaccine non-respondents are coming from the five Gaza governorates. For each "non-respondent" case, two "respondent" controls selected by systematic random sampling method, from the same sex and local health center.

Closed ended questionnaire filled from vaccination files. For non-recorded data (15.9%), child mother interviewed face-to-face and supported by immunization cards. This step is

followed by designing an entry model using computer software SPSS, where data was entered and analyzed.

Several factors increase the risk of non- response to HB vaccination studied and classified into Socio-demographic factors: residency, sex, mother education level and type of immunization place, were all found not statically significant on non-response to HB vaccination; additionally response to HB vaccination did not correlated with family size.

Health status factors: Birth weight, history of hospitalization before vaccination, history of infection, nutrition status, feeding during immunization and suffering from adverse event after vaccine, none is statically significant.

Immunization factors: all children in the study received three doses of vaccination; the manufacture and difference of lot numbers of vaccines (1st, 2nd & 3ed) doses were not statistically significant. In addition, response to HB vaccination not correlated with the interval from birth to first vaccine, interval between first and second dose, interval between second and third dose. While the interval between last vaccination dose and Blood sample testing date was found to be negatively correlated and statically significant (P-value= 0.024).

Environmental factors, the change of seasons of (1st, 2nd & 3ed) vaccinations and the presence of a sewage net in area was not statistically significant.

Tentatively, this study could be a model to define further risks factors, which are not included in this study, and may affect non-response to HB vaccination in developing community as Gaza Governorates. Such study and similar studies will help in institute successful intervention program to reduce the non- respondent percentage of infants to HB vaccination in Gaza, Palestine and other similar countries.

"تقييم برنامج تطعيم التهاب الكبد البائي (B) لأطفال محافظات غزه، فلسطين، 2007م"

ملخص

يعتبر فيروس التهاب الكبد البائي (B) أحد الإمراض الرئيسة التي تصيب البشرية، بصمت وبطريقة غير ملحوظة يقتل و يدمر الكبد ويحفز على تطور سرطان الكبد في شخص قد يعتقد انه سليم. التطعيم من أنجح أدوات الوقاية من التهاب الكبد البائي، بعد تطعيم الأطفال بثلاث جرعات أكثر من 90% منهم يكون لديهم مستويات من الأضداد السطحية لالتهاب الكبد البائي Anti-HBs (بمقدار يساوي أو يزيد عن 10 مل وحده دولية / ملليتر)، تقريبا 5–15 % من الأطفال يفشلوا في تكوين مستوي حماية من الأضداد السطحية (بمقدار يقل عن 10 مل وحده دولية / ملليتر).

الدراسة مبنية علي بحث عُمِلَ في فلسطين عام 2003 عن الحصبة والحصبة الألمانية والتهاب الكبد البائي، علي الأطفال من سن 18–30 شهر، نتائج التهاب الكبد البائي كانت عدد الأطفال الذين ليس لديهم مستويات كافية من الأضداد السطحية في الضفة الغربية 66، و محافظات غزه 63. هدف الدراسة هو تقييم برنامج تطعيم التهاب الكبد البائي (B) لأطفال محافظات غزة ، فلسطين ، 2007م ، وكذلك دراسة العوامل المرتبطة بهذه المناعة التي قد تؤدي إلي عدم الاستجابة لتطعيم الالتهاب الكبد البائي لتكوين الأضداد السطحية عند الأطفال المُطعمين عام 2001 م في محافظات غزه ، فلسطين. مجتمع الدراسة يشمل جميع الحالات (63) التي لم تستجب للتطعيم في محافظات غزه بالإضافة إلي (126) حالة استجابت للتطعيم أخذت كعينات ضابطة، أجريت الدراسة في مراكز الصحة العامة الحكومية ووكالة الغوث.

الدراسة كانت كمية، بأثر رجعي، من نوع الحالة والضابطة. الحالات التي لم تستجب للتطعيم كانت من محافظات غزة الخمسة، لكل حالة "لم تستجب للتطعيم" تم اختيار عينتين ضابطتين "استجابتا للتطعيم" بطريقة العينة العشوائية المنتظمة من نفس الجنس و مكان التطعيم. تم تعبئة الاستبيانات من ملفات التطعيم الخاصة بالأطفال و في حالة عدم وجود الملف (15.9%) تم تعبئة الاستبيان بمقابلة الأم وجهاً لوجه بالاستعانة بكرت التطعيم. تم إدخال المعلومات وتحليلها باستخدام برنامج SPSS الإحصائي.

عدة عوامل تزيد من خطورة عدم الاستجابة لتطعيم التهاب الكبد البائي تم دراستها وتم تصنيفها إلي العوامل الاجتماعية– السكانية وهي مكان الإقامة، الجنس، مستوي تعليم الأم ومكان التطعيم، لا يُعْتَدُّ بأيٍ منها إحصائياً بعدم استجابتها لتطعيم الكبد البائي. كذلك الاستجابة للتطعيم لا يرتبط ولا يُعْتَدُّ إحصائياً بحجم العائلة و الوزن عند الولادة.

العوامل الصحية مثل الوزن عند الولادة، دخول المستشفي قبل التطعيم، التغذية "الـــوزن" ووجـــود عدوى خلال التطعيم، الرضاعة خلال التطعيم والمضاعفات بعد التطعيم لا يُعْتَدُّ إحصائياً بأي منها.

العوامل المناعية وُجِدَ أن كل الأطفال الذين شملتهم الدراسة وُجِدُوا مُطعمين بثلاث جرعات، ووجد أن الاختلاف في أنواع وأرقام تصنيع التطعيم المختلفة في كلِ من الجرعات الأولي والثانية والثالثة لم يُعْتَدُّ به إحصائيا، كذلك عدم الاستجابة للتطعيم لا يرتبط ولم يُعْتَدُّ به إحصائيا في كلِ من الفتـــرة ما بين الولادة والجرعة الأولي، الفترة ما بين الجرعة الأولي والثانية، والفترة مـــا بـــين الجرعـــة الثانية والثالثة، بينما الفترة ما بين الجرعة الثالثة وتاريخ فحص عينة الدم وجد بأنه يرتبط ســـلبياَ و يُعْتَدُّ به إحصائياَ (بقوة احتمال = 0.024) .

بالنسبة للعوامل البيئية من تغيير في فصول التطعيم في الجرعات الأولي والثانية والثالثـــة وكـــذلك وجود شبكة مجاري في مكان السكن، وجد أنه لا يُعْتَدُّ بأيٍ منها إحصائياَ.

مبدئيًا هذه الدراسة قد تكون نموذج لتحديد عوامل خطورة إضافية لم تشملها الدراسة والتي ممكـــن أن تُؤَثر علي عدم الاستجابة لتطعيم التهاب الكبد البائي في المجتمعات النامية مثل محافظات غزة ، هذه الدراسة والدراسات المشابهة تساعد في تأسيس برنامج وقاية ناجحة لتقليل نسبة الأطفال الـــذين لا يستجيبوا لتطعيم الالتهاب الكبد البائي في فلسطين والدول الشبيهة.

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List of abbreviations

ALT	Alanine Transferase
ANOVA	Analysis of Variance
Anti-HBc	Antibody to hepatitis B core antigen
anti-HBe	antibody to HBeAg
anti-HBs	antibody to HBsAg
AST	Aspartate Tansferase
BCG	Bacillus Calmette-Guerin
CBR	Crude Birth Rate
CDC	Centres for Disease Control & Prevention
CDR	Crude Death Rate
CI	Confidence Interval
df	Degree of Freedom
DPT	Diphtheria, Pertussis and Tetanus
ELISA	Enzyme Linked Immunosorbent Assay
EMRO	Eastern Mediterranean Regional Office
EPI	Expanded Programme on Immunization
GAVI	Global Alliance for Vaccines and Immunization
GG	Gaza Governorates
GHSRC	Gaza Health Service Research Centre
GMT	geometric mean titer
GNP	Gross National production
HBcAg	Hepatitis B core antigen
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immune globulin
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCC	Hepto Celluar carcinoma
HCV	Hepatitis C Virus
Hib	Haemophylus influenzae Sereotype b
HIV	Human Immuno-deficiency Virus
IMCI	Integrated Management of Childhood Illnesses
MCH	Maternal & Child Health
MMR	Measles, Mumps and Rubella
MOH	Ministry of Health
NCDs	Noncommunicable Diseases
NGOs	Non Governmental Organization
OPV	Oral Polio Vaccine
OR	Odds Ratio
PCBS	Palestinian Centre Bureau of Statistic
PCR	Poly Chain Reaction
PHC	Primary health care system
PNA	Palestinian National Authority
SPSS	Statistical Package for Social Sciences
TB	Tuberculosis
UN	United Nations
UNICEF	United Nations Children's Fund
UNRWA	United Nations Relief and Works Agency For Palestine Refugees in the Near East

UNSCO	United Nations Special Coordinator in the Occupied Territories
USAID	United Sates Agency for International Development
WB	West Bank
WHO	World Health Organization
WHO,V&B	WHO, Vaccines and Biological

Chapter One

Introduction

Chapter one

Introduction

1.1 Background

Hepatitis B virus (HBV) is one of the major diseases of mankind, HBV is a silent, unnoticed killer destroying the liver or stimulating the development of liver cancer in someone who thinks he is completely well. HBV is a serious global public health problem, chronic HBV infection is one of the most common and persistent viral infections in humans. More than 350 million people worldwide are chronically infected and at high risk of death from liver cancer and cirrhosis (WHO, HB Fact sheet, 2004). People with chronic HBV infection are at high risk for 2 serious liver diseases: cirrhosis and primary liver cancer. From 500,000 to 700,000 people die each year from HBV-related liver disease (WHO, W.E., 2004). Adults with acute HB 1 to 2 % develops fulminate hepatitis for which the mortality rate is between 60 and 90% in the absence of liver transplantation (CDC, 2004). In a study by WHO,V&B, 2000, there were over 5.5 million cases of acute HBV infection and over 520,000 deaths from HBV-related diseases (470,000 from cirrhosis and liver cancer and 52,000 from acute HBV infection), an other study by Parkin, et al, 2001, reports primary liver cancer is ranked the 6th most common cancer globally; over 50% are caused by chronic HBV infection.

According to a study by Margolis, Alter & Hadler, 1997, HBV is spread by either skin puncture or mucous membrane contact with infected blood or other body fluids, HBV is not spread by air, food or water, the highest concentrations of the virus occur in blood and wound secretions, moderate concentrations of HBV are found in semen and vaginal fluid, and lower concentrations occur in saliva. Similar to HIV, HBV is spread by skin or mucous membrane contact with infected blood or body fluids (Mast, et al, 2004). HBV,

however, is 100 times more infectious than HIV (WHO/CDS, 2002). HBV can be transmitted vertically, through sexual or household contact, or by unsafe injections, but chronic infections acquired during infancy or childhood account for large share of worldwide morbidity and mortality (By CDC, MMWR, 2005).

In 1991, Global Alliance for Vaccines and Immunization (GAVI) recommended that the routine immunization of infants and adults should take the highest priority and decided to include HBV immunization in the EPI and should be integrated in all countries by 1997. The younger the age at infection the higher the chance of becoming a carrier as many 95% of infected infants, but only around 10 % of adults, become long term carriers. According to McIntyre, 1995, vaccination is the most successful tool for HB prevention over 90% of susceptible children develop a protective antibody response (Anti-HBs>10 mIu/ml) following three doses of vaccine and the efficacy of the vaccine in preventing chronic carriage in most cohorts of children. According to WHO, EPI., GEN., 1996, expanded Program of Immunization (EPI) is a program adopted by World Health Organization (WHO) to protect against six targets of these infectious diseases by child immunization and vaccination of women

Several factors that increase the risk of non-response to HBV vaccination have been identified, family size, mother educational level, increasing age, sex, the cold chain system. The number of doses of vaccination, and a delay in receiving the 1st dose of vaccine, the interval between the 1st and 2nd doses, the interval between the 2nd and 3rd doses, the time between the last dose of vaccine and taking the blood sample, the manufacture and change of lot numbers of vaccines. In addition, to seasonal variation: season of 1st immunization (birth), season of 2nd immunization, season of 3ed immunization (Minuk, Bohme & Bowen, Jun, 1989; Alper, et al, 1989 & Inskip, et al, 1991).

Middle East countries represent the global epidemiology of HBV infection, with the prevalence of chronic carriers showing considerable variation between and within the countries, studies in the middle east show the prevalence of HB Surface Antigen (HBsAg) to range from 3% to 11% (WHO,1995). Within the Palestinian population there is a high morbidity rate of HB, a high infectivity rate among newborns due to vertical transmission from positive pregnant women, and delays in vaccination for confirmed cases of HB are a result of the current political situation. Palestine as other Countries in Middle East falls in the region of intermediate prevalence rate from 3% to 11%. of HBV infection. Routine immunization for HB for all newborns was instituted in Palestine, during 1992/1993 as recommended by WHO (Palestine, MOH, 2004).

1.2 Statement of the problem

Based on a sero-survey in Palestine for Measles Rubella and HBV in the year 2003, conducted among Palestinian children, 66 (5.5%) and 63 (7.9%) non- respondent to HB vaccination, were found in West Bank and Gaza Governorates respectively.

Since the very young are most at risk from the HBV, 70 to 90 % of infants infected at birth become chronic HBV patients and develop fatal complication. Although vaccination is the most tool for HB prevention, approximately 5 to 15% of infants failed to produce protective levels of antibodies to HBV vaccination after the initial 3-doses vaccination. The risk factors lead to a poor respone to HB vaccination present in Palestine.

HBV infectin as insidious, silent disease and can be transmitted by different methods. Many of millions infected with this disease will not know about their case unless they do laboratory serological investigations, those become infectious to others. This leaves us

with an increasing number of potentialy succeptable individuals, espacialy as this number is commulitatively increased year by year.

The evaluation and management of the vaccine program from time to time will survive for keeping the success in improvement of health services by reducing the non-respondent percentage of infants, continuing in strengthening, supporting of the success of prevention, controlling of HB vaccination and prevent deteriorating health services.

1.3 Justification of the study

This disease is associated with morbidity and mortality, it is also considered as insidious and silent disease, many of millions infected with this disease will not know about their case unless they do laboratory serological investigations.

Palestine falls in the region of intermediate prevalence rate from 3% to 11% of HBV infection**,** although the immunization programme is instituted since 1992/1993. In the beginning there was decrease in the incidense of HB cases and carriers; then it becomes approximatly steady which keep Palestine to stay in the region of intermediate prevalence rate of HBV infection. Up to now, in Palestin follow just one option of WHO immunization policy for HBV.

Barriers due to instability of political situations enforced by the Israeli occupation, which will continue in the negative impact on health services by reducing access to health services and reducing the efficacy of the vaccines by destruction of the cold chain system,

For all of the above mentioned, it was believed to survive for keeping the success in improvement of health services and to continue in strengthening, supporting the success of prevention and control of HB vaccination, also it is believed that study will participate in

the early detection and management of HB vaccination failure, which was one cause of reducing the percentage of the non-respondent infants in Palestine.

For all of these reasons, the resarcher decided to study the evaluation of HB immunization program for children in Gaza governorates, in the year 2001, Palestine, 2007.

1.4 The aim of the study

To evaluate Hepatites B immunization program, in the year 2001, for children in Gaza governorates, Palestine, 2001.

1.5 Objectives

1. To evaluate the immune response to HB vaccine.
2. To study the associated factors that lead to a poor response for HB vaccination among vaccinated children in years 2001 in Gaza Governorates, Palestine.
3. To identify high-risk areas with low response to HB vaccine.
4. To spot lighting to follow the different opptions of HB immunization, which is recommended by WHO for detecting HBeAg-positive mothers

1.6 Demography

Palestine is situated on the Eastern coast of the Mediterranean Sea. It is of an ancient and of strategic important location. Now, Palestine comprises two areas separated geographically: the West Bank and Gaza governorates, the total area is 6,020 sq. Km. with total population living in is 3,762,005 individuals in 2005 with capita per sq Km 625. Gaza governorates is a narrow piece of land lying on the coast of the Mediterranean sea. Its position on the crossroads from Africa to Asia made it a target for occupiers and conquerors over the centuries. The last of these was Israel who occupied the Gaza

governorates from Egyptians in 1967. Gaza governorates is very crowded place with area 365 sq. Km and constitute 6.1% of total area of Palestinian territory land. In mid year of 2005 the population number is to be 1,389,789 mainly concentrated in the cities, small village, and eight refugee camps that contain two thirds of the population of Gaza governorates. In Gaza governorates, the population density is 3,808 inhabitants/km2 that comprises the following main five governorates: North of Gaza, Gaza City, Mide-Zone, Khan-younis, Rafah. West Bank is divided into four geographical regions. The North of West Bank includes the districts of Jenin, Tulkarem, Qalqylia, Salfit and Tubas districts. The Center includes the districts of Ramallah and al-bireh, and Jerusalem. The South includes the Bethlehem and Al-Khaliel districts, and the sparsely populated Jordan valley including Jericho. The population density is 420 inhabitants/ km2 and constitutes 93.9% of total area of Palestinian territory land (Palestine, MOH, October, 2006).

According to UNRWA, 2005, by the end of 2005, the total number of Palestine refugees registered in the Agency's area of operation according to UNRWA registration statistics was 4,349,946, which represents an overall increase of 2.7 per cent over 2004 registered population, Agency-wide. The registered population was distributed as follows: Jordan 1,827,877, Lebanon 404,170, Syria 432,048, Gaza governorates 986,034, and the West Bank 699,817. Approximately one third of the registered refugees live in 58 official camps and the remaining population lives in unofficial camps, towns and villages side to side with host country population. The distribution of camp refugee population varies significantly from one field to another, with the highest rates in Lebanon and Gaza governorates and the lowest in Jordan. (Annex no.1).

According to Palestinian MOH, October, 2006, the Population natural increase rate in Palestine is 2.5% in 2005 (3.1% GG & 2.1% WB), which differ from Palestinian Centre

Bureau of Statistic (PCBS) estimation the natural increase rate in Palestine at 3.3% (3.0% in WB and 3.8% in GG), the percentage of population under 15 years old is 46.3% of the total population in Palestine (44.2% in WB and 49.1% in GG). The estimated number of males in Palestine is 1,905,642 compared with 1,856,363 females; the sex ratio in Palestine is 102.7. There is a slight increase in the median age for population in Palestine between 1997 and 2005, where it increased from 16.4 years in 1997 to 16.7 years in 2005. Palestinian Ministry of Health (MOH) has reported that, the crude birth rate (CBR) in Palestine is 27.5/1000 population in 2005 (33.7 GG& 23.9 WB) but According to PCBS data, CBR in Palestine dropped from 42.7 births per 1000 population in 1997 to 37.5 per 1000 population in 2005. MOH has reported that, the crude death rate (CDR) in Palestine is 2.7/1000 population in 2005 (3.1 GG& 2.5 WB) but According to PCBS data, CDR in Palestine declined from 4.8 deaths per 1000 population in 1997 to 4.0 in 2005.

1.7 Israeli Unilateral Disengagement

In August, 2005 the Israel evacuated the occupied Gaza governorates, including all existing Israeli settlements (22) and all military installations which redeployed outside Gaza governorates. After this process it should be no longer for permanent presence of Israeli security forces in areas of GG territory which have been evacuated. In August 2005, Israel evacuated the occupied Northern area of West Bank existing Israeli settlements (4) and all military installations in this area, and redeploed it outside the vacated area. In reality, the Israeli unilateral disengagement imposed huge prison for the Palestinian people introduced by Israeli government for the first time in modern world. This is the newest and most dangerous reoccupation of people with disavowal from their rights and the entitled to live with self determination in their occupied land. Also, all these Israeli activities violate the UN human rights conventions and UN decisions.

1.8 Socio-economic context

According to Ministry of Finance estimation, the year 2005 showed a further steep decline in all Palestinian economic indicators in comparison with 2000, which affect all aspects of the Palestinians life specially health care. The Gross National production (GNP) decreased from 5,275 in 2000 to 4,709 million USD in 2005, and GNP per capita decreased from 1,674 in 2000 to 1,174 USD in 2005. According to W.B., 2005, report which state that, despite positive growth rates during 2003 to 2005, Palestinian incomes remain considerably lower than their pre-intifada levels with real GNP per capita in 2005 about 31% lower than in 1999, the real growth of GNP was 6.3% and the growth of GNP per capita was 2.7%. Unemployment rate increased from 14% in 2000 to 24.5% in 2005 of the workforce. Around 43% of the Palestinian population still falls below the poverty line, with perhaps 15% living in deep poverty and not able to meet substantial needs. In the last two years the situation became worse.

1.9 Health care system

MOH is the main health care provider in Palestine with other health care providers, UNRWA, Medical Services for Police and General Security, health services of national and international Non Governmental Organizations (NGOs), and private health sector. MOH is the health authority responsible for supervision, regulation, licensure and control of the whole health services. Primary health care system (PHC) is a major component of Palestinian health care system; wkich provides health care to all Palestinian people especially for children. Primary health care centers in Palestine provide primary, secondary and tertiary health care services. In the Last five Years and after the uprising of

second Intifada (Al Aqsua), PHC centers in Palestine have been developed in a dynamic way to face instability of Palestinian situation were Israeli occupied Forces tends to divide Palestinian localities into isolated geographical areas. PHC centers try to offer accessible and affordable health services for all Palestinians regardless the geographical locations. According to MOH policy, PHC centers classified from level I to level IV. They offer different health services according to clinic level, theses services include maternal and child health, care of chronic diseases, daily care, family planning, dental, mental services and other services according to center level, at the end of 2005, there are 654 (129 in GG and 525 in WB) PHC centers in Palestine; are cared for about 3.7 million people (Palestine, MOH, October, 2006).

In Palestine the secondary healthcare is provided by governmental, non-governmental, UNRWA and private sectors. MOH is responsible for a significant portion of the secondary healthcare delivery system (60-70% of general and specialized hospital beds) and more than this proportion in hospital services (about 70% of hospital services). In 2005, there are 43 general hospitals with 3,726 beds, 10 specialized hospitals with 812 beds, 19 maternity hospitals with 322 beds and four rehabilitation centers with 165 beds (Palestine, MOH, October, 2006).

1.9.1 Communicable diseases in Palestine:

The Palestinian health authorities have succeeded in the prevention and complete control of many infectious diseases. Where there are no cases of schistosomiasis, leprosy, diphtheria, plague, poliomyelitis, rabies, relapsing fever or malaria has been reported in the last years. Other infectious diseases, such as meningococcal meningitis, brucellosis, HIV, hepatitis, tuberculosis, diarrhea, pneumonia and parasitic infestation remain challenges. Regular notification is needed for the success of their prevention and control programs.

According to Palestine, MOH, October, 2006, 1,044 deaths were reported due to the infectious diseases in 2005 with a proportion of 10.3% of total deaths, with a rate of 27.8 per 100,000 populations. Among infants and children under five years, 179 and 233 deaths were reported with a rate of 1.7 and 0.3 per 1000 infant respectively. 44 deaths and 159 deaths were reported among ages 5-19 and 20-59 with a rate of 2.9 and 10.8 per 100,000 population respectively. The mortality rate due to the infectious diseases among adult aged 60 and above was 369.4 per 100,000 population. Distribution of mortality by sex due to the infectious diseases was 53.4% among males with a rate of 29.2 per 100,000 and 46.6% among females with a rate of 26.2 per 100,000. Mortality rate due to pneumonia and other respiratory infections still the highest incidence rate of infectious disease, per 100,000 population which constituted 17.8, septicemia 7.7, diarrhea and gastroenteritis 0.2 and meningococcal disease 0.4. Moreover 65 deaths (47 deaths in G and 18 deaths in WB) were reported due to other infectious diseases with mortality rate of 1.7 per 100,000 population, including hepatitis and pulmonary TB.

In the year 2005, There is notable decrease of HB acute cases in the year 2005, where 40 cases were reported with an incidence rate of 1.06 per 100,000 population, compared with 104 cases in 2004 with an incidence rate of 2.9 per 100,000 with a decreasing percentage of 160%. No significant change of HBV carriers incidence rate between 2004 and 2005, it remains moderately endemic at incidence rate of 52.5 per 100,000 in 2005, and 53 in 2004. The prevalence of HBV carriers among blood donors was 2.3% (Annex no. 2). In addition to continuous decline in hepatitis C cases and carrier to 0.05 per 100,000 population. On the other hand slightly increase of reported hepatitis A cases to reach 85 per 100,000. The low incidence and prevalence of HBV is due to the efficacy of vaccination program among infants and other groups at high risk in addition to success of health education programs and importance of early detection and management. The current policy of the MOH

routinely examines all blood donors, screening were carried out among 50,309 in the year 2004; with a prevalence rate of 2.4% with an annual average prevalence rate of 2.6% in the last five years. In addition, 38,699 blood samples were examined for patients with a prevalence rate of 4.8% with an annual average prevalence rate of 6.1% in the same period (Palestine, MOH, October, 2006).

1.9.2 Immunization and child health:

Palestinian system for disease prevention and control programs include the EPI, which aimed to reduce the incidence of communicable diseases. The immunization program is the major success of PHC where the services are available, accessible and affordable almost in all the PHC centers in both GG and WB. It is worth to mention that UNRWA plays an important role in providing immunization to refugees children with no cost through the coordination and cooperation with MOH. The MOH and UNRWA offered two main programs of vaccination, the EPI during infancy and early childhood, and the second program is the booster doses of DT, OPV and d.T. vaccines, in addition to, rubella for female students at 12 years. As recommended by WHO, EPI is conducted to cover the following infectious disease: Diphtheria, Pertussis, Tetanus, HB, Polio, Measles and Tuberculosis as well as German measles and Mumbs (Anex no. 3).

Vaccines are provided from different sources such as MOH,UNICE and WHO, Situation regarding the availability of vaccines to cover all population is generally good and immunization activities are regular in MOH and UNRWA Clinics. Immunization is provided at MCH/PCH centers and with the help of mobile immunization team regularly visiting villages in addition to UNRW health center services. Vaccination is the most important tool for HB prevention, and HB vaccine is fully integrated into the national immunization program for children under 1 year of age since 1993 with high coverage rate

of 99%. HB vaccination is given on a voluntary basis for medical and paramedical personnel who are at risk of exposure to this virus, the vaccine is also given a voluntary and free of charge to the contact members of a family has infected person. Immunization program performance is now increasingly measured not only by immunization coverage rates, but also, and more important, by measuring the reduction in the incidence of EPI target diseases. Surveillance data are crucial in assessing whether disease eradication, elimination and reduction targets are being met and where resources should be targeted for maximum cost-effectiveness (Anex no. 4). In Palestine immunization coverage remains high, based on the reports received from Immunization department, the average coverage rates were more than 95% for all vaccines, which had clear impact on reduction in the incidence of vaccine preventable diseases (Annex no. 5).

Chapter two

Literature Review

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Literature Review

2.1 History of HBV

According to Lai, et al, 2003, HBV was first discovered in 1963 by Dr. Baruch Blumberg and colleagues, who identified a protein (Australia antigen) that reacted to antibodies from patients with hemophilia and leukemia. The association of this protein with infectious hepatitis was discovered 3 years later by several investigators, and HBV was specifically seen by electron microscopy in 1970 (Mast, et al, 2004). HBV is a double-stranded hepatotropic DNA virus belonging to the family Hepadnaviridae. It is a 42 nm spherical particle with a 27 nm diameter, electron-dense, nucleocapsid core and a 7 nm thickness outer lipoprotein envelope containing the surface antigen (HBsAg), the viral genome is 3.2 kb in length, and possesses four partially overlapping open-reading frames that encode various antigens (Seeger & Mason, 2000), and an active polymerase enzyme that is linked to a single molecule of double-stranded HBV DNA, virus can be subdivided into 8 different genotypes, based on the degree of variation. The clinical importance of these is still uncertain, however (Lai, et al, 2003).

HBV infects only humans and some other non-human primates, HBV can survive outside the body for up to 1 week, and viral replication takes place predominantly in hepatocytes and to a lesser extent in the kidney, pancreas, bone marrow, and spleen. Intracellular HBV is non-cytopathic and causes little or no damage to the cell (Ganem & Schneider, 2001).

2.2 Magnitude of HBV problem

Chronic HBV infection is one of the most common and persistent viral infections in humans, more than 350 million people worldwide are chronically infected and at high risk of death from liver cancer and cirrhosis (WHO, HB Fact sheet, 2004). People with chronic HBV infection are at high risk for 2 serious liver diseases: cirrhosis and primary liver cancer, from 500,000 to 700,000 people die each year from HBV-related liver disease (WHO, W.E., 2004). In Africa and Asia, liver cancer is the second most frequent cause of cancer deaths among adult males, most of which are attributed to HBV infection (Shibuya, et al, 2003). 1 to 2 % of adults with acute HB develops fulminate hepatitis for which the mortality rate is between 60 and 90% in the absence of liver transplantation (CDC, 2004). In a study by WHO,V&B, 2000, liver cirrhosis and HCC cause an estimated 470 000 deaths per year, an other study by Parkin, et al, 2001, primary liver cancer is ranked the 6th most common cancer globally; over 50% are caused by chronic HBV infection.

HBV is considered, after tobacco, the number two carcinogen. In 1996, it was estimated that more than 1 million people acquired acute HB infection in the 51 countries of the WHO European Region; of these, 90000 cases progressed to chronic infection (FitzSimons, et al, 2002).

2.2.1 International magnitude of HBV problem:

In United States mortality from HB was five times that from Haemophilus influenzae type B and 10 times that from measles before routine vaccination of children was introduced (Roure, 1995). Approximately 5%–25% of persons with chronic HBV and HCV infection will die prematurely from cirrhosis and liver cancer. Approximately 1 million persons in the United States have chronic HBV infection, and 3 million have chronic HCV infection

(Kim, et al, 2002). In CHINA, HB infection is highly endemic (approximately 60% of the total population has been infected and 9-10% are chronic carriers), (China, 2004).

In Europe the level of endemicity generally increases from north to south and from west to east, but factors such as changes in family size, high risk lifestyles, and population migration from areas of high to low endemicity are also affecting the distribution of the virus, the Regional Office for Europe of the WHO estimates that a million people are infected in Europe every year, of these, about 90 000 will become chronically infected carriers and about 22 000 will die from cirrhosis and liver cancer. Unexpectedly high prevalence's of HB carriage have been found in many parts of central and eastern Europe and the newly independent states of the former Soviet Union. In the Central Asian republics of the former Soviet Union and in some countries of central and eastern Europe (such as Albania, Bulgaria, Moldova, Romania), HB is a serious threat to community health, with an estimated annual incidence of 520 infections/100 000. The remaining countries of central and Eastern Europe have an estimated annual incidence of 130 infections /100000. These countries have intermediate or high endemic (Roure, 1995). In the UK, each year there are an estimated 4300 acute HB infections, more than 7500 new cases of chronic infection with HB (mainly in immigrants), and up to 430 cases of HB related hepatocellular carcinoma (FLRHB, 2004).

2.2.2 Magnitude of HBV problem in Mediterranean area:

By WHO,1995, middle east countries represent the global epidemiology of HBV infection, with the prevalence of chronic carriers showing considerable variation between and within the countries, studies in the middle east show the prevalence of HBsAg to range from 3% to 11%. In Lebanon a study done by Baddoura, Haddad & Germanos, january, 2002, 2893 blood samples were examined and a questionnaire were answered, exposure to HBV

antigen was 18.9%; 1.9% were carriers and acute HB point prevalence was 0.1%, exposure to HCV antigen was 0.7%, exposure to both HBc and HCV antibodies was 0.2%. In Jordan a study by Said, Saleh & Jumaian, 2001, to determine the prevalence of HBsAg among 192 chronic schizophrenia patients, 14 were positive for HBsAg while only 5 of control subjects tested positive. According to a study in Egypt conducted by Darwish, et al, on 70 patients with HCC, and sera from patients were tested for anti-HCV and HBsAg markers. 30% were anti HCV positive alone, 21.4% were HBsAg positive alone, 40% were positive for both anti-HCV and HBsAg and the remaining 8.6% were negative for the two markers. The total positivety for anti-HCV and for HBsAg in these patients was 70% and 61.4% respectively. The comparable figures in a recent study on 90 blood donors from Egypt were 24.4% for anti-HCV and 4.4% for HBsAg.

2.2.3 Magnitude of HBV problem in Palestine:

Palestine as other Countries in middle east falls in the region of intermediate prevalence rate of HBV infection, within the Palestinian population there is a high morbidity rate of HB, a high infectivity rate among newborns due to vertical transmission from positive pregnant women, and delays in vaccination for confirmed cases of HB as a result of the current political situation. In a study by Yassin, et al, 2002, the prevalence and risk factors of HB surface antigen (HBsAg) were investigated and simulated the incidence of HBV infection from reported cases of acute hepatitis due to HBV. Blood samples from 810 randomly selected individuals from the general population and from 17,060 blood donors were tested for HBsAg. The prevalence of HBsAg was found to be 3.5% in the general population and 3.8% in blood donors. The simulation model revealed the incidence of HBV infection decreased between 1990 and 1999 from 233 to 56 per 100,000/year. On an other sero-survey was carried out in cooperation between MOH and Unicef in 2003,

among children aged 18-30 months old for measles, rubella and HB, the result was the HB immune response was 92%, ranging between 83.3% in Jericho governorate and 98% in Qalqilia governorate (Palestine, MOH, 2003).

2.3 The economic burden of HBV infection

By Beutels, 2001, from an economic standpoint, HB vaccination is considered cost-effective or a good 'buy' for the public health services. The economic burden of HBV infection is substantial because of the high morbidity and mortality associated with the above-mentioned complications. In Italy, the estimated yearly cost of hospitalization for chronic liver disease related to HBV infection is 60 million euros. One United States-based study estimated the average cost per hospitalization at 8464$ (in 1999 US dollars) for a patient with hepatitis, increasing to 14 063$ for a patient with Cirrhosis (Metcalf, et al, 1999). The cost of a liver transplant is higher still (estimated at 89 076$). In Germany, total HBV-related costs have been estimated at DM 1200 million (95% CI 924.2–1536.7) in 1997 (Harbarth, et al, 2000). In 1997 a South Korean study conducted by Yang, et al, 2001, the annual societal cost (direct and indirect costs) was estimated to be 957.7$ million, of the total societal cost, 126.7$ million was attributable to prevention (vaccine) and the rest to HBV-related disease (including 434.7$ million for cirrhosis). For HBV-related disease, direct costs amounted to 632.3$ million (or 1219$/year/patient), and indirect costs to 200.3$ million. The direct cost (prevention- and disease-related), was equivalent to 3.2% of the South Korean healthcare expenditure for 1997.

The full economic impact of HB mass vaccination programs cannot be evaluated yet because the complications generally start to appear after 15 years. Nevertheless, the results of numerous cost-effectiveness studies showed cost savings for universal immunization programs in most countries regardless of the level of Endemicity (Beutels, 2001).

According to CDC, September, 2003, by providing countries with technical and financial support, the Global Alliance for Vaccines and Immunization (GAVI) and the Vaccine Fund have made significant contributions to the introduction of HB vaccine into EPI. Although the price of monovalent HB vaccine for developing countries has decreased from approximately 3.00$ per dose in 1990 to 0.30$ per dose in 2001, the cost remains higher than that of the older vaccines included in childhood immunization programs. The price of DTP, measles, and polio vaccines range from 0.06$ to 0.10$ per dose. Many countries now recognize the cost-effectiveness of HB vaccine as childhood immunization reduces the disease burden of chronic HBV infection – deaths from cirrhosis and liver cancer. These are important factors in promoting the integration of HB vaccine into national childhood immunization schedules.

2.4 HB virus infection

2.4.1 Clinical features of HBV:

According to Hollinger & Liang, 2001, the sera of infected patients may contain as many as (10^{10}) **i**nfectious virions per ml. The complete virion has a buoyant density of about 1.22 g/cm3 in CsCl and a sedimentation coefficient of 280 S in sucrose gradients, and present in two type of viral particles:

- Infectious HBV particle: 42 to 47 nm double-shelled particles, outer envelope containing lipid and three forms of HBsAg, 27nm nucleocapsid made of 180 copies of core protein, containing the polymerase and HBV DNA.
- Empty noninfectious particles: 22 nm spheres and filaments of variable length containing lipid and mainly one form of HBsAg usually present in 10000 to 1000000-fold excess over Dane particles.

Titers of the virus in the blood can range between <104/ml and >109/ml. The incubation period of HBV ranges from 45 to 160 days (mean = 100 days). Symptoms therefore range widely in severity, from asymptomatic, sub clinical infection to fulminate, fatal disease (Nair & Perrillo, 2003).

2.4.2 Diagnosis:

HBV can be diagnosed by two scales:

- Large-scale screening for HBV infection: biochemical assessment of liver function include total and direct bilirubin, ALT, AST, alkaline phosphatase, prothrombin time, total protein, albumin, globulin, complete blood count, and coagulation studies (Robinson, 1995; Hollinger & Liang, 2001). Diagnosis is confirmed by three clinical useful antigen-antibody systems:
    1. HBsAg and antibody to HBsAg (anti-HBs)
    2. Antibody (anti-HBc IgM and anti-HBc IgG) to HB core antigen (HBcAg)
    3. HB e antigen (HBeAg) and antibody to HBeAg (anti-HBe)

HBsAg can be detected in the serum from several weeks before onset of symptoms to months after onset, HBsAg is present in serum during acute infections and persists in chronic infections, the presence of HBsAg indicates that the person is potentially infectious (Robinson, 1995; Mahoney & Kane, 1999 and Hollinger & Liang, 2001). The first detectable viral marker is HBsAg followed by HBeAg and HBV DNA, titers may be high during incubation period, but HBV DNA and HBeAg levels begin to fall at the onset of illness and may be undetectable at time of peak clinical illness (Ganem & Prince, 2004). Core antigen does not appear in blood, but anti-HBc is detectable with the onset of clinical symptoms. The immunoglobulin M (IgM) fraction is used in an important diagnostic assay for acute HB infection. Before current molecular assays were available, it was the only

marker detectable at the time between when HBsAg disappears and anti-HBs appears, the "window period" (Weber, et al, 2001; Kuhns, et al, Jun, 2005). The presence of a precore mutant, causing HB e antigen-negative chronic hepatitis, has a number of implications regarding the natural history, as well as treatment options and outcomes (Okamoto, et al, 1994; Scaglioni, Melegari & Wands, 1997; Shindo, et al, 1999).

Anti-HBc is the first antibody to appear, demonstration of anti-HBc in serum indicates HBV infection, current or past, IgM anti-HBc is present in high titre during acute infection and usually disappears within 6 months, although it can persist in some cases of chronic hepatitis. This test may therefore reliably diagnose acute HBV infection. IgG anti-HBc generally remains detectable for a lifetime (Robinson, 1995; Mahoney & Kane, 1999 And Hollinger & Liang, 2001).

Anti-HBe appears after anti-HBc and its presence correlates to a decreased infectivity. Anti-HBe replaces HBeAg in the resolution of the disease (Robinson, 1995; Mahoney & Kane, 1999 And Hollinger & Liang, 2001).

Anti-HBs replace HBsAg as the acute HBV infection is resolving. Anti-HBs generally persists for a lifetime in over 80% of patients and indicates immunity (Robinson, 1995; Mahoney & Kane, 1999 And Hollinger & Liang, 2001).

Acute hepatitis patients who maintain a constant serum HBsAg concentration, or whose serum HBeAg persists 8 to 10 weeks after symptoms have resolved, are likely to become carriers and at risk of developing chronic liver disease. The presence of anti-HBsAb and anti-HBcAb (IgG) indicates recovery and immunity in a previously infected individual, whereas a successful vaccination response produces antibody only to HBsAg (Liang &

Ghany, 2002). Patients with chronic infection will spontaneously clear surface antigen at a rate of 0.5% a year (Kuhns, et al, Jun, 2005).

- Small-scale screening for HBV infection: Immunofluorescence studies, in situ hybridization, immunohistochemistry, and thin-section electron microscopy are used to examine pathological specimens for the presence of HBV-associated antigens or particles, providing information about the relationship between HBV DNA replication and HBV gene expression (Hollinger & Liang, 2001). Within the hepatocyte, HBsAg localizes in the cytoplasm and HBcAg is seen in the nucleus and/or the cytoplasm. Detection of complete virions in the liver is uncommon (Hollinger & Liang, 2001).

DNA hybridization techniques and RT-PCR assays have shown that almost all HBsAg/HBeAg-positive patients have detectable HBV DNA in their serum, whereas only about 65% of the HBsAg/anti-HBe reactive patients are positive. All patients who recover from acute HB are negative for HBV DNA. On the other hand, some patients infected chronically who have lost their HBsAg remain HBV DNA positive (Robinson, 1995; Hollinger & Liang, 2001).

2.4.3 Treatment:

No specific treatment exists for acute HB, persons who have chronic HBV infection require medical evaluation and regular monitoring (Lok & McMahon, 2001; Lok & McMahon, 2004). There are two main classes of treatment:

1. Antiviral: aimed at suppressing or destroying HBV by interfering with viral replication.

2. Immune modulators: aimed at helping the human immune system to mount a defense against the virus.

Neither corticosteroids, which induce an enhanced expression of virus and viral antigens, and a suppression of T-lymphocyte function, nor adenine arabinoside, acyclovir or dideoxyinosine, have been shown to be beneficial for the treatment of chronic HB. Currently, chronic HB is treated with interferons (Mahoney & Kane, 1999; Hollinger & Liang, 2001).

2.5 Age distribution for HBV

According to Robinson, 1995, Mahoney & Kane, 1999, the infecting dose of virus and the age of the person infected are important factors that correlate with the severity of acute or chronic HB. Primary HBV infection may be associated with little or no liver disease or with acute hepatitis of severity ranging from mild to fulminate. HBV infection is transient in about 90% of adults and 10% of newborn, and persistent in the remainder, most cases of acute hepatitis are sub clinical, and less than 1% of symptomatic cases are fulminate. By WHO/V&B, 2001, only a small proportion of acute HBV infections are recognized clinically, less than 10% of children and 30-50% of adults with acute HBV infection will have icteric disease. According to two publications by WHO/UNICEF, August, 2005; WHO /V&B/ September, 2005, estimated deaths in 2002 due to HB: 600 000, of which less than 1000 were under age five. By CDC, 2005, fatality rate among persons with reported acute HB is 0.5–1.5%, with highest rates in adults aged >60 years (Annex no. 6).

2.6 Global distribution of HBV and Geographic patterns of transmission

According to WHO/V&B, 2001; Mast, et al, 2004, approximately 45% of the world population live in areas where chronic HBV infection is highly endemic (>8% of the

population are HBsAg-positive), include most of Asia and Africa, where the lifetime risk of HBV infection is more than 60% and most infections are acquired from perinatal and child-to-child transmission. 43% live in areas of intermediate endemicity (2-7% HBsAg-positive), include India and most of northern Africa, Middle East and Eastern Europe, where lifetime risk of HBV infection is 20-60% and infections occur in all age groups, acute HB is common in these areas because many infections occur in adolescents and adults. However, high rates of chronic infection are maintained mainly because of infections occurring in infants and children. 12% live in areas of low endemicity (<2% HBsAg-positive), include most of North America, Western Europe and Australia, where lifetime risk of HBV infection is less than 20%, most HBV infections in these areas occur in adults in relatively well-defined risk groups, but a high proportion of chronic infections may occur as a consequence of perinatal and child-to-child transmission (annex no. 19).

2.7 Risk factors of HBV

2.7.1 Risk factors of HBV from pernatal transmission:

Pernatal transmission usually happens at the time of birth; in utero transmission is relatively rare, accounting for fewer than 2% of perinatal infections in most studies, (Lee, et al, 1991). The risk of perinatal transmission depends on the presence of HBeAg in the blood of mother infected with HBV (Margolis, Alter & Hadler, 1997). Areas with intermediate HBV endemicity, include the Mediterranean countries, the Middle East and the Indian subcontinent. Perinatal, household was one of the major sources of infection in the past (Rosina, et al, 1999). CDC estimates that perinatal HBV infection in the United States declined 75% during 1987--2000 (CDC, preview, 2000). Studies in Egypt also suggest that perinatal transmission is relatively high. El-Nawawy, et al. detected HBsAg in

8% of pregnant mothers and 17% of their infants; none of the HBsAg-positive mothers or their infants was HBeAg positive.

2.7.2 Risk factors of HBV from Child-to-child transmission:

Transmission usually happens in household settings but may also occur in child day care centers and in schools (Oleske, et al, 1997; Martinson, et al, 1998). The most probable mechanisms of child to child spread involve contact of skin sores, small breaks in the skin, or mucous membranes with blood or skin sore secretions (Margolis, Alter & Hadler, 1997). HBV may also spread because of contact with saliva through bites or other breaks in the skin, and as a consequence of the premastication of food (Williams, et al, 1997), in addition the virus may spread from inanimate objects such as shared towels or toothbrushes, since it can survive for at least seven days outside the body and can be found in high titers on objects, even in the absence of visible blood (Martinson, et al, 1998).

2.7.3 Risk factors of HBV from Sexual transmission:

By CDC, MMWR, 2005, high-risk sexual behaviors (unprotected sex with multiple partners) and injection drug use are the major risk factors. About 5% of people in the U.S. have evidence of past infection with HBV and approximately 1.25 million people have chronic HBV infection. HBV is efficiently transmitted by sexual contact, which can account for a high proportion of new HB infections among adolescents and adults in countries with low and intermediate endemicity of chronic HBV infection (Alter & Margolis, 1990). According to a study by Rosina, et al, 1999, it was in the past sexual transmission probably represented the major sources of infection. In highly endemic countries, sexual transmission does not account for a high percentage of cases because most persons are already infected during childhood (Alter & Margolis, 1990; Maddrey,

2001 and Goldstein, et al, 2002). In a study to Goldmann, 2002, the risk increases with the number of partners, years of sexual activity, history of other sexually transmitted infections, and with receptive anal intercourse.

2.7.4 Risk factor of HBV from Blood transfusion:

Blood transfusion is a major source of HBV transmission in countries where the blood supply is not screened for HBsAg (Hutin & Chen, 1999), even when blood products are tested for HBsAg there is still a minor risk of transmission, (Gerlich & Caspari, 1999). In well-developed countries it appears to be 2–16 cases per million units of blood, depending on the prevalence of HBsAg carriers in the population, some countries also screen for anti-HBc to further decrease HBV transmission by transfusion. The risk of transfusion related HBV infection is unknown in poor countries, where screening of donors is not always performed. WHO estimates that globally about 6 million units of blood are not properly tested (Simonsen, et al, 1999). In epidemiologic study of chronic HB virus infection in male volunteer blood donors in Karachi, Pakistan, HBsAg prevalence in the male volunteer blood donors was 2.0 % (Akhtar, et al, 2005).

2.7.5 Risk factor of HBV among Hemodialysis patients:

HBV and HCV infections are important causes of morbidity and mortality in Hemodialysis patients and pose problems in the management of patients in the renal dialysis units, because chronic renal failure patients do not clear these viral infections efficiently (Saha & Agarwal, 2001; Moreira, et al, 2003), HBV infection is usually less prevalent than HCV in haemodialysis units (Oesterreicher, et al, 1995), moreover dual infection with HBV and HCV leads to more aggressive liver disease (Devi, et al, 2004), primary infections also become chronic more fre-quently in immunosuppressed persons (Polish, et al, 1992). In

USA, with only 3.5% of all centers reporting newly acquired infections, prevalence of positive HBsAg among hemodialysis patients declined from 7.8% in 1976 to 3.8% in 1980 and to 0.9% by 1999. In 1999, a total of 27.7% of 3,483 centers provided dialysis to ≥1 patient with either acute or chronic HBV infection (Tokars, et al, 2000). Due to the Introduction of HBV vaccination, isolation of HBV positive patients, use of dedicated dialysis machines and regular surveillance for HBV infection dramatically reduced the spread of HBV (Fabrizi, Poordad & Martin, 2002). In India a study was done on 134 haemodialysis patients were screened for HBsAg and anti-HCV antibodies, the result showed that the prevalence of HBV was 1.4% and HCV 5.9% while infection with both viruses was observed in 3.7% of the patients (Reddy, et al, 2005). A study in Brazil on 434 haemodialysis patients from three different haemodialysis units in Belo Horizonte showed that the average prevalence of seropositivity to HCV (anti- HCV) was 20.3% and 4.4% for HBV, while co infection was detected in two patients only. The prevalence of HCV RNA among HCV seropositive patients was 94.3% (Busek, et al, 2002).

In Gaza governorates, about 210 end stage renal disease patients receive haemodialysis in four centers at El-Shifa, Nasser, Abu-Yousef Al-Najar and Shuhada El-Aqsa Hospitals, there is almost no data about the situation in these centers.

2.7.6 Risk factors of HBV from Dental Clinic:

In a study by Tullman & Boozer, 1997, Samples of blood from 327 new patients at a dental school were tested by radioimmunoassay for the presence of HBsAg and anti-HBs. The data were compared to the patients' histories of hepatitis. Through a statistical analysis, it was indicated that significant numbers of patients with no history of hepatitis had been infected with HBV. Although HBV infection is uncommon among adults in the United States (1%-2%) serologic surveys have indicated that 10%-30% of health-care or dental

workers show evidence of past or present HBV infection (CDC, 1989). Studies of seropositivity for HBV infection, carried out among dentists in the pre-vaccination years show that. In the United States in (1991, 1996) respectively showed (15%, 9%) (Gruninger, et al, 1991). 7% among dentists from Berlin, in Germany (Ammon, et al. 2000). Unsatisfactory infection control practices, including the reuse of contaminated medical or dental equipment, failure to use appropriate disinfection and sterilization practices for equipment and environmental surfaces, and improper use of multi dose medication vials (Hutin & Chen, 1999). In Brazil a study By Batista, et al, May, 2006, Blood samples from 474 dentist, the result was 10.8% dentists showed seropositivity for HBV. 0.6% were HBsAg/anti- HBc/anti-HBe positive, 9.1% were anti-HBc/anti-HBs positive, and 1.1% had only anti-HBc.

2.7.7 Risk factor of HBV between health care workers and patients:

Nosocomial infections occasionally occur in discrete epidemics related to failures in the implementation of universal precautions and safe injection practices, (Rosina, et al, 1999), infected health care workers can infect others (Puro, et al, 2001), the risk of transmission from infected medical personnel to patients is much higher for HBV than for HCV or HIV (Goldstein, et al, 2002), in this high-risk group, harm reduction counseling, drug substitution (such as methadone) and needle exchange programs have resulted in a reduction in the incidence of blood borne viral infections (Gerlich & Caspari, 1999). Uninfected workers are themselves at risk, particularly from percutaneous injuries like needle stick (Mahoney, et al, 2003). A study in Brazil was done on serum from 813 patients, 149 haemodialysis workers from all the 22 dialysis units at Santa Catarina, and 772 healthy controls assayed for HBV markers. The study showed that the frequency of HBV infection was 10.0%, 2.7% and 2.7% among patients, haemodialysis workers and

controls, respectively (Carrilho, et al, 2004). In across sectional study of 399 healthcare personnel was conducted in governmental healthcare settings of the southern region of Gaza governorates. the results revealed that, the prevalence of HBsAg was 2.8% among health workers. Needle injection showed a highly significant association as a main risk factor for infection. The rate of infection among non-vaccinated health workers was approximately (4.1%) that among vaccinated participants (2.0%). However, among those who had less than 3 doses of vaccine, the rate of infection was higher (3.9%) than those who had received 3 doses (1.5%) (El-astal & Edher, 2004).

2.7.8 Risk factor of HBV from Transplantation of organs:

Transmission of HBV by bone marrow and non-liver solid organ transplantation has been largely eliminated by screening donors for serum HBsAg. Transmission from donors with isolated serum anti-HBc can occur, but the risk is low for non-liver solid organs. Liver graft from donors with HBV serum markers can transmit HBV infection. The risk is almost 100% for liver grafts from HBsAg-positive donors, over 70% for donors with isolated anti-HBc, and very low for grafts from anti-HBs and anti-HBc positive donors (Rosen & Martin, 2000). According to many studies by Davis, Gretch & Carithers, 1995; Martin, et al, 1995 and Law, et al, 2005, re infection or reactivation of latent HBV infection has been reported among certain groups of immunosuppressed persons, including renal transplant recipients, HIV-infected patients, bone marrow transplant recipients, and patients receiving chemotherapy.

2.7.9 Risk factor of HBV from Injection transmission:

By CDC, MMWR, 2005, high-risk sexual behaviors and injection drug use are the major risk factors for evidence of past infection with HBV.

a. Tattoos:

Tattooing is a risk factor of HBV in areas with intermediate HBV endemicity, (Rosina, et al, 1999). Hepatitis C and B viruses have a association in some modes of transmission, Robert Haley and colleagues reported that individuals who had received a tattoo in a commercial tattoo parior were more likely to be infected than people who had not been tattooed (nine times with HCV), and a study of prisoners in Norway found that tattooing was significantly associated with drug use. The data showed that people who reported having a tattoo had higher rates of HCV infection. However the risk of HCV was greatly increased if the tattoos had been done in jail (Baeumler, et al, 2000).

b. Unsafe injections:

Transmission occurs because of non-compliance with universal precautions and with safe injection techniques (e.g. through overuse of injections to administer medications, re-use of equipment in the absence of sterilization, inadequate cleaning and sterilization practices, and contamination of sterile equipment/medication vials). It has been estimated that globally 8–16 million new HBV infections occur annually due to the use of unsafe injections (Simonsen, et al, 1999), Unsafe injection practices are a major source of transmission of HBV and other blood borne pathogens (e.g. hepatitis C virus, HIV) in many countries, (Kane, et al, 1999). In many developing countries, up to 50% of injections are administered with needles and syringes that are reused without sterilization. Moreover, a substantial proportion of therapeutic injections, accounting for approximately 90% of the estimated 12 billion injections administered each year throughout the world, are unnecessary, inject able medications are often inappropriately used, and most medications given in primary care settings can be administered orally (Hutin & Chen, 1999). In countries of Eastern Europe, a high incidence and prevalence of HBV infection in the last

decades was often connected to re-use of medical equipment coupled with inadequate methods of sterilization (Magdzik, 2000).

c. Intravenous injection of illicit drugs:

Intravenous injection of illicit drugs is a major source of infection worldwide, and proportionally more so in countries of low endemicity (Goldstein, et al, 2002), needle sharing among injecting drug users is a risk factor in areas with intermediate HBV endemicity, (Rosina, et al, 1999).

2.8 Vaccine and Prevention for HBV

2.8.1 Implementation and Need for HBV Vaccination:

"Vaccines are the corner-stone of contemporary medicine and are considered the best approach to reduce morbidity and mortality due to infectious disease." (Nature Medicine, 2005).

According to WHO, 2005, estimated number of deaths averted by immunization in 2003: more than 2.1 million, as well as an additional 600 000 hepatitis-B-related deaths that would otherwise have occurred in adulthood. In a publication by WHO/V&B/ 01.01, 2000, the number of countries including HB vaccination in their national immunization program increased progressively from 20 in 1991 to 129 in 2000, while a study by Healy, et al, 2001, show that, only 116 of 215 countries in 2000 have such a policy. Thus, despite the availability of an effective vaccine for more than 15 years, most of the world's children remain at risk for HBV infection. Immunization strategies in developed countries vary widely. According to two publications by WHO/UNICEF, August 2005 & WHO /V&B/ sept., 2005, the number of countries that integrated HB vaccine into their routine infant

immunization schedules by 2004: 153, this is a five-fold increase compared to the number of countries that used the vaccine in 1992 and is the result of tremendous global advocacy, a decrease in HB vaccine prices, and the availability of resources to the poorest countries. Despite this significant increase, less than half of the world's infants had received three doses of HB vaccine by the end of 2004. Continued efforts will protect millions more and achieve the 2007 HB introduction goal, and at regional and country level By the end of 2005: Nineteen countries in the Eastern Mediterranean Region had introduced HB vaccine into their routine immunization programs. Forty-four countries in the European Region had implemented universal HB immunization. HB vaccine had been introduced in some or all districts of all countries in the South-East Asia Region (except Timor-Leste). All countries in the Western Pacific Region (accounting for half the global disease burden of HB) had HB control programs through immunization.

According to Mast, et al, 2004, HB vaccine is the first vaccine against cancer. Primary liver cancer caused by HBV is the leading cause of cancer death in males in sub-Saharan Africa and much of Asia. When countries include HB vaccine as part of routine childhood immunization programs, HBV infection in children is essentially eliminated in 10 to 15 years. In 30 to 40 years after the vaccine's introduction, there will be no new victims of liver cancer and cirrhosis caused by HBV.

According to CDC, MMWR, 1995, in the United States, the immunization strategy has evolved over time and now includes: prevention of perinatal HBV infection through routine screening of all pregnant women and appropriate postexposure immunoprophylaxis of infants born to HBsAg positive women, routine vaccination of infants, routine vaccination of adolescents who have not previously been vaccinated, vaccination of adults at increased risk of infection. In a study by Van Steenbergen, et al, 2001, most countries in

western Europe have focused efforts on prevention of perinatal infection and routine vaccination of adolescents; rarely, routine immunization of infants also has been included.

According WHO, 2005 highlights, since the creation of GAVI, whose main aims include the provision of new and under-used vaccines (particularly HB vaccine) to the poorest countries, an acceleration occurred. As a consequence, nations with routine infant immunization against HB have reached 154 in June 2002. Of the 74 countries eligible for support from GAVI, 38 have already received approval to introduce routine HB vaccination, and many others are in the process of application. However, about 37 million of the 132 million children born each year do not even receive the basic vaccination originally included in the EPI, 25 million of which live in the poorest countries.

2.8.2 Types of HB Vaccine:

There are two types of HB vaccine are available:

- Recombinant or genetically engineered vaccines are made using HBsAg synthesized in yeast or mammalian cells into which HBsAg gene has been inserted.
- Plasma-derived vaccines are prepared from purified HBsAg from the plasma of persons with chronic HBV infection.

The two types are similar with respect to safety, immunogenicity and efficacy. HB vaccines are available in monovalent for mulations that protect only against HB; it does not protect against other types of hepatitis or jaundice. While combination formulations that protect against HB and other diseases (e.g. DTP-HepB, DTP-HepB+Hib, Hib-HepB), there is speciality in use of each type:

- Monovalent HB vaccine **must be used** for the birth dose.
- Combination vaccines that include HB vaccine **must not be used** to give birth dose of HB vaccine because DTP and Hib vaccines should not be administered at birth.

- Either monovalent HB vaccine or combination vaccines **may be used** for later doses in the HB vaccine schedule. Combination vaccines can be given whenever all the antigens in the vaccines are indicated.

The types and formulations of HB vaccines can be interchanged. Vaccines of different types and from different manufacturers can be used for each dose that a child receives. HB vaccines are available in liquid single-dose and multidose glass vials, and in profiled single-dose injection devices. Multidose vials generally contain 2, 6 or 10 doses.

In Palestin from the instituation of HB immunization program in year 1993 up to the year 2007, the recombenent DNA type is given.

2.8.3 Dose of HB Vaccine:

The standard pediatric dose is 0.5 ml. The quantity of HBsAg protein per dose that induces a protective immune response in infants and children varies with the manufacturer, ranging from 1.5 μg to 10 μg, because of differences in HB vaccine production processes. HB vaccine is given by intramuscular injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children). It can safely be given on the same day as other vaccines (e.g. DTP, OPV, Hib, measles, BCG, and yellow fever vaccine). In addition, it can be given at any time before or after a different inactivated or live vaccine because inactivated vaccines such as HB vaccine generally do not interfere with the immune response to other inactivated or live vaccines (CDC, ACIP, 1994). If HB vaccine is administered on the same day as another injectable vaccine, it is preferable to give the two vaccines in different limbs. If more than one injection has to be given in the same limb, the thigh is the preferred site of injection because of the greater muscle mass, and the injection sites should be 2.5 cm to 5 cm apart so that any local reactions are unlikely to overlap (CDC, ACIP, 1994).

2.8.4 Schedule of HB Vaccine:

According to WHO recommendations in WHO/V&B/01.31, HB vaccine schedules are very flexible and there are multiple options for adding the vaccine to existing national immunization schedules without requiring additional visits for immunization (Annex no. 10). Programmatically, it is usually easiest if the three doses of HB vaccine are given at the same time as the three doses of DTP (Annex no.10, Option I). This schedule prevents infections acquired during early childhood, which account for most of the HBV-related disease burden in countries of high endemicity. It also prevents infections acquired later in life. However, this schedule does not prevent perinatal HBV infections because it does not include a dose of HB vaccine at birth. Two schedule options can be used to prevent perinatal HBV infections: a three-dose schedule of monovalent HB vaccine, the first dose being given at birth and the second and third being given at the same time as the first and third doses of DTP vaccine (Annex no.10, Option II); or a four-dose schedule in which a birth dose of monovalent HB vaccine is followed by three doses of a combination vaccine (e.g. DTP-HepB) (Annex no.10, Option III).

- The three-dose schedule (Annex no.10, Option II) is less expensive but may be more complicated to administer because infants receive different vaccines at the second immunization visit than at the first and third visits. Moreover, it may be difficult to achieve a high level of completion of three-dose vaccine series with this schedule in countries where a high percentage of children are not born in hospitals.
- The four-dose schedule (Annex no.10, Option III) may be easier to administer programmatically but is more costly.
- Other factors to consider in deciding which HB vaccine schedule to use in a particular country include the following.

- The minimum interval between dose 1 and dose 2 is four weeks, and the minimum interval between dose 2 and dose 3 is four weeks.
- Schedules should optimize the percentage of children completing the HB vaccine series; higher coverage is usually achieved with earlier administration of vaccines.
- If a dose is missed it should be given as soon as possible. There is no need to start the schedule again.

2.8.5 "Success" Response for HBV Immunization:

A. Pre-exposure immunization: A course of three doses of HB vaccine induces protective levels of anti-HBs in over 95% of healthy infants and children when given in a variety of schedules, including the following: at 6 weeks, 10 weeks and 14 weeks, at 2 months, 4 months and 6 months, at birth, 1 against acute HB and chronic infection (Hadler & Margolis,1992; Courseget & Kane, 1993).

B. Post-exposure immunization: Beginning at birth with either HB vaccine alone or with HB vaccine & HB immune globulin (HBIG), can prevent the spread of more than 90% of HBV infections from mother to baby, the efficacy of giving recombinant HB vaccines alone is similar to giving HB vaccine with HBIG (Andre & Zuckerman, 1994).

Studies by Mclntyre, 1995; Jack, et al, 1999 and Lok & McMahon, 2004, show that Anti-HBs is the only easily measurable correlate of vaccine-induced protection. In a study by Banatvala & Van Damme, 2003, the mechanism for continued vaccine-induced protection is thought to be the preservation of immune memory through selective expansion and differentiation of clones of antigen specific B and T lymphocytes. In a study by Mast, et al, 2003, no clinical cases of HB have been observed in follow-up studies conducted 15–20 years after vaccination among immunocompetent vaccinated persons with antibody levels

>10 mIU/mL, certain studies have documented breakthrough infections detected by the presence of anti-HBc or HBV DNA) in a limited percentage of vaccinated persons. In Egypt A seroepidemiologic study was conducted by Reda, et al, 2003, the result was, rate of HbsAg positively among the vaccinated group was found to be 0.8% compared to 2.2% among the non-vaccinated group, the study showed that the efficacy of HB vaccine in preventing the carriage of HbsAg, 5 years after full course vaccination, was estimated to be around 67%.

According to different studies around the world universal immunization of neonates has resulted in a dramatic reduction in the incidence of acute HB in children and adolescents**.** In United States**,** during 1990–2004, incidence declined 75%, the greatest decline (94%) occurred among children and adolescents (CDC, MMWR, 2005). In Canada, the Province of Québec incidence rates fell dramatically from approximately (5 / 100,000) in 1997 to (1 / 100,000) in 2002 (Duval, et al, 2000). In Italy the incidence dropped by 80% between 1991 and 2003 compared with data for 1985 to 1990 (Mele, Stroffolini & Zanetti, 2002; Italy, VHPB, 2003). In Tuscany the incidence in the age group at highest risk (15–24 years) was halved from 12 in 1991 to 6 in 1994 and 49% decline was registered between 1992 and 1996 (Bonanni, et al, 1999). In Bulgaria, a drop of incidence reached 5.6/100 000 in 1992 vs. 25-35/100 000 during the 1980s (Gatcheva, Vladimirova & Kourtchatova, 1995). In addition to other studies, In Taiwan HBsAg prevalence in the population of under-15-year-olds changed from 9.8% (1984) to 0.7% (1999) (Ni YH, et al, 2001) (Annex no. 11). A study after 5 years of implementation of HB vaccination none of about 600 vaccinated children showed HBsAg reactivity (Tsebe, et al, 2001). In Saudi Arabia a Comparative data for the years 1989 and 1997 show that HBsAg prevalence in Saudi children declined in all areas of the country (Al-Faleh, et al, 1992; Al-Faleh, et al, 1999).

In Thailand a study by Poovorawan, et al, 2000, HBV carrier rate decreased from 3.4% to 0.7% following implementation of the EPI strategy (Poovorawan, et al, 2000).

According to WHO/V&B, 2001, routine immunization of infants almost eliminates chronic HBV infection and will reduce the incidence of liver cancer in immunized children when they reach adulthood. It is also expected that routine infant immunization will decrease the incidence of cirrhosis among adults who were immunized as infants. In Taiwan, the impact of vaccination by mortality rates was studied by Kao, et al, 2001, the result was, the average mortality from culminant hepatitis in infants changed from 5.36/100 000 in 1975–1984 (prior to mass vaccination) to 1.71/100 000 in 1985–1998. A study by Ni YH, et al, 2001, following introduction of mass vaccination during the 15 years, HBsAg prevalence in the population of under-15-year-olds changed from 9.8% (1984) to 0.7% (1999). The impact of mass HB immunization on the chronic consequences of infection have been studied by Chang, et al, 1997, the result was liver cancer death rates fell dramatically among children in Taiwan, in children aged 6–14 years, incidence of HCC progressively declined from 0.7/100 000 in the period 1981–1986 to 0.57/100 000 in 1986–1990, to 0.36/100 000 in 1990–1996 (Annex no. 12).

2.8.6 Factors affecting "Failure" to non- response for HBV Immunization:

A recent study showed a 31% HBV vaccine non-response rate in patients with chronic hepatitis C, and the response to vaccine was independent of HCV RNA titers or the presence of cirrhosis (Idilman, et al, 2000). Approximately 5 to 15% of infants and at least 5 to 10% of most healthy adult population failed to produce protective levels of antibodies to HB vaccination (MEI-HWEI, 2004). In primary non-responders, protective levels of anti-HBs develop in 10-30% of subjects after a single additional dose of vaccine and in 50-

70% after 3 additional doses. Some studies found that higher response rates occur in non-responders who receive additional doses intradermally (Emmet, et al, 2004).

According to a study conducted by Inskip, et al, 1991, to study factors influencing antibody response to HB vaccine in the Gambian EPI, the result show that, the dominant effect was the time between the last dose of vaccine and taking the blood sample. There was considerable variation in vaccine response by area of residence which could not be explained by any other factor. Residence was substantially associated with antibody level (p-value=0.01). The differences could not be attributed to ethnic differences, seasonal variation, season of birth, or season of 1st immunization. The HBsAg status of the mother and the age at vaccination did not appear to have an effect, but there was some indication that a delay in receiving the second dose of vaccine led to a marginally lower response. The greater the interval between the 1st and 2nd doses the lower the antibody response (p-value=0.03). For example, the recommended interval between the 2 doses is 4 weeks, but in those cases where the interval was doubled the antibody response fell 12%. On the other hand, increasing the interval between the 2nd and 3rd doses or the 3rd and the 4th doses did not affect antibody level.

According to a study conducted by Jafarzadeh, et al, 2004, to study the influence of ethnicity and environmental factors of immunogenicity of A recombinant HB Vaccine in Iranian neonates. A total of 521 healthy neonates attending the health centers of Kerman and Urmia were included in this study. Gestational age, birthweight and sex of the neonates were registered and only physically healthy neonates with a minimum weight of 2500 g were enrolled into study. The result was 96.1% and 98.3% of vaccinees in Kerman and Urmia cities developed protective titer of anti-HBs (>10 IU/L), respectively. By measueing geometric mean titer (GMT), no significant differences were observed in

seroprotection rate between neonates of two cities. The percentage of non-responders, low responders and intermediate responders, collectively, was found to be higher in Kermanian neonates than Urmian vaccinees (p-value <0.01). Consequently, the proportion of high responder neonates was lower in the Kermanian group compared to Urmian vaccine recipients (p-value <0.01). the GMT was higher in females compared to males, this difference was not statistically significant. The GMT of both male and female neonates from Urmia (11433 and 12309 IU/L) was significantly (p-value <0.001) higher than those from Kerman (5772 and 6400 IU/L).

In a study by Chang, et al, 1997, the lower efficacy in China is related to the large number of HBeAg-positive mothers, highlighting the need for immediate prophylaxis using HBIG in countries with a high prevalence of HBeAg among HBV carriers.

According to a study by Minuk, Bohme & Bowen, Jun, 1989, some population groups have a poor response to vaccination. Male gender, over weight, smoking, renal failure, chronic liver disease and immunodeficiency are predictive factors for a poor response. In these individuals, additional vaccine doses can increase the response rate. In a study conducted by Alper, et al, 1989, despite the extraordinary efficacy of second-generation HBV vaccines, immunization failure may occur and can sometimes be explained by variables such as improper storage or administration, advanced age, obesity, renal failure, chronic liver disease and especially, immunosuppression.

According to a study by Gold, et al, 2003, to study the decreased immune response to HB eight years after routine vaccination in Israel, by measuring antibody levels in 122 healthy children who were vaccinated in a routine vaccination program, the result was 77.1% of children had detectable Anti-HBs titer (>10mIU/ml), while 22.9% had undetectable Anti-HBs titer (<10mIU/ml). When the children were divided into three groups according to the

time elapsed since vaccination, it was found that the antibody levels declined with time (p-value < 0.009). No correlation was found between Anti-HBs titers and gestational age, birth weight and parental origin, although females generated higher mean antibody levels than males (207.3 ± 217 mIU/ml vs 141.9 ± 218.9 mIU/ml, p-value < 0.05).

According to a study conducted by Yen, et al, 2005, to evaluate the etiology of non-responsiveness to HB vaccination in adults from an endemic area. A total of 250 subjects who were HBsAg negative and anti-HBs<10 mIU/ml received three-dose HB-vaccine series, the result was three variables were associated with non-responsiveness by univariate analysis: anti-HBc positive, male gender, and age >40 years. Multivariate analysis additionally showed that anti-HBs negative was associated with non-responsiveness. Among 23 non-responders in anti-HBc positive subjects, post-vaccination serum was available in 16 subjects. HBV-DNA in all subjects was under detectable level by PCR assay. Anti-HBe positive were found in 13 of 16 subjects.

According to a study in Mongolia by Davaalkham, et al, 2007, where in rural areas, the frequency of immunity induced by vaccine was significantly lower among those with winter administration of birth HB than those vaccinated during non-winter months (p-value= 0.007). However, this difference was not evident in urban areas, after stratifying by residence, the association between winter vaccination and total HBV infection was evident for rural (p-value= 0.008) but not for urban areas (p-value= 0.294). There were no significant differences, in the distributions of sex, HBV-infected mother.

According to a study by Seung-Dae, et al, April, 2007. A significantly (p-value < 0.05) higher proportion of subjects in the Celiac Disease group (53.9%) failed to respond to HBV vaccine compared with controls (11.1%).

According to a study in Egypt by Shaaban, July/August, 2007, only 39.4% of the children had protective (≥ 10 IU/L) Anti-HBs. This proportion decreased with age but the decrease was not statistically significant. The mean level of Anti-HBs decreased significantly with increasing age (p-value= 0.026). A significant negative correlation was found between current age and HBsAb levels (r = –0.31, p-value= 0.041).

In a study by Hill, et al, 2002, by comparing 101 breast-fed infants with 268 formula-fed infants. There was no significant difference between the two groups with respect to the number of women who were positive for HBeAg (22% versus 26%, p-value= 0.51). There were nine cases of HBV infection transmission (2.4%). None of the 101 breast-fed infants and nine formula-fed infants (3%) were positive for HBsAg after the initial vaccination series (p-value= 0.063). the conclusion is appropriate immunoprophylaxis, including HB immune globulin and HB vaccine, breast-feeding of infants of chronic HBV carriers poses no additional risk for the transmission of the HB virus.

2.8.7 Monitoring and Impact of HBV Vaccination:

By Bonanni, et al, 2003, when the decision to introduce a universal program of HB vaccination is taken, the first step is to implement it and to monitor coverage. This may be accomplished by comparing the vaccination register (number of subjects receiving the basic immunization course) with the number of subjects of the same age group supplied by the birth register of each area where the study is performed. If a significant number of irregular immigrants are present, a precise estimate of their number and of their immunization status should be obtained in order to get the real coverage in that area. A first consequence of the implementation of routine vaccination is the decline of the incidence of HB in the age cohorts covered by immunization. As to this aspect, it is particularly important to investigate the risk factors and reasons of possible cases occurring

in age groups subject to recommended or mandatory vaccination. When a case occurs in a vaccinated subject, it should be investigated whether this is due to a wild-type or to a mutant virus, in order to monitor the long term effectiveness of the currently used vaccine and foresee possible need of changes in vaccine composition. As a second step, it is important to monitor the changing prevalence of HBV markers in different age groups, which is consequent to the implementation of immunization programs. In the long term, it is possible to verify a decline in the incidence and prevalence of chronic liver diseases. Safety issues are becoming increasingly important in the perception of the public with regard to acceptance of routine immunization. Since frequent and minor side effects are usually seen during clinical trials preceding vaccine registration, but rare and important adverse events are reported only after a large use of the new product, it is necessary to perform a continuous post-marketing surveillance to verify the safety in the field.

There were many studies in the effectiveness of routine immunization of infants against HB in significantly reducing or eliminating the prevalence of chronic HBV infection has been demonstrated in a variety of countries and settings, number of subjects tested in follow-up serosurveys after implementation of program: In Alaska by Harpaz, et al, 2000, 268 subjects followed- up from 1-10 years, with vaccine coverage 96%, the prevalence of chronic HBV infection in children reduced from 16 before to 0.0 after integration of HB vaccination. In Federated States of Micronesia by Mahoney, et al, 1993, 544 subjects followed- up for 2 years, with vaccine coverage 37%, the prevalence reduced from 12 before to 2.9 after integration. In Gambia by Viviani, et al, 1999, 675 subjects followed- up for 9 years, with vaccine coverage 100%, the prevalence reduced from 10 before to 0.6 after integration. In Saipan by Moulia-Pelat, et al, 1994, 200 subjects followed- up from 3 to 4 years, with vaccine coverage over 94%, the prevalence reduced from 9 before to 0.5 after integration. In Saudi Arabia by Al-Faleh, et al, 1999, 4791 subjects followed- up

from 1 to 8 years, with vaccine coverage over 85%, the prevalence reduced from 6.7 before to 0.3 after integration. In Taiwan by Chen, et al, 1996, 424 subjects followed- up from 7 to 10 years, with vaccine coverage over73%, the prevalence reduced from 10 before to 1.1 after integration.

Chapter Three

Conceptual Framework

Chapter 3

Conceptual Framework

3.1 Conceptual Framework for risk factors to non- response to HB vaccination

When I look to construct a conceptual framework for risk factors lead to a poor response for HB vaccination, some of these were studied and classified into:

A- Socio- demographic factors

1. Residency area
2. Family size
3. Sex
4. Education level
5. Age
6. Type of immunization place

B- Health status (personal) factors

1. Birth weight
2. History of Hospitalization
3. History of Infection
4. Nutritional status
5. Feeding during immunization
6. Adverts event after immunization

C- Immunization factors

1. Number of doses of vaccination
2. A delay in receiving 1st dose of vaccine

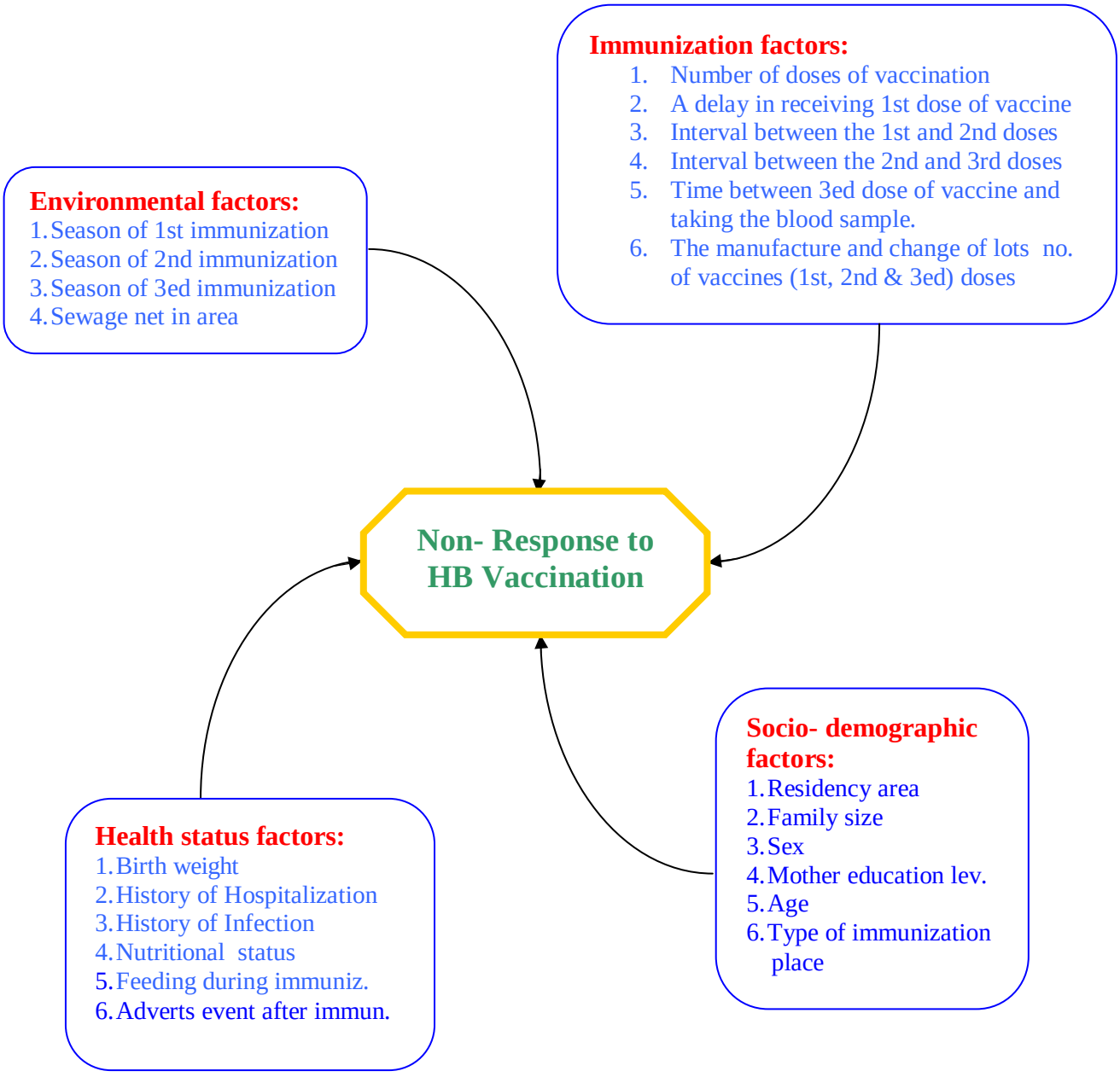
3. Interval between the 1st and 2nd doses
4. Interval between the 2nd and 3rd doses
5. Time between 3ed dose of vaccine and taking the blood sample
6. The manufacture and change of lots no. of vaccines (1st, 2nd & 3ed) doses

D- Environmental factors

1. Season of 1st immunization (birth)
2. Season of 2nd immunization
3. Season of 3ed immunization
4. Sewage net in area

Approximately 5 to 15% of infants and at least 5 to 10% of most healthy adult population faile to produce protective levels of antibodies to HBV vaccination after the initial 3-dose vaccination series (MEI-HWEI, 2004). Acording to a study by Minuk, Bohme & Bowen, Jun, 1989, some population groups have a poor response to vaccination, increasing age, male gender, over weight and changes in family size are predictive factors for a poor response. In a study by Chang, et al, 1997, the lower efficacy in China is related to the large number of HBeAg positive mothers. While a study conducted by Alper, et al, 1989, despite the extraordinary efficacy of second-generation HBV vaccines, immunization failure may occur and can sometimes be explained by factors such as improper storage or administration. Safety issues are becoming increasingly important in the perception of the public with regard to acceptance of routine immunization. Since frequent and minor side effects are usually seen during clinical trials preceding vaccine registration, but rare and important adverse events are reported only after a large use of the new product.

3.2 Theoretical Diagram of Conceptual Framework:



Chapter Four

Methodology

Chapter 4

Methodology

4.1 Introduction

This study based on a sero-survey in Palestine for Measles Rubella and HBV in the year 2003, conducted by ministry of health, in cooperation with UNICEF in occupied Palestinian territory and with funds from USAID (Palestine, MOH, 2003). The sero-survey was conducted among Palestinian children (GG and WB) aged 18-30 months old, children who were born after Sept. 2000 and had completed their immunization program at 15 months of age. A representative sample of 1:200 used, the sample size was 2004 samples, and samples taken randomly from selected cities, villages and camps by using immunization files from local health centers (Palestine, MOH, 2003). The samples were distributed 1197 from West Bank (66 Negative Anti HBs, 17 Equivocal, 1114 positive Anti HBs), 807 from Gaza Governorates (63 Negative Anti HBs, 13 Equivocal, 731 positive Anti HBs) as illustrated in table no. (4.1).

Table No. (4.1)

Distribution of Anti-HBs results by residency in Gaza governorates

Residency	No. of -ve Anti HBs	No. of Equivocal	No. of +ve Anti-HBs	No. of Samples
North Gaza	11	2	125	138
Gaza City	28	6	274	308
Mid Zone	5	2	99	106
Khan younis	14	2	136	152
Rafah	5	1	97	103
Total	63	13	731	807

The sero-survey result for HBV also showed that the immune response was 92%, ranging between 83.3% and 98%. The blood samples collected by trained nurses and analyzed by qualified laboratory technicians in MOH central laboratories by enzyme immunoassay system (ELIZA) test for the qualitative detection of antibodies against HBsAg.

The Anti-HBs test is a solid phase enzyme immunoassay system, which utilizes a sandwich method to detect Anti-HBs in serum, plasma or decalcified plasma. Test sample and peroxides conjugated added to micro wells coated with purified HBsAg, the amount of peroxidase – HBsAg conjugate bound well is proportional to the concentration of Anti-HBs in the specimen, which acts as a link between the fixed and HRP conjugate HBsAg. After incubation the unbound enzyme conjugate washed off, substrate solution added, and during further incubation, a blue color develops, the intensity of color, changes to yellow after the reaction is halted with acid solution and is proportional to the amount of Anti-HBs present in the specimen. Within certain limits, the optical density at 450 nm reflects the level of Anti-HBs antibody in the specimen. The optical density reading interpreted as:

Cut-off value (COV) = 0.033

Positive "Respondent to HB vaccination": if specimens with absorbance values equal or greater than 1.1 × COV (Positive ≥ 0.036)

Negative "Non-respondent to HB vaccination": if specimen with absorbance values less than 0.9 × COV (Negative < 0.030)

Equivocal: if specimen with absorbance values within ± 10% of the cut-off value should be retest to confirm the original reading (Equivocal > 0.030 to < 0.036)

Conversion Factor: to convert the absorbance value to mIu/ml multiply the absorbance result by the factor (320), which obtained by inducing serial dilutions of positive controls with known concentration and absorbance for each have been taken. Then concentrations

against absorbance plotted, the relation was linear. All negative result was confirmed by using micro particles enzyme immunoassay (AxSYM CORE) abbott laboratories.

4.2 Design

This study is a quantitative, case-control, retrospective study. In a case-control study design exposure data collected retrospectively and it is very important to decide how the controls will be selected from same population, the controls should be similar to cases except have not the outcome. The advantages of a case-control study are less expensive, time consuming and efficient for studying rare diseases. In the researcher study, the design is comparing negative anti-HBs "Non-respondent" to positive anti-HBs "respondent" as controls from same population in sero-survey, 2003.

4.3 The study population

The study population is 189 include (63) all negative Anti-HBs "Non-respondent" and 126 positive Anti-HBs "Respondent" in Gaza Governorates from the sero-survey, 2003.

4.4 Setting of the study

The study is carried on Governmental and UNRWA public health centers in Gaza Governorates, Palestine.

4.5 Sample and Sampling

The distribution of Anti-HBs results by residency and place of immunization in Gaza governorates, 2003, done and all the places of immunization which have negative Anti-HBs result in the different residencies has been chosen as illustrated in table no. (4.2). All the reported negative Anti-HBs are Included, the distribution of negative Anti-HBs and

controls by residency is 8illustrated in table (4.3).

Table No. (4.2)

Distribution of Anti-HBs results by Residency and Immunization place

Resid	Immunization place	Anti- HBs			Tot. Clinic Samples
		-ve	Equiv.	+ve	
NORTH GAZA	U. BET HANOON	1	0	20	21
	U. JABALIA	7	0	71	78
	G. SHOHDA BEIT LAHIA	1	0	14	15
	G. SHIMA' BEIT LAHIA	2	2	20	24
	Total NORTH GAZA Samples	11	2	125	**138**
GAZA CITY	G. SHOHDA ALREMAL	9	0	64	73
	G. SHOHDA ALDRAJ	6	0	37	43
	G. ALRHMA	4	0	34	38
	U. SOIDI	5	5	84	94
	U. ALZAITON	3	1	28	32
	U. ALSHATE'	1	0	27	28
	Total GAZA CITY samples	28	6	274	**308**
MID ZONE	G. DER ALBALAH	0	1	13	14
	U. ALMAKHAZI	0	0	19	19
	U. ALBREJ	3	0	24	27
	U. ALNSERAT	2	1	43	46
	Total MID ZONE Samples	5	2	99	**106**
KHAN YOUNIS	G. ALKRARA	2	0	23	25
	G. BANI SOHELLA	5	0	31	36
	U. MAEN	5	0	27	32
	U. ALMOASKER	2	2	55	59
	Total Khan Younis Samples	14	2	136	**152**
RAFAH	G. SHOHDA RAFAH	1	0	20	21
	U. TALASOLTAN	4	1	43	48
	G. SHOHDA TALASOLTAN	0	0	5	5
	U. ALSHABORA	0	0	29	29
	Total RAFAH samples	5	1	97	**103**
Sero-Survey Size		**63**	**13**	**731**	**807**

U. : UNRWA clinic

G. : Governmental clinic

Table No. (4.3)

Distribution of Negatives and Controls by Residency

Residency	No. of Cases	No. of Controls	Total
North Gaza	11	22	33
Gaza City	28	56	84
Mid Zone	5	10	15
Khan younis	14	28	42
Rafah	5	10	15
Total	63	126	189

The distribution of negative Anti-HBs and controls by residency and place of immunization is represented in table (4.4), the place of immunization which have no negative Anti-HBs result is excluded. For each case "negative Anti-HBs" two Controls "positive Anti-HBs" were selected by systematic random sampling method from the same sex and local health center, the selection was by taking the case name with negative Anti-HBs result first from the list, then if the negative is male we chose the previous two positive Anti-HBs male names as two controls, if one of these is not found is substituted by the previous before, this continue until we get two controls, the same way followed if the negative Anti-HBs is female.

4.6 Selection of cases

All negative results to Anti-HBs "Non-respondent to HB vaccination" from Gaza governorates, in the sero-survey, 2003 were chosen.

Table No. (4.4)

Distribution of Cases and controls by Residency and Immunization place

Residency		No. of Cases	No. of Controls	Total
NORTH GAZA	U. BET HANOON	1	2	3
	U. JABALIA	7	14	21
	G. SHOHDA BEIT LAHIA	1	2	3
	G. SHIMA' BEIT LAHIA	2	4	6
	Total NORTH GAZA Samples	**11**	**22**	**33**
GAZA CITY	G. SHOHDA ALREMAL	9	18	27
	G. SHOHDA ALDRAJ	6	12	18
	G. ALRHMA	4	8	12
	U. SOIDI	5	10	15
	U. ALZAITON	3	6	9
	U. ALSHATE'	1	2	3
	Total GAZA CITY samples	**28**	**56**	**84**
MID ZONE	U. ALBREJ	3	6	9
	U. ALNSERAT	2	4	6
	Total MID ZONE Samples	**5**	**10**	**15**
KHAN YOUNIS	G. ALKRARA	2	4	6
	G. BANI SOHELLA	5	10	15
	U. MAEN	5	10	15
	U. ALMOASKER	2	4	6
	Total Khan Younis Samples	**14**	**28**	**42**
RAFAH	G. SHOHDA RAFAH	1	2	3
	U. TALASOLTAN	4	8	12
	Total RAFAH samples	**5**	**10**	**15**
Sero-Survey Size		**63**	**126**	**189**

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4.7 Selection of controls

Positive Anti-HBs "Respondent to HB vaccination" is the one who had been chosen from Gaza Governorates, and the result was positive Anti-HBs in the sero-survey, 2003.

Controls were chosen from all positive results to Anti-HBs from Gaza Governorates, in the sero-survey, 2003, has the same sex and place of immunization of the negative case.

4.8 Criteria of inclusion

Any case from Gaza Governorates, in sero-survey, 2003, with negative Anti-HBs result is included.

4.9 Criteria of Exclusion

Any case which was not included in the sero-survey, 2003, Gaza Governorates.

Any case included in sero-survey, 2003, Gaza Governorates with equivocal Anti-HBs result.

4.10 Setting

The cases "Non-respondent" are coming from the five Governorates in Gaza Governorates: Rafah, Khanyounis, Middle region, Gaza and North region. At the time, controls "Respondent" are selected from the same sex and immunization place.

4.11 Tool of the study

Closed ended questionnaire has been constructed, the questionnaire was including socio-demographic factors, Health (personal) factors, immunization factors and environmental factors to evaluate the HB immunization program (Annex no. 13).

4.12 Pilot study

Pilot test was carried on 4 cases and 8 controls prior to the beginning of data collection to chick the validity of the questionnaire and to evaluate the outcome, the pilot interviews were conducted by the researcher and the suitability of the questionnaire was evaluated.

The misunderstanding, ambiguously and some changes was introduced over the questionnaire to reach the final version.

4.13 Data collection

The cases and controls vaccination files reviewed by the researcher and a questionnaire has been filled, If the vaccination file is not found for any one, the questionnaire was filled by home visit from the immunization cards issued by the public health centers, and information was reviewed face-to-face with child mother, the percentage of interviewee was (15.9%).

4.14 Data entry

Over reviewing of the questionnaires was the first step, prior to data entry. This step followed by designing an entry model using the computer Software Statistical Package for Social Sciences (SPSS) version 11. Then the coded questionnaires entered into the computer by the researcher. Data cleaning is done through checking out a random number of the questionnaires and through exploring descriptive statistics frequencies for all factors. All suspected or missed values were checked by revising the available sheets.

4.15 Data analysis

In data analysis many different statical tests were used, through frequency of the study factors, description of the study population. Frequency Tabulation and Pie Chart are used to disseminate the study factors. A comparison between controls and cases for the factors, chi- square test, odds Ratio, and p- value are calculated, statistically significant values are considered at p-value is equal or less than 0.05. Additinally comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test), Correlation and regression tests are also used.

4.16 Ethical consideration

Agreement from ministry of health had been obtained to use the sero-survey, 2003 data in the study (annex no. 14).

A permission to the study from Helsinki committee was obtained, Attached Helsinki agreement for the project as a whole (annex no. 15).

All the administrated procedures were completed, and a permission from MOH and UNRWA health office obtained before data collection (annex no 16, 17 respectively).

A consent form is done and offered to the child family (Annex no. 18).

Confidentiality had been maintained at all times during the study.

The result of the study will be public and will allow being use for further studies.

4.17 Limitations

In some public health centers (Governemental And UNRWA) the vaccination files was dameged after three years end of vaccination, according to their policy.

The sample size was small, which does not help in reflect the differnces between the comparitive groups in some risk factors.

The nature of the study as retrospective study, does not help to study some risk factors which related to the Israeli occupation, which need prospective study.

Chapter Five

Results & Discussion

Chapter 5

Results & Discussion

5.1 Distribution of Cases

The researcher will study the distribution of some risk factors in Gaza Governorates, which may affect non-response to HB vaccination, then disseminate, explore the results.

5.1.1 Distribution of Cases by Governorates:

The 63 cases "Non-respondent" distributed as shown in figure no. (5.1), the percentage of cases in Gaza City is the highest 44.4%, while 22.2% in Khanyounis, North Gaza 17.5%,

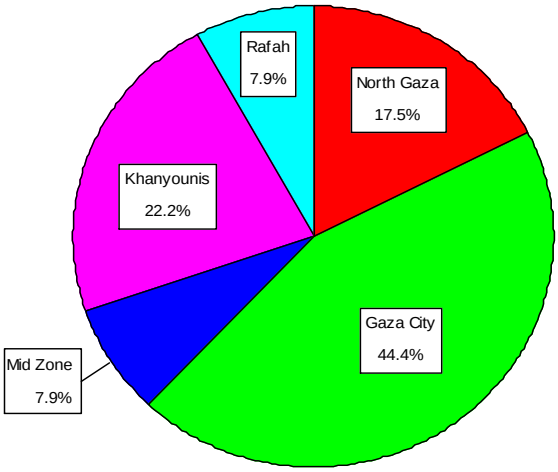

Figure No. (5.1): Distribution of cases by Governorates

Mid Zone and Rafah, the percentage is the same 7.9%. We emphasize that, these reported cases do not reflect the variation in the number of population in each governorate.

Table no. (5.1) indicates, the prevalence of cases "Non-respondent" in Khan younis is the highest (9.2%), followed by Gaza city (9.1%) while the middle zone is the lowest (4.7%).

These findings disagree with a study result in Palestine by Kuhail, El-Khodary & Ahmed, 2000, where more non-responders in the North area (62%) and Rafah (50%). I think the difference between the two studies results from the selection way of control groups that in

Table No. (5.1)

Prevalence of Cases by Residency

Residency	No. of Cases	No. of Examined children	Prevalence Rate (%)
North Gaza	11	138	7.8
Gaza city	28	308	9.1
Middle Zone	5	106	4.7
Khan Younis	14	152	9.2
Rafah	5	103	4.9

my study there was completely matching in selection controls from the same age, sex and residency, while in the other study, the controls was aged more than cases.

5.1.2 Distribution of Cases by Sex:

Table no. (5.2) illustrates that, 52.4% of cases are male, while 47.6% are female. The prevalence of cases among females are higher than males (8.0%, 7.7%) respectively.

Table No. (5.2)

Distribution of Cases by Sex

Sex	No. of Cases	% of Cases	No. of Examined children	Prevalence Rate (%)
Male	33	52.4	431	7.7
Female	30	47.6	376	8.0
Total	63	100.0		

5.1.3 Distribution of Cases by Type of Immunization Place:

Figure no. (5.2) shows, 52.4% of the cases received vaccination in UNRWA clinics, while 47.6% in Governmental clinics.

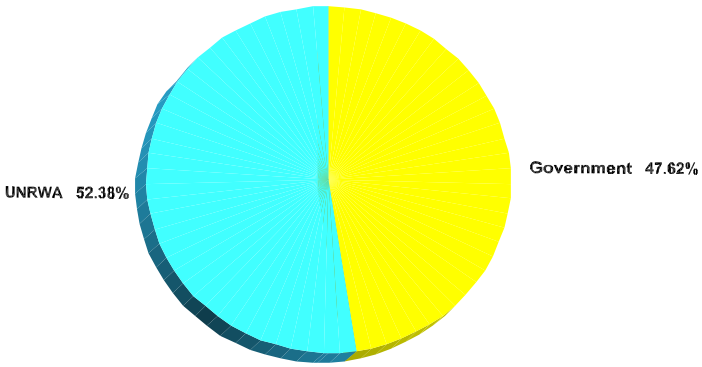

Figure No. (5.2): Distribution of cases by Type of Immunization Place

The prevalence rate of non-respondent to HB vaccination was highest among child who received immunization in governmental clinics (10.2) more than UNRWA clinics (6.4), as represented in table no. (5.3).

Table No. (5.3)

Prevalence of Cases by Type of immunization place

Type of Immunization place	No. of non-respondent	No. of Examined Children	Prevalence Rate (%)
Government	30	294	10.2
UNRWA	33	513	6.4

5.1.4 Distribution of Cases by Mother Education Level:

According to figure no. (5.3), most of Cases (62%) are with mothers who have secondary educational level, then (16%) of Cases are with mothers who have preparatory educational level, while the lowest cases (5%) with mothers have university or more educational level.

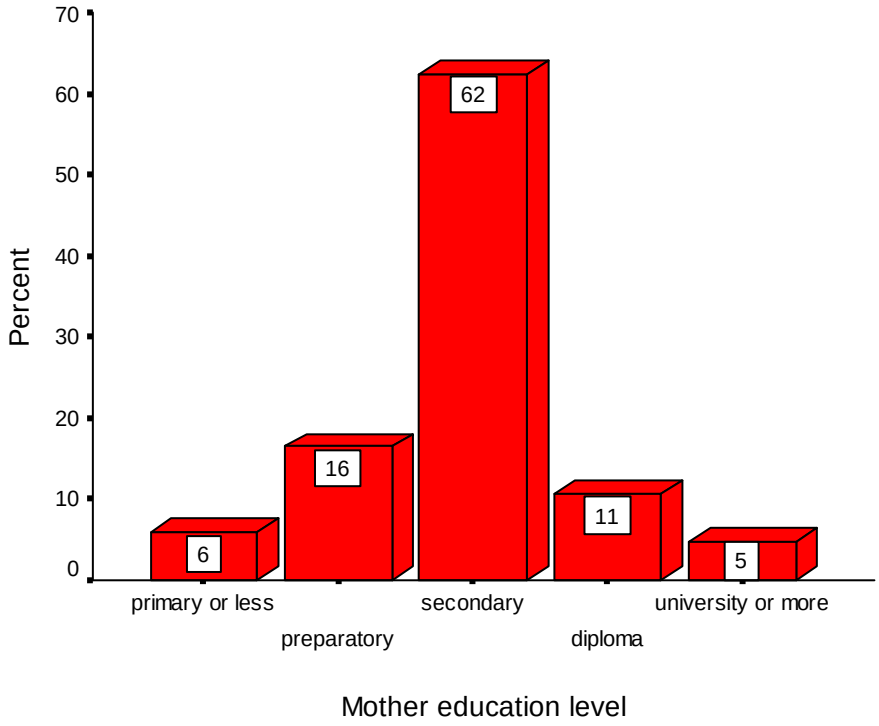

Figure No. (5.3): Distribution of Cases by Mother Education Level

5.1.5 Distribution of Cases by Places of immunization:

The percentage of cases in Shohda Alremal clinic is the highest (14%), in Jabalia clinic (11%), while in clinics of Beit Hanon, Shohda Beit Lahia, Alshate' and Shohda Rafah the percentage is the same (2%), as illustrated in Figure no. (5.4).

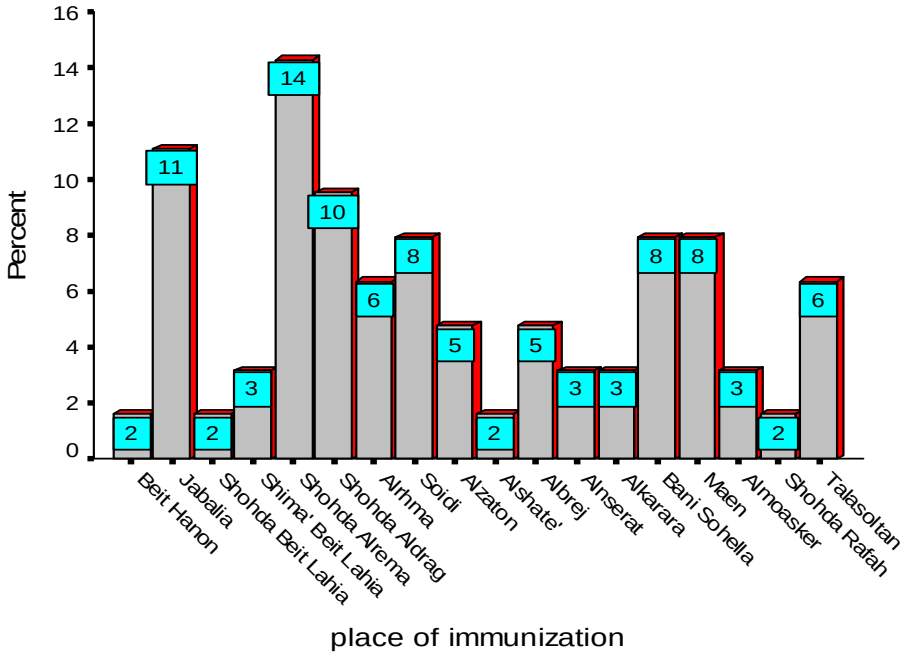

Figure No. (5.4): Distribution of Cases by Places of immunization

5.2 Risk Factors for non- response to HB vaccination

The researcher will analyze the results of some risk factors in Gaza Governorates, which may affect non-response to HB vaccination, which classified into socio- demographic factors, Health (personal) factors, immunization factors and environmental factors. The difference between cases and controls will differ in their statistically significant level, one risk factor to another, this will depend on different situations and we will discuss each situation alone. In addition to comparison by others studies, to see where there is matching and conflicting.

5.2.1 Socio- Demographic Factors for non-response to HB vaccination

In this section, the researcher will study the distribution of cases by some of socio-demographic factors that may be cause of non-response to HB vaccination in Gaza governorates, such as Residency area, family size, sex, mother education level, place of immunization, type of immunization place and age.

5.2.1.1 Anti- HBs Level and Residency:

As illustrated in table no. (5.4), comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) between residency categories: Khan Younis and Middle Zone had the highest and the same mean scores (238 mIu/ml), while North Gaza had the lowest mean score (147 mIu/ml). The difference between means does not reach a statically significant level (p-value= 0.824). This means the risky of non-respondent to HB vaccination in North Gaza is the highest.

Table No. (5.4)

Comparisons between Anti-HBs Levels (mIu/ml) in Residencies, Categories of Total House Number and Mother Education Levels

	Socio- Demographic Factors		Anti-HBs Mean (mIu/ml)	p-value
Anti-HBs Levels (mIu/ml)	Residencies	North Gaza	147	0.824
		Gaza city	173	
		Middle Zone	238	
		Khan Younis	238	
		Rafah	208	
	Categories of Total House Number	Less than 5	177	0.938
		between 5 to 10	197	
		More than 10	184	
	Mother Educational Levels	Preparatory or less	202	0.370
		Secondary	172	
		Higher than second.	251	

Table number (5.5) indicates multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between North Gaza and Mid Zone (91.9 mIu/ml) was the highest, followed by North Gaza and Khanyounis (91.8 mIu/ml), while the mean difference between Mid Zone and Khanyounis was the lowest (0.1 mIu/ml). Residencies differ not statically significant from each others, for example North Gaza differ not statically significant from Mid Zone (p- value = 0.993) and others.

Table No. (5.5)

Multiple Comparisons between Anti- HBs Levels in Residency Groups

(I) residency	(J) residency	Anti- HBs Mean Difference (mIu/ml) (I-J)	p-value
North Gaza	Gaza City	-26.6	0.993
North Gaza	Mid Zone	-91.9	0.871
North Gaza	Khanyounis	-91.8	0.695
North Gaza	Rafah	-61.4	0.968
Gaza City	Mid Zone	-65.3	0.941
Gaza City	Khanyounis	-65.2	0.791
Gaza City	Rafah	-34.8	0.994
Mid Zone	Khanyounis	0.1	1.000
Mid Zone	Rafah	30.5	0.999
Khan younis	Rafah	30.4	0.997

These findings disagree with the result of a study in Iran, by Jafarzadeh, et al, 2004, which result was 2 cities Kerman and Urmia developed Anti- HBs (> 10 IU/L), with GMT 6104 and 11869 IU/L respectively. No significant differences were observed in sero-protection rate between neonates of two cities, but the GMT was found significantly higher in Urmian neonates as compared to vaccinees of Kerman city (P-value <0.001). Also disagree with

the result of a study in Mongolia by Davaalkham, et al, 2007, where after stratifying by residency, the association between winter vaccination and total HBV infection was evident for rural (p-value= 0.008) but not for urban areas (p-value= 0.294). Additionally disagree with the result of a study in Gambia by Inskip, et al, 1991; where considerable variation in vaccine response by residency. Residence was substantially associated with Anti-HBs level (p-value= 0.01). I think that the difference results from the nature of each country, where Iran and Gambia are large in area and difference groups in relative to Palestine.

5.2.1.2 Anti- HBs Level and Total Household (or Category) Number:

Table no. (5.6) illustrates that: the highest percentage of cases was in the category of between 5 to 10 members (54.0%), but it was the lowest for category of more than 10

Table No. (5.6)

Relationship between Anti- HBs and Categories of total house Number

Categories of total house number	Subject			
	Case		Control	
	No	%	No	%
less than 5	18	28.6	26	20.6
between 5 to 10	34	54.0	87	69.0
more than 10	11	17.5	13	10.3
Total	63	100.0	126	100.0

Chi-Square= 4.32 df= 2 p- value= 0.116

members (17.5%). The difference between the three categories is not reach a statically significant level (p-value = 0.116).

As shown in table no. (5.4), comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for the total house categories: the mean for the category

between 5 to 10 was the highest (197 mIu/ml), category more than 10 (184 mIu/ml) and for category less than 5 (177 mIu/ml). The difference between means does not reach a statically significant level (p-value= 0.938). This means, never mind the total house number, the response to HB vaccination was not affected.

Table number (5.7) indicates multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between less than 5 category and between 5 to 10 category was the highest (20.9 mIu/ml), while the mean

Table No. (5.7)

Multiple Comparisons between Categories of total house no. on Anti- HBs Level

(I) Category of total House number	(J) Category of total house number	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
less than 5	between 5 to 10	-20.9	0.905
less than 5	more than 10	-7.6	0.994
Between 5 to 10	more than 10	13.4	0.975

difference between less than 5 category and more than 10 category was the lowest (7.6 mIu/ml). Categories of total house number differ not statically significant from each others, for example the category less than 5 differed not statically significant from the category between 5 to 10 (p- value = 0.905) and others categories. Also table no. (5.12) reports that, Anti- HBs Level is not correlated by the total number in household (p- value = 0.562).

5.2.1.3 Anti- HBs Level and Sex:

Table no. (5.8) illustrates comparison of anti- HBs level means by t- test, anti- HBs mean level of males (201 mIu/ml) scoring higher than of female (179 mIu/ml). The difference

between the two means did not reach a statically significant level (t= 0.58, p-value= 0.566), this means there is female gender. This finding disagree with many studies results,

Table No. (5.8)

Comparisons between Anti-HBs Levels (mIu/ml) in

Sex and Types of immunization place

Anti-HBs Levels (mIu/ml)	Socio- Demographic Factors	Groups	Anti-HBs Mean (mIu/ml)	t	p-value
	Sex	Male	201	0.58	0.566
		Female	179		
	Types of immunization place	Govern.	189	0.38	0.704
		UNRWA	184		

where no sex differences in antibody level were apparent, and the difference was not statistically significant. One is a study result in Palestine by Kuhail, El-Khodary & Ahmed, 2000; one in hongKong by Lok, et al, Dec, 2005 and an other in Egypt by El-Sawy & Mohamed, 1999, the difference was not statically significant (p-value= 0.916, p-values > 0.05) respectively. This finding disagree also with many studies results, where there Male gender, and the difference was not statistically significant, a study in North America by Minuk, Bohme & Bowen, Jun, 1989; in Taiwan by Yen, et al, 2005 and in Iran by Jafarzadeh, et al, 2004, where GMT was higher in females compared to males; this difference was not statistically significant. The GMT of both male and female neonates from Urmia (11433 and 12309 IU/L) was significantly (p-value<0.001) higher than those from Kerman (5772 and 6400 IU/L). However, a study in Israel by Gold, et al, 2003, there was Male gender, and the difference was statistically significant, where females generated higher mean Anti-HBs than males (207.3-± 217 mIU/ml vs 141.9-± 218.9 mIU/ml, p-value < 0.05). In addition, disagree with study result in Mongolia by Davaalkham, et al, 2007, where, there no significant differences, in the distributions of sex. Moreover, to a study result by Blumberg, Dec, 2005, where HBV infection appears to affect the sex ratio at birth

of their offspring. A couple in which either parent is carriers have higher sex ratios (higher proportion of males) compared with couples in which neither parent is positive HBsAg. Couples in which mother is positive anti-HBs have children with lower sex ratios than either carriers or uninfected couples

5.2.1.4 Anti- HBs Level and Mother Education Levels:

Table no. (5.9) shows that: the highest percentage of cases was in secondary level (66.7%), followed by preparatory or less level (23.8%), while level higher than secondary was the lowest (9.5%). The difference between the three levels did not reach a statically significant level (p-value = 0.292).

Table No. (5.9)

Relationship between Anti- HBs and Mother Education Levels

Mother Education Levels	Subject			
	Case		Control	
	No	%	No	%
Preparatory or less	15	23.8	27	21.4
Secondary	42	66.7	76	60.3
Higher than secondary	6	9.5	23	18.3
Total	63	100.0	126	100.0

Chi-Square = 2.47 df = 2 p-value = 0.292

Table no. (5.4) illustrates, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for levels of mother education: the mean of mother with education level higher than secondary (251 mIu/ml) was the highest , while the mean for mother with secondary level was the lowest (172 mIu/ml). The difference between means

does not reach a statically significant level (p-value= 0.370). We can conclude that, the response to HB vaccination not affected by mother education level.

Table number (5.10) shows, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between Secondary level and higher than secondary level was the highest (78.8 mIu/ml), while the mean difference between preparatory or less level and secondary level was the lowest (29.5 mIu/ml).

Table No. (5.10)

Multiple Comparisons between Levels of Mother Education on Anti- HBs Level

(I) mother education level	(J) mother education level	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
preparatory or less	Secondary	29.5	0.824
preparatory or less	Higher than secondary	-49.3	0.742
Secondary	Higher than secondary	-78.8	0.357

Levels of Mother education differ not statically significant from each others, for example the category of preparatory or less differed not statically significant from the category of secondary (p-value = 0.824) and others educational levels.

5.2.1.5 Anti- HBs Level and Age

According to table no. (5.22), the researcher findings, Anti- HBs Level is not correlated by (age at immunization) the interval from birth to first vaccine (t= 1.372, p-value= 0.172), but correlated negatively with the interval between last vaccination dose and Blood sample testing date (p-value= 0.024). This findings agree with a astudy in hongKong by Lok, et al, Dec, 2005, where there was a decrease in response rate and anti-HBs titre with age, and

an other in Egypt by Shaaban, July/August, 2007, where Anti-HBs proportion decreased with age, but the decrease was not statistically significant. while mean level of Anti-HBs decreased significantly with increasing age (p-value= 0.026). A significant negative correlation was found between current age and HBsAb levels (r = –0.31, p-value = 0.041). My results agree with a study in Gambia by Inskip, et al, 1991, where age at vaccination did not appear to have an effect.

5.2.1.6 Anti- HBs Level and Type of Immunization Place :

The findings in table no. (5.11) that: the percentage of cases and controls for type of immunization place is the same (47.6%) for governmental clinics and (52.4%) for UNRWA clinics. This because there was marching in selection of controls from the same type of immunization places.

Table No. (5.11)

Anti- HBs and Type of Immunization Place

Type of immunization place	Subject			
	Case		Control	
	No	%	No	%
Government	30	47.6	60	47.6
UNRWA	33	52.4	66	52.4
Total	63	100.0	126	100.0

Table no. (5.8) illustrates comparison of anti- HBs level means by t- test. Children who get vaccination on governmental clinics with mean (189 mIu/ml) slightly higher than UNRWA clinics (184 mIu/ml). The difference between the two means does not reach statically significant level (t= 0.38, p-value= 0.704). The researcher findings disagree with the result of a study by Jafarzadeh, et al, 2004 in Iranian neonates, which result was for 2 cities, Kerman and Urmia the GMT 6104 and 11869 IU/L respectively. The GMT was

found significantly higher in Urmian neonates as compared to vaccinees of Kerman city (P-value <0.001).

5.2.2 Health (Personal) Factors for non- response to HB vaccination

The researcher will study the distribution of cases by some personal health factors which, may be a predictive of a poor response to HB vaccination in GG, birth weight, history of hospitalization, history of infection, nutritional status, feeding during immunization and Suffering from adverse event after vaccine.

5.2.2.1 Correlation between Anti-HBs Level and Total No. in Household, Birth Weight:

The regression of Anti- HBs Level on total number in household and birth weight accountable for 0.4% of the variance and was not significant at the level 0.540. Anti- HBs Level is not correlated by the total number in household (p-value= 0.562) and the birth weight (p-value= 0.381), as represented in table no. (5.12). The researcher findings agree with a study result by Gold, et al, 2003, in Israel, where no correlation was found between

Table No. (5.12)

Correlation between Anti- HBs Level and Total No. in Household, Birth Weight

	Model	T	p-value	R	Adjusted R Square	F	p-value
Anti- HBs Level	(Constant)	1.962	0.051	0.081	-0.004	0.618	0.540
	Total no. in Household	-0.582	0.562				
	Birth Weight	-0.878	0.381				

Anti-HBs titers and birthweight, while disagree with a study result by Losonsky, et al, February, 1999 in USA, where the finding was the seroprotection response rate after 3

doses of vaccine increased with birth weight. Of all infants who did not achieve protective levels of antibody after 3 doses of vaccine, 96% weighed <1700 g at birth. Of 36 children with a birth weight >1500 g, (91%) achieved levels of Anti-HB_S >100 mIU/mL after 3 doses of vaccine, compared with (71%) of infants with birth weight <1500 g.

5.2.2.2 Anti- HBs Level and History of Hospitalization:

4.8% of cases are from children those were hospitalized before vaccination, compared to 3.2% of controls. However, 95.2% of cases from children have not hospitalization, compared to 96.8% of controls as indicated in table no. (5.13). The difference between the two groups did not reach a statically significance level (p-value = 0.586).

Table No. (5.13)

Anti- HBs and History of Hospitalization

History of Hospitalization	Subject			
	Case		Control	
	No	%	No	%
Yes	3	4.8	4	3.2
No	60	95.2	122	96.8
Total	63	100.0	126	100.0

OR = 1.53 CI = 0.33 – 7.03 P- value = 0.586

From table no. (5.14), the mean for children who has not history of hospitalization before vaccination (194 mIu/ml) was higher than who has (121 mIu/ml) on their response to HB vaccination. The difference between two means did not reach a statically significant level (t= 0.72, p-value= 0.475). This finding agrees with a meta-analysis study by Fibrizi, et al,

Nov. 2004, where the result demonstrated a significantly decreased risk of response to HB vaccine among older dialysis patients (overall risk ratio: 0.74; 95% C. I: 0.70–0.79).

Table No. (5.14)

Comparisons between Anti-HBs Levels (mIu/ml) in History of hospitalization, Feeding during immunization and Adverse event after vaccine

	Health (Personal) Factors	Groups	Anti-HBs Mean (mIu/ml)	t	p-value
Anti-HBs Levels (mIu/ml)	History of Hospitalization	Yes	121	0.72	0.475
		No	194		
	Feeding during Immunization	Breast	193	0.23	0.815
		Breast+ Artificial	181		
	Suffering from adverse event after vaccine	Yes	189	0.97	0.336
		No	370		

5.2.2.3 Anti- HBs Level and History of Infection:

The highest percentage of cases was, with no history of infection (90.5%), while with diarrhea was the lowest (1.6%). The difference between the categories of history infection did not reach a statically significant level (p-value = 0.774), as reported in Table no. (5.15)

Table No. (5.15)

Relationship between Anti- HBs and Categories of History Infection

History of Infection	Subject			
	Case		Control	
	No	%	No	%
No history of infection	57	90.5	112	88.9
Diarrhea	1	1.6	1	0.8
Respiratory	5	7.9	13	10.3
Total	63	100.0	126	100.0

Chi-Square = 0.51 df = 2 p-value = 0.774

Table no. (5.16) indicates, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for categories of history infection: children who were vaccinated and with out a history of infection through vaccination (mean= 169 mIu/ml) is higher than those with respiratory infection (mean= 18 mIu/ml) and diarrhea infection (mean= 2 mIu/ml). The difference between means did not reach a statically significant level (p-value = 0.598).

Table No. (5.16)

Comparisons between Anti-HBs Levels (mIu/ml) in History of Infection and Nutritional status

	Health (Personal) Factors		**Anti-HBs Mean (mIu/ml)**	**p-value**
Anti-HBs Levels (mIu/ml)	History of Infection	No History of infect.	169	0.598
		Diarrhea	2	
		Respiratory	18	
	Nutritional status	Under weight	7	0.170
		Normal	178	
		Over weight	4	

Table number (5.17) shows, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that, the anti- HBs levels mean difference between no infection category and diarrhea category (164.8 mIu/ml) is the highest, while the mean difference between no infection category and respiratory category (4.7 mIu/ml) is the lowest. Categories of history infection differ not statically significant from each other's, for example no infection category differed not statically significant from diarrhea category (p-

value=0.683) and others categories. The researcher findings disagree with the findings of a study by Blumberg, Dec, 2005, Couples in which mother is positive anti-HBs have

Table No. (5.17)

Multiple Comparisons between Categories of History Infection on Anti- HBs Level

(I) History of Infection	(J) History of Infection	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
No infection	Diarrhea	164.8	0.683
No infection	Respiratory	4.7	0.997
Diarrhea	Respiratory	-160.0	0.721

children with lower sex ratios than either carriers or uninfected couples. In addition to, a study by Seung-Dae, et al, April, 2007, where was a significantly (P-value < 0.05) higher proportion of subjects in the Celiac disease group (53.9%) failed to respond to HB vaccine compared with controls (11.1%).

5.2.2.4 Anti- HBs Level and Nutritional status:

From the finding in table no. (5.18), most of cases was with normal status (96.8%), over weight (2.0%), while no case reported under weight.

As shown in table no. (5.16), comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for nutritional status: children with normal weight (mean = 178 mIu/ml) was higher than those with abnormal weights: under weight (mean= 7 mIu/ml) and over weight (mean= 4 mIu/ml). The difference between means does not reach statically significant level (p-value= 0.170).

Table No. (5.18)

Relationship between Anti- HBs and Nutritional status

Nutritional status	Subject			
	Case		Control	
	No	%	No	%
Under weight	0	0	7	5.6
Normal	61	96.8	117	92.9
Over weight	2	3.2	2	1.6
Total	63	100.0	126	100.0

Table no. (5.19) shows multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between under weight status and over weight status (256.9 mIu/ml) is the highest, while the mean difference

Table No. (5.19)

Multiple Comparisons between Nutritional status on Anti- HBs Level

(I) nutritional status	(J) nutritional status	Mean Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Under weight	Normal	162.1	0.282
Under weight	Over weight	256.9	0.300
Normal	Over weight	94.9	0.776

between normal status and over weight status (94.9 mIu/ml) is the lowest. Nutritional status of children differ not statically significant from each others, for example Under weight status differed not statically significant from normal status (p- value = 0.282) and others nutritional status.

between normal status and over weight status (94.9 mIu/ml) is the lowest. Nutritional status of children differ not statically significant from each others, for example Under weight status differed not statically significant from normal status (p- value = 0.282) and others nutritional status.

5.2.2.5 Anti- HBs Level and Feeding during Immunization:

Table no. (5.20) shows, the cases of children who get breast-feeding during immunization (82.5%) are higher than by breast and artificial (17.5%). The difference between the two groups did not reach a statically significance level (p-value = 0.893).

Table No. (5.20)

Anti- HBs and Feeding during immunization

Feeding during Immunization	Subject			
	Case		Control	
	No	%	No	%
Breast	52	82.5	103	81.7
Breast + Artificial	11	17.5	23	18.3
Total	63	100.0	126	100.0

OR= 1.06 CI= 0.47 – 2.33 P- value= 0.893

Table no. (5.14) illustrates that, the mean for children who got feeding during Immunization by breast (193 mIu/ml) was slightly higher than by breast and artificial (181 mIu/ml) on their response to HB vaccination. The difference between two means did not reach a statically significant level (t= 0.23, p-value= 0.815). The findings disagree with a study by Hill, et al, 2002, None of the 101 breast-fed infants and (3%) formula-fed infants were positive for HBsAg after the initial vaccination series (P-value = 0.063).

5.2.2.6 Anti- HBs Level and Suffering from adverse event after vaccine:

98.4% of cases compared to 99.2% of the controls are suffering from adverse event after vaccine, while 1.6% of cases compared to 0.8% of the controls arte not suffering from adverse event after vaccine. This difference between the two groups did not reach a statistically significant level (p-value = 0.615), this represented in table no. (5.21).

Table No. (5.21)

Anti- HBs and Suffering from adverse event after vaccine

Suffering from adverse event after vaccine	Subject			
	Case		Control	
	No	%	No	%
Yes	62	98.4	125	99.2
No	1	1.6	1	0.8
Total	63	100.0	126	100.0

OR = 0.50 CI = 0.03 – 8.06 P- value = 0.615

Table no. (5.14) indicates, the mean for children who were suffering from adverse event after vaccine (189 mIu/ml) was lower than who are not (370 mIu/ml) on their response to HB vaccination, the difference between the two means did not reach a statically significant level (t= 0.97, p-value= 0.336). This means that in HB vaccination, there is no effect on response to HB vaccination from adverse event after vaccine, if it is happen. This agree with a study result by Alper, et al, 1989, where rare and important adverse events are reported only after a large use of the new product.

5.2.3 Immunization factors for non- response to HB vaccination:

In this section, the researcher will study the distribution of cases by some of immunization factors that may be cause of a poor response to HB vaccination in Gaza governorates, such as the number of vaccination doses, a delay in receiving 1st dose of vaccine, interval between 1st and 2nd dose, interval between 2nd and 3ed dose. The time between 3ed dose of vaccine and taking blood sample, the cold chain system of vaccines, the manufacture and change of lots number of vaccines which include lots no. of 1st, 2nd and 3ed vaccine.

5.2.3.1 Correlation between Anti- HBs Level and five predictor factors:

According to table no. (5.22) the regression of Anti- HBs Level on five predictor factors, which included (age at immunization) interval from birth to first vaccine, interval between

Table No. (5.22)

Correlation between Anti- HBs Level and five predictor factors

	Model (Predictors)	**t**	**p-value**	**R**	**Adjusted R Square**	**F**	**p-value**
Anti- HBs Level	(Constant)	-0.304	0.761	0.250	0.037	2.435	0.036
	Interval from birth to 1st vaccine in days	1.372	0.172				
	Interval between 1st and 2nd dose in days	0.744	0.458				
	Interval between 2nd and 3ed dose in days	0.200	0.842				
	Interval between last vaccination dose and Blood sample testing date in months	-2.280	0.024				
	Age at blood sample drawal in months	1.792	0.075				

1st and 2nd dose, interval between ed and 3ed dose, age at blood sample drawal and the interval between last vaccination dose and Blood sample testing date, accounted for 3.7% of the variance and was not significant at the level (p-value= 0.036). Anti- HBs Level is not correlated by the interval from birth to first vaccine (p-value= 0.172), interval between 1st and 2nd dose (p-value= 0.458) and interval between 2nd and 3ed dose (p-value = 0.842). and age at blood sample drawal (p-value= 0.075) but correlated negatively with the interval between last vaccination dose and Blood sample testing date (p-value= 0.024).

In studying the delay in receiving the 2nd dose of vaccine, the researcher finding disagree with a study result in Gambia by Inskip, et al, 1991, where there was some indication that a delay in receiving the 2nd dose of vaccine led to a marginally lower response. But, in studying factors influencing Anti-HBs, the result show that, the dominant effect was the time between the last doses of vaccine and taking the blood sample. The study result agree with other studies; one in Palestine by Kuhail, El-Khodary & Ahmed, 2000, where Anti-HBs among the immunized children were lower in the older age group (> 36 months). Other in Egypt, by El-Sawy & Mohamed, 1999, where the differences in sero-protection rates were highly significant (p-value= 0.0097) and there was a significant association between the time lapse since the last vaccine dose and the sero-protection rate (p-value= 0.00028), where the longer the time lapse after vaccination, the lower the sero-protection rate. In addition to the findings of a study in Israel by Gold, et al, 2003, where children divided into three groups according to the time elapsed since vaccination, the finding was the Anti-HBs levels declined with time (p-value < 0.009).

5.2.3.2 Anti- HBs Level and Lots number of 1st vaccine dose:

From table no. (5.23), in the first HB vaccine dose, the highest percentage of cases was vaccinated by Lot No. ENG3166A3 (46%), while the lowest by Lot No. ENG3321A3

(15.9%). The difference between the three lot numbers did not reach a statically significant level (p-value = 0.107).

Table No. (5.23)

Relationship between Anti- HBs and Lots number of 1st dose

Lots number of 1st dose	Subject			
	Case		Control	
	No	%	No	%
Lot No. ENG3166A3	29	46.0	39	31.0
Lot No. ENG3171A3	24	38.1	66	52.4
Lot No. ENG3321A3	10	15.9	21	16.7
Total	63	100.0	126	100.0

Chi-Square = 4.47 df = 2 p-value = 0.107

Table no. (5.24) indicates, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for Lots number of 1st vaccine dose: children those were vaccinated by Lot No. ENG3321A3 (mean= 236 mIu/ml) was higher than those vaccinated with others lots numbers. The difference between means does not reach a statically significant level (p-value= 0.180). We conclude that, in the first vaccine dose what ever the lot number of the vaccine was, the response to HB vaccination was not affected.

Table number (5.25) shows multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between Lot No. ENG3166A3 and Lot No. ENG3321A3 was the highest (96.1 mIu/ml), while the mean difference between Lot No. ENG3171A3 and Lot No. ENG3321A3 was the lowest (22.3 mIu/ml). Lots number of First vaccine dose differ not statically significant from each

Table No. (5.24)

Comparisons between Anti-HBs Levels (mIu/ml) in Lots Numbers of 1st, 2nd, 3ed dose

	Immunizational factors		Anti-HBs Mean (mIu/ml)	p-value
Anti-HBs Levels (mIu/ml)	Lots no. of 1st dose	Lot No. ENG3166A3	140	0.180
		Lot No. ENG3171A3	214	
		Lot No. ENG3321A3	236	
	Lots no. of 2nd dose	Lot No. ENG3166A3	159	0.489
		Lot No. ENG3171A3	197	
		Lot No. ENG3321A3	220	
	Lots no. of 3ed dose	Lot No. ENG3166A3	35	0.268
		Lot No. ENG3171A3	183	
		Lot No. ENG3321A3	194	
		Lot No. ENG3422A3	222	

others, for example Lot No. ENG3166A3 differed not statically significant from Lot No. ENG3171A3 (p- value = 0.220) and others lots numbers of first vaccine dose.

Table No. (5.25)

Multiple Comparisons between Lots no. of 1st dose on Anti- HBs Level

(I) Lots number of 1st dose	(J)) Lots number of 1st dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p-value
Lot No. ENG3166A3	Lot No. ENG3171A3	-73.8	0.220
Lot No. ENG3166A3	Lot No. ENG3321A3	-96.1	0.243
Lot No. ENG3171A3	Lot No. ENG3321A3	-22.3	0.920

5.2.3.3 Anti- HBs Level and Lots number of 2nd vaccine dose:

Table no. (5.26) demonstrates, in the second HB vaccine dose, the highest percentage of cases was vaccinated by Lot No. ENG3171A3 (47.6%), while the lowest by Lot No. ENG3321A3 (20.6%). The difference between the three lots numbers did not reach a statically significant level (p-value = 0.699).

Table No. (5.26)

Relationship between Anti- HBs and Lots number of 2nd dose

Lots number of 2nd dose	Subject			
	Case		Control	
	No	%	No	%
Lot No. ENG3166A3	20	31.7	33	26.2
Lot No. ENG3171A3	30	47.6	67	53.2
Lot No. ENG3321A3	13	20.6	26	20.6
Total	63	100.0	126	100.0

Chi-Square = 7.2 df = 2 p-value = 0.699

Table no. (5.24) illustrates, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for Lots no. of 2nd vaccine dose: children those vaccinated by Lot No. ENG3321A3 with mean (220 mIu/ml) was higher than those vaccinated with others lots numbers. The difference between means does not reach a statically significant level (p-value= 0.489). We can conclude that, in the 2nd vaccine dose what ever the lot number of the vaccine was, the response to HB vaccination was not affected.

Table number (5.27) shows, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between Lot No.

ENG3166A3 and Lot No. ENG3321A3 was the highest (60.7mIu/ml), while the mean difference between Lot No. ENG3171A3 and Lot No. ENG3321A3 was the lowest (22.6 mIu/ml). Lots number of second vaccine dose differ not statically significant from each others, for example Lot No. ENG3166A3 differed not statically significant from Lot No. ENG3171A3 (p- value = 0.702) and others lots numbers of second vaccine dose.

vaccine dose differ not statically significant from each others, for example Lot No. ENG3166A3 differed not statically significant from Lot No. ENG3171A3 (p- value = 0.702) and others lots numbers of second vaccine dose.

Table No. (5.27)

Multiple Comparisons between Lots no. of 2nd dose on Anti- HBs Level

(I) Lots number of 2nd dose	(J)) Lots number of 2nd dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Lot No. ENG3166A3	Lot No. ENG3171A3	-38.1	0.702
Lot No. ENG3166A3	Lot No. ENG3321A3	-60.7	0.555
Lot No. ENG3171A3	Lot No. ENG3321A3	-22.6	0.904

5.2.3.4 Anti- HBs Level and Lots number of 3ed vaccine dose:

From table no. (5.28), in the third HB vaccine dose the highest percentage of cases was vaccinated by Lot No. ENG3166A3 (46.0%), while the lowest by Lot No. ENG3166A3 (4.8%). The difference between the four lots numbers did not reach a statically significant level (p-value = 0.579).

Table no. (5.24) shows, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for Lots number of third vaccine dose: children who vaccinated by Lot No. ENG3422A3 with mean (222 mIu/ml) was higher than those

vaccinated with others lots numbers. The difference between means did not reach a statically significant level (p-value= 0.268).

Table No. (5.28)

Relationship between Anti- HBs and Lots number of 3ed dose

Lot number of 3ed dose	Subject			
	Case		Control	
	No	%	No	%
Lot No. ENG3166A3	3	4.8	2	1.6
Lot No. ENG3171A3	29	46.0	55	43.7
Lot No. ENG3321A3	18	28.6	42	33.3
Lot No. ENG3422A3	13	20.6	27	21.4
Total	63	100.0	126	100.0

Chi-Square = 1.97 df = 3 p-value = 0.579

Table number (5.29) shows, multiple comparison between groups by one- way ANOVA

Table No. (5.29)

Multiple Comparisons between Lots no. of 3ed dose on Anti- HBs Level

(I) Lots number of 3ed dose	(J)) Lots number of 3ed dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Lot No. ENG3166A3	Lot No. ENG3171A3	-148.7	0.685
Lot No. ENG3166A3	Lot No. ENG3321A3	-159.0	0.645
Lot No. ENG3171A3	Lot No. ENG3321A3	-187.8	0.526
Lot No. ENG3171A3	Lot No. ENG3321A3	-10.4	0.997
Lot No. ENG3171A3	Lot No. ENG3422A3	-39.2	0.898
Lot No. ENG3321A3	Lot No. ENG3422A3	-28.8	0.963

(include Post Hoc test) that: anti- HBs levels mean difference between Lot No. ENG3171A3 and Lot No. ENG3321A3 was the highest (187.8mIu/ml), while the mean difference between Lot No. ENG3171A3 and Lot No. ENG3321A3 was the lowest (10.4 mIu/ml). Lots numbers of third vaccine dose differ not statically significant from each other's, for example Lot No. ENG3166A3 differed not statically significant from Lot No. ENG3171A3 (p- value = 0.685) and others lots numbers of third vaccine dose.

Generally

The researcher findings show that, the manufacture and change of lots number of vaccines had no effect on response to HB vaccination in Gaza governorates. This for Palestinian children in Gaza Governorates aged 18-30 months old, children who born after Sept. 2000 and had completed their immunization program at 15 months of age.

5.2.4 Environmental factors for non- response to HB vaccination

In this section the researcher will study the distribution of cases by some of environmental factors which, may affect response to HB vaccination in Gaza governorates, season of vaccine which include season of 1st, 2nd and 3ed immunization and sewage net in area.

5.2.4.1 Anti- HBs Level and Seasons of 1st dose of vaccine:

Table No. (5.30)

Relationship between Anti- HBs and Seasons of 1st dose

Seasons of 1st dose	Subject			
	Case		Control	
	No	%	No	%
Winter	22	34.9	35	27.8
Spring	21	33.3	31	24.6
Summer	8	12.7	30	23.8
Autumn	12	19.0	30	23.8
Total	63	100.0	126	100.0

Chi-Square = 4.88 df = 3 p-value = 0.181

From table no. (5.30), in the 1st dose, the highest percentage of cases was vaccinated in winter (34.9%), while the lowest in summer (12.7%). The difference between the seasons did not reach a statically significant level (p-value = 0.181).

As shown in table no. (5.31), comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for seasons of the first vaccination dose: children those

Table No. (5.31)

Comparisons between Anti-HBs Levels (mIu/ml) in

Seasons of 1st, 2nd, 3ed dose

	Environmental factors		**Anti-HBs Mean (mIu/ml)**	**p-value**
Anti-HBs Levels (mIu/ml)	Seasons of 1st dose	Winter	193	0.938
		Spring	169	
		Summer	205	
		Autumn	202	
	Seasons of 2nd dose	Winter	180	0.901
		Spring	191	
		Summer	183	
		Autumn	223	
	Seasons of 3ed dose	Winter	196	0.946
		Spring	206	
		Summer	195	
		Autumn	173	

were vaccinated in summer (mean = 205 mIu/ml) was higher than others, who were vaccinated in other seasons. The difference between means did not reach statically

significant level (p-value= 0.938). We can conclude that, in the first vaccine dose what ever the season of vaccination was, the response to HB vaccination was not affected.

Table number (5.32) shows, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between spring and summer was the highest (35.5 mIu/ml), while the mean difference between summer and autumn (2.5 mIu/ml) was the lowest. Seasons of first vaccine dose differ not statically significant from each others, for example winter differed not statically significant from spring (p- value = 0.974) and others seasons of first vaccine dose.

Table No. (5.32)

Multiple Comparisons between Seasons of 1st dose on Anti- HBs Level

(I) season of 1st dose	(J) season of 1st dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Winter	Spring	23.8	0.974
Winter	Summer	-11.6	0.998
Winter	Autumn	-9.2	0.999
Spring	Summer	-35.5	0.942
Spring	Autumn	-33.0	0.948
Summer	Autumn	2.5	1.000

5.2.4.2 Anti- HBs Level and Seasons of 2nd dose of vaccine:

From table no. (5.33), in the second HB vaccine dose, the highest percentage of cases was vaccinated in spring (31.7%), while the lowest in autumn (12.7%). The difference between the seasons did not reach a statically significant level (p-value = 0.840).

Table no. (5.31) shows, comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for seasons of the second vaccination dose: children those

Table No. (5.33)

Relationship between Anti- HBs and Season of 2nd dose

Seasons of 2nd dose	Subject			
	Case		Control	
	No	%	No	%
Winter	19	30.2	34	27.0
Spring	20	31.7	37	29.4
Summer	16	25.4	33	26.2
Autumn	8	12.7	22	17.5
Total	63	100.0	126	100.0

Chi-Square = 0.84 df = 3 p-value = 0.840

vaccinated in autumn (mean = 223 mIu/ml) was higher than others who vaccinated in

Table No. (5.34)

Multiple Comparisons between Seasons of 2nd dose on Anti- HBs Level

(I) season of 2nd Dose	(J) season of 2nd dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Winter	Spring	-10.9	0.997
Winter	Summer	-3.6	1.000
Winter	Autumn	-43.0	0.918
Spring	Summer	7.3	0.999
Spring	Autumn	-32.2	0.962
Summer	Autumn	-39.4	0.938

others seasons. The difference between means did not reach statically significant level (p-value= 0.901). We can conclude that, in the second vaccine dose response to HB vaccination did not affected by season of vaccination.

Table number (5.34) show, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between winter and autumn was the highest (43.0 mIu/ml), while the mean difference between winter and summer (3.6 mIu/ml) was the lowest. Seasons of second vaccine dose differ not a statically significant from each others, for example winter differed not statically significant from spring (p- value = 0.997) and others seasons of first vaccine dose.

5.2.4.3 Anti- HBs Level and Seasons of 3ed dose of vaccine:

Table no. (5.35) illustrates, the highest percentage of cases was vaccinated in autumn (36.5%), while the lowest in winter (12.7%). The difference between the seasons did not reach a statically significant level (p-value = 0.158).

Table No. (5.35)

Relationship between Anti- HBs and Seasons of 3ed dose

Seasons of 3ed dose	Subject			
	Case		Control	
	No	%	No	%
Winter	8	12.7	30	23.8
Spring	12	19.0	31	24.6
Summer	20	31.7	30	23.8
Autumn	23	36.5	35	27.8
Total	63	100.0	126	100.0

Chi-Square = 5.19 df = 3 p-value = 0.158

As shown in table no. (5.31), comparison of anti- HBs level means by one- way ANOVA (include scheffe- Post Hoc test) for seasons of the third vaccination dose: children those were vaccinated in spring (mean = 206 mIu/ml) was higher than others who vaccinated in others seasons. The difference between means did not reach a statically significant level (p-value= 0.946). We can conclude, third vaccine dose what ever the season of vaccination was, the response to HB vaccination was not affected.

Table number (5.36) shows, multiple comparison between groups by one- way ANOVA (include Post Hoc test) that: the anti- HBs levels mean difference between spring and autumn was the highest (33.7 mIu/ml), while the mean difference between winter and summer (1.9 mIu/ml) was the lowest. Seasons of third vaccine dose differ not a statically significant from each others, for example winter differed not statically significant from spring (p- value = 0.999) and others seasons of first vaccine dose.

Table No. (5.36)

Multiple Comparisons between Seasons of 3ed dose

on Anti- HBs Level

(I) season of 3ed dose	(J) season of 3ed dose	Anti- HBs Mean Difference (mIu/ml) (I-J)	p- value
Winter	Spring	-10.0	0.999
Winter	Summer	1.9	1.000
Winter	Autumn	23.9	0.980
Spring	Summer	11.8	0.997
Spring	Autumn	33.7	0.941
Summer	Autumn	21.9	0.980

In studying the seasonal variation as a factor influencing antibody response to HB vaccine, the researcher findings was what ever the season of vaccination was, the response to HB vaccination was not affected. This findings agree with the study result conducted by (Inskip, et al, 1991), in Gambia, where there was no effect to seasonal variation, season of birth, or season of 1st immunization.

5.2.4.4 Anti- HBs Level and Sewage net in the area:

It is clear from table no. (5.37) that, the percentage of cases from areas with sewage net (79.4%) was higher than areas with out (20.6%).

Table No. (5.37)

Anti- HBs and Sewage net in the area

Sewage net in the area	Subject			
	Case		Control	
	No	%	No	%
Yes	50	79.4	100	79.4
No	13	20.6	26	20.6
Total	63	100.0	126	100.0

The mean for children who lives in places have not a sewage net (227 mIu/ml) was higher

Table No. (5.38)

Comparisons between Anti-HBs and Sewage net in the area

Anti-HBs	Groups	Mean	t	p- value
Sewage net in the area	Present	182	0.95	0.344
	Not-present	227		

than with a sewage net (182 mIu/ml) on their response to HB vaccination, as recorded in table no. (5.38). the difference between the two means did not reach a statically significant level (t= 0.95, p-value= 0.344). We conclude that, the presence or absence of sewage net have not effect on response to HB immunization.

Generally

In studying the seasonal factor as apredictive factor to a poor response to HB vaccination, the researcher findings was what ever the season of vaccination was, the response to HB vaccination was not affected. This findings agree with the study result conducted by Inskip, et al, 1991, in Gambia, where there was no effect to seasonal variation, season of birth, or season of 1st immunization. While disagree with the findings of a study in Mongolia by Davaalkham, et al, 2007, where, administration of HB vaccine during winter is an important predictor of the low effectiveness of vaccination in rural Mongolia, the result was in rural areas, the frequency of immunity induced by vaccine was significantly lower among those with winter administration of birth HB than those vaccinated during non-winter months (p = 0.007). However, this difference was not evident in urban areas.

Chapter Six

Conclusion and Recommendation

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6.1 Conclusion

In an attempt to study the evaluation of Hepatites B immunization program for children in Gaza governorate, Palestine, 2007, the current study was conducted as a part of my study at school of public health.

The study findings might help in determining the associated factors lead to a poor response for HB vaccination among vaccinated children in year 2001 and continue monitoring the immunization program and adopting suitable polices for prevention of HBV.

Globally, several factors that increase the risk of non-response to HBV vaccination have been identified: male gender, area of residence, ethnic differences. The manufacture and change of lots no. of vaccines (1st, 2nd & 3ed) doses. A delay in receiving the 1st dose of vaccine, interval between the 1st and 2nd doses, interval between the 2nd and 3rd doses, the time between the last dose of vaccine and taking the blood sample. In addition to seasonal variation, season of birth, 2nd and 3ed immunization. HBsAg status of the mother and the age at vaccination.

In this study some of these factors have been studied, it is found that, most are not statically significant on non-response to HB vaccination, while the dominant effect was the time between the last dose of vaccine and taking the blood sample, which was statically significance (p-value = 0.024).

Tentatively This study could be a model to study and define the risk factors, which may affect non-response to HB vaccination in developing community as Gaza governorates. Such study and similar studies will help in institute successful intervention program to reduce the non- respondent percentage of infants to HB vaccination in Gaza, Palestine and other similar countries.

6.2 Recommendation

1. People must be aware about risk factors, that increase the risk of non-response to HB vaccination on infants in Palestine.
2. Assessing policy, to keep the vaccination files as long as possible or to computerize the data.
3. To continue monitoring the EPI and ensure cold chain system preservation.
4. We rcommend to follow the different opptions of HB immunization, which recommended by WHO for detecting HBeAg-positive mothers.
5. We rcommend to follow other opptions of WHO immunization policy for HB, that will help in decreasing the incidence and prevalence of HBV in Palestine, and in reducing the percentage of the non-respondent infants in Palestine.
6. To assess a strtigy to follow up after immunization for giving a poster dose in case of vaccine failure.

6.3 Future Research Recommendation

1. Risk factors associated with non-response to HB vaccination in Palestine.
2. The prevalence of HBsAg among pregnant women in Palestine
3. HBsAg- Mother, as a predictive factor of non-response to HB vaccination on infants in Palestine.

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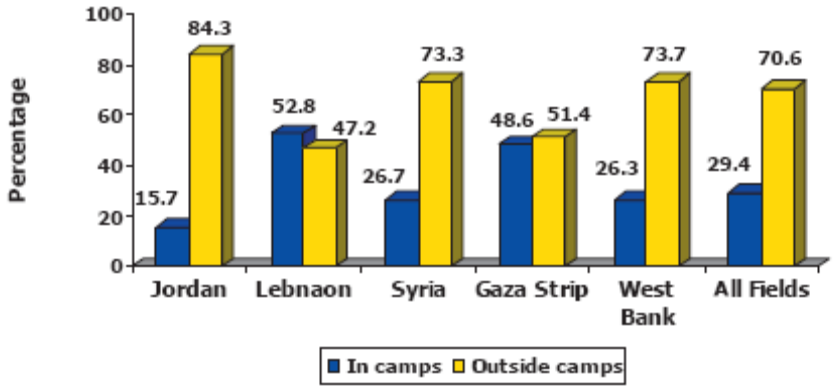
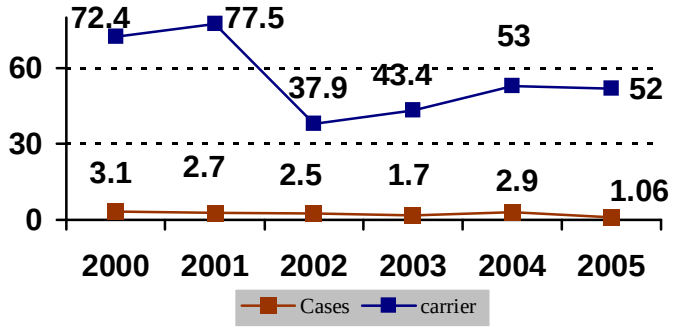
Annexes

Annex No. (1)



Distribution of the refugee population in and outside camps

Annex No. (2)



Incidence rate of HB cases and carrier in Palestine,

2000-2005, (per 100,000)

Annex No. (3)

Vaccination schedule in Palestine from Jan, 1995

Vaccines	Age
B.C.G , HB1	1 day
HB2 , I.P.V1	1 month
D.P.T.1 , T.O.P.V1 , I.P.V2	2 months
D.P.T.2 , T.O.P.V2	4 months
HB3 , D.P.T.3 , T.O.P.V3	6 months
Measles	9 months
D.P.T.4 , T.O.P.V4	12 months
MMR	15 months
DT , O.P.V	6 years
Rubella , for female students only	12 years
Dt	15 years

Annex No. (4)

Distribution of used basic vaccines by type and cost, Palestine, 2005

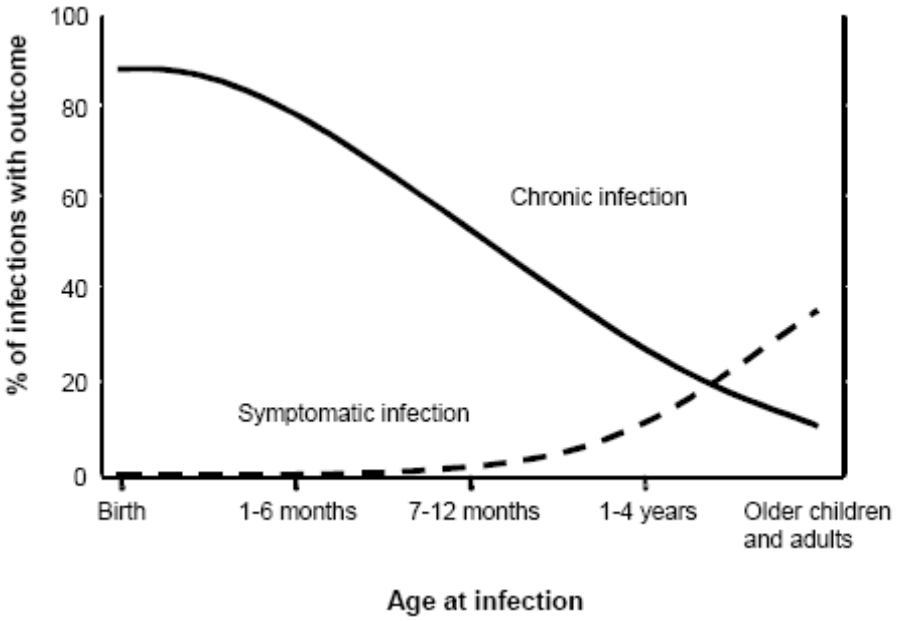
Vaccine	No. of doses	Cost (US$)	cost per dose (US$)
BCG 0.1 ml vial	138,210	13,148	0.1
DPT	371,680	72,587	0.2
IPV	316,330	358,342	1.1
OPV	993,800	66,170	0.1
HB infant	417,950	100,879	0.2
Rubella vaccine	74,420	19,778	0.3
Measles	50,690	5,442	0.1
MMR	830,121	844,682	1.0
Mantoux test PPD 5 U/0.1 ml	4,380	8,865	2.0
Basic vaccines	3,197,581	1,489,893	0.47

Annex No. (5)

HB Vaccination Coverage in Palestine 2000-2005.

Year	2000	2001	2002	2003	2004	2005
HepB3	95%	96%	91.7%	98.3%	97.9%	98.7%

Annex No. (6)



From: McMahon, Alward & Hall, 1985

Outcome of HB virus infection by age at infection

Annex No. (7a)

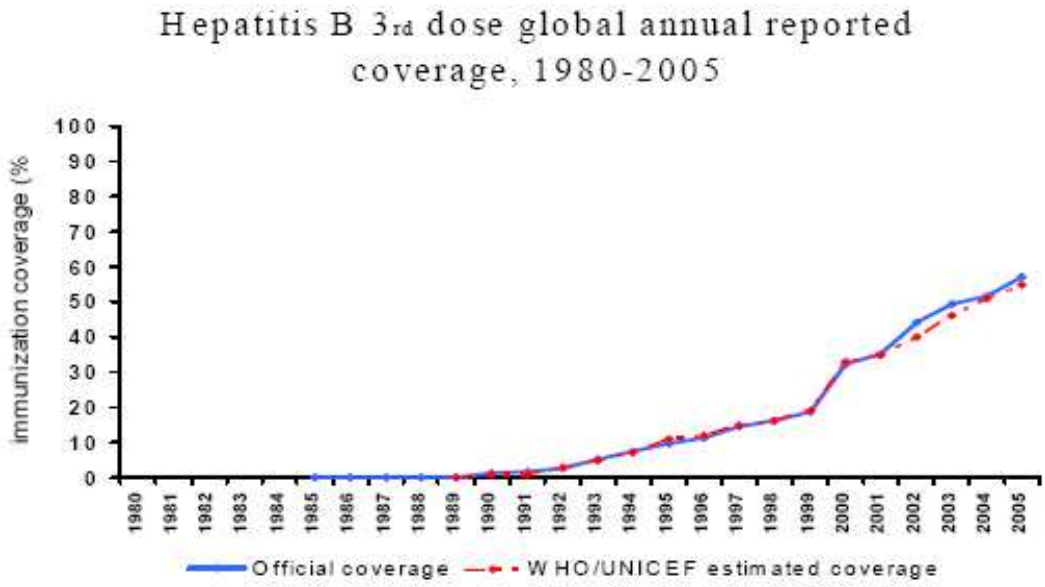
Regional and global summaries of reported, and WHO/UNICEF estimates of, vaccination coverage (%), HepB3 < 1 year of age: 1980, 1990, 1996-2005.

	1980	1990	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
AFR	-	0	1	1	1	1	6	5	26	30	36	45
	-	*0*	*1*	*4*	*5*	*5*	*6*	*6*	*23*	*29*	*34*	*39*
AMR	-	0	21	33	37	53	73	75	75	78	84	85
	-		*22*	*30*	*32*	*50*	*69*	*71*	*72*	*78*	*83*	*85*
EMR	-	3	31	35	32	36	39	42	44	64	65	74
	-	*3*	*30*	*34*	*31*	*36*	*40*	*43*	*45*	*64*	*66*	*74*
EUR	-	7	15	23	23	27	43	49	66	70	75	77
	-	*4*	*19*	*23*	*28*	*29*	*42*	*50*	*65*	*68*	*74*	*76*
SEAR	-	0	10	11	12	12	11	10	11	15	17	29
	-		*10*	*11*	*12*	*12*	*11*	*10*	*11*	*13*	*20*	*27*
WPR	-	2	5	7	12	12	55	65	81	83	80	76
	-	*2*	*8*	*7*	*8*	*8*	*60*	*68*	*67*	*74*	*76*	*76*
Global	-	1	11	15	16	19	32	35	44	49	51	57
	-	*1*	*12*	*15*	*16*	*19*	*33*	*35*	*40*	*46*	*51*	*55*
% population	-	2	13	21	23	25	44	46	50	59	87	85
N° countries	-	10	44	62	68	78	87	100	104	128	142	152

Unless otherwise specified, data provided by Member States through WHO-UNICEF Joint Reporting Form and WHO Regional offices.

1)Source: "World Population Prospects: The 2004 Revision", New York, United Nations, 2005.

Annex No. (7b)


Hepatitis B 3rd dose global annual reported coverage, 1980-2005
immunization coverage (%
100
90
80
70
60
50
40
30
20
10
0
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
Official coverage
WHO/UNICEF estimated coverage

Annex No. (8a)

Eastern Mediterranean Region

Population data in thousands [1]

	2005	2004	2003	2002	2001	2000	1990	1980
Total population	538'001	526'772	515'735	504'879	494'186	483'637	381'832	283'466
Live births	15'502	15'296	15'091	14'893	14'708	14'547	14'291	12'343
Surviving infants	14'504	14'290	14'078	13'873	13'683	13'515	13'146	11'041
Pop. less than 5 years	69'036	68'030	67'071	66'210	65'507	65'001	63'470	49'664
Pop. less than 15 years	195'233	193'737	192'389	191'154	189'987	188'839	165'432	124'198
Female 15-49 years	135'164	131'506	127'833	124'146	120'438	116'714	85'024	62'408

Number of reported cases

Diphtheria	251	145	287	924	96	175	3'604	19'970
Measles	15'069	59'804	52'110	42'616	41'103	38'592	59'058	341'624
Mumps	14'241	26'492	12'351	19'861	35'431	65'935	-	-
Pertussis	5'164	81'987	1'161	2'650	4'257	2'112	27'437	171'631
Polio	730	187	113	110	143	505	1'498	12'622
Rubella	14'967	8'368	510	569	1'328	3'122	-	-
Rubella (CRS)	1	3	1	0	2	0	-	-
Tetanus (neonatal)	802	910	1'299	1'986	1'815	3'140	4'666	5'190
Tetanus (total)	914	766	1'618	2'900	2'038	2'134	9'815	17'721
Yellow fever	0	0	0	0	0	0	-	-

Percentage of target population vaccinated, by antigen

based on WHO-UNICEF estimates
TT2plus and YFV are based on reported coverage

BCG	84	83	82	81	76	77	83	18
DTP1	91	86	85	84	83	81	85	36
DTP3	82	78	77	76	75	73	71	18
HepB3	74	66	64	45	43	40	3	-
Hib3	15	12	12	10	5	1	-	-
MCV	82	79	75	75	75	72	67	15
Pol3	84	78	78	77	75	73	71	21
TT2plus	51	52	57	53	50	48	46	1
YFV	0	0	0	0	0	0	0	0

Annex No. (8b)

Regional and global summaries of reported, and WHO/UNICEF estimates of, vaccination coverage (%), HepB3 < 1 year of age

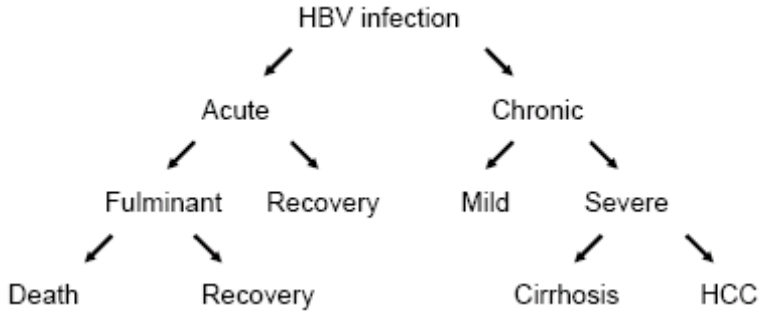
Vacc. Coverage %		1990	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
world	%population	2	13	21	23	25	44	46	50	59	87	85
	Countries N.	10	44	62	68	78	87	100	104	128	142	152
EMR	Reg. Report.	3	31	35	32	36	39	42	44	64	65	74
	Who/unicef	3	30	34	31	36	40	43	45	64	66	74

Note: the vaccination coverage % in year 1989 was not reported.

Source: "World Population Prospects: The 2004 Revision", New York, United Nations, 2005.

Annex No. (9)

Spectrum of liver disease after HBV infection



From: Chisari & Ferrari, 1997

Annex No. (10)

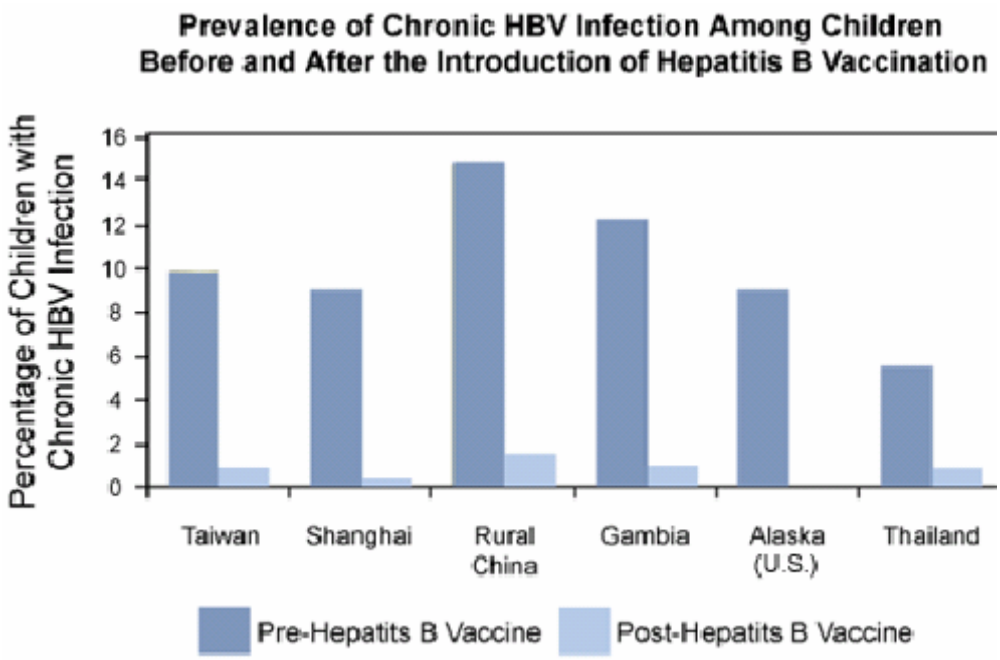
						Hepatitis B vaccine options		
						No birth dose	With birth dose	
Age	Visit		Other antigens			I	II	III
Birth	0	BCG [OPV0][1]				HepB -birth[2]	HepB -birth[2]	
6 weeks	1		OPV1	DTP1		HepB1[3]	HepB2[2]	DTP-HepB1[4]
10 weeks	2		OPV2	DTP2		HepB2[3]		DTP-HepB2[4]
14 weeks	3		OPV3	DTP3		HepB3[3]	HepB3[2]	DTP-HepB3[4]
9–12 months	4				Measles			

Options for adding HB vaccine to childhood immunization schedules

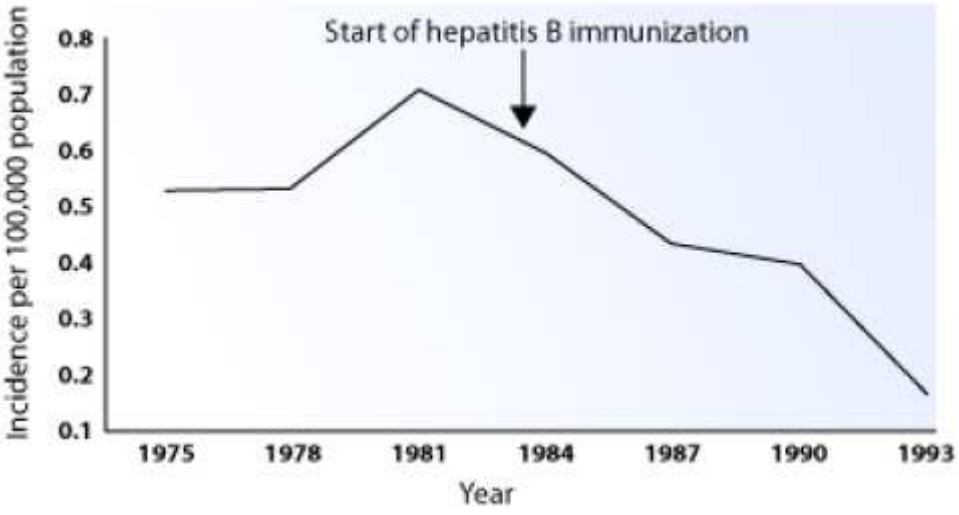
Notes: 1. Only given in high polio endemic countries, 2. Monovalent vaccine,

3. Monovalent or combination vaccine, 4. Combination vaccine

Annex No. (11)



Annex No. (12)



Liver cancer death rates among children in Taiwan, 1975 to 1993

Annex No. (13)

Questionnaire

Serial Number: _ _ _ _ _ _

Child Name: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

ID. No.: _ _ _ _ _ _ _ _ _

Date of birth: _ _ _ / _ _ _ / 200_ _

Address: _ _ _ _ _ _ _ _ _ _ _ _ _ _

District: ☐ North Gaza ☐ G. City ☐ M. zone ☐ Khanyounis ☐ Rafah

Sex: ☐ Male ☐ Female

Total number in household: ☐

Mother Years of education: ☐ Primary Or less ☐ Preparatory ☐ Secondary ☐ Diploma ☐ University or more

Father Years of education: ☐ Primary Or less ☐ Preparatory ☐ Secondary ☐ Diploma ☐ University or more

Father work: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Health Determinants:

1. **Anti- HBs Level:** ☐ Positive ☐ Negative
2. **Place of Immunization:** _ _ _ _ _ _ _ _ _ _ _ _ _
3. **Type of Immunization:** ☐ Government ☐ UNRWA ☐ G.+ U. ☐ Others Specify _ _ _ _ _ _ _ _ _ _
4. **Birth Weight (kg):** _ _ _ _ _ _ _
5. **Lot number of First vaccine dose:** _ _ _ _ _ _ _
6. **Lot number of Second vaccine dose:** _ _ _ _ _ _ _
7. **Lot number of Third vaccine dose:** _ _ _ _ _ _ _

8. Number of doses: ☐ Doses

9. Dates of HB Vaccination:

1st	2nd	3ed
/ / 200_	/ / 200_	/ / 200_

10. Interval between doses in days:

Birth - 1st	1st - 2nd	2nd - 3ed

11. Date of Blood Sample Drawal: _ _ _ /_ _ _ / 200_ _

12. Age at blood sample drawal in months: _ _ _ _ _ _ _

13. Interval between last vaccine. dose and Blood sample test in months: _ _ _ _

14. Season of First vaccine dose: ☐ Winter ☐ Spring ☐ Summer ☐ Autumn

15. Season of Second vaccine dose: ☐ Winter ☐ Spring ☐ Summer ☐ Autumn

16. Season of Third vaccine dose: ☐ Winter ☐ Spring ☐ Summer ☐ Autumn

17. Vaccine delay: ☐ Yes ☐ No

18. If yes, Period of delay: ☐ Days

19. Reason of delay: _ _ _ _ _ _ _ _ _ _ _

20. Are you traveled long distance to have vaccine:

☐ Yes ☐ No

21. Are your child suffered from adverse events after vaccine:

☐ Yes ☐ No

22. Do you consult a clinic or a doctor for adverse events:

☐ Yes ☐ No

23. Nutritional Status: ☐ Underweight ☐ Normal

☐ Overweight

24. History of Infection: ☐ No ☐ Diarrhea

☐ Respiratory ☐ Others specify _ _ _ _ _ _ _

25. History of Hospitalization before immunization:

☐ Yes ☐ No

26. Feeding during Immunization:

☐ Breast ☐ Artificial

☐ Breast + Artificial

27. Sewage net in the area: ☐ Present ☐ Not presen

Annex No. (14)

Agreement of Ministry of Health to use the sero- survey, 2003, data

Annex No. (14)

السيد/ مدير عام الصحة العامة ومختبر الصحة العامة

السيد/ أسعد رملاوي المحترم

أفيد سيادتكم علماً بأنني اعمل في وزارة الصحة - دائرة المختبرات وبنوك الدم وأحضر لرسالة الماجستير في موضوع التطعيمات للأطفال بخصوص التهاب الكبد الوبائي B في كلية الصحة العامة - جامعة القدس.

Sero- Conversion of Hepatitis B Surface Antibody among vaccinated Children in Palestine

وبعد اطلاعي على دراستكم بخصوص

Sero- Survey For Measles Rubella And Hepatitis B

أرجو من سيادتكم السماح لي إن أمكن باستخدام المعلومات في دراستكم وتزويدي بها .

ولكم فائق الاحترام والتقدير

الأخ شحدة خليل/ هذه المعلومات وجدت للاستفادة منها ومن تشجيعك وتشجيعي أي طالب شحدة خليل برهوم

جوال: 0599- 476097

أن يستعين ويستغل أي معلومة موجودة.

أما إذا أردت أي معلومة أرجو الاتصال بالأخت مي أبو ردا ضحى في مختبر الصحة العامة: 02/2983034

055

نسخة الأخت مي أبو ردا في

أنا مستعد للمساعدة في رسالتك

082840066

Annex No. (15)

Agreement of Helsinki committee

Annex No. (15)

Palestinian National Authority
Ministry of Health
Helsinki Committee

السلطة الوطنية الفلسطينية
وزارة الصحة
لجنة هلسنكي

Date: 26 / 9 /2006

التاريخ: 2006/ 9/ 26

Mr./ Shehda Barhoum

السيد: شحدة برهوم

I would like to inform you that the committee has discussed your application about:

نفيدكم علما بأن اللجنة قد ناقشت مقترح دراستكم حول:-

Evaluation of Hepatitis B Immunization Programme for Children in Gaza Governorate, Palestine 2007

In its meeting on September 2006 and decided the Following:-

To approve the above mention research study.

و ذلك في جلستها المنعقدة لشهر سبتمبر 2006

و قد قررت ما يلي:-

الموافقة على البحث المذكور عاليه.

Signature

توقيع

Member

عضو

Member

عضو

Chairperson

Ministry of Health
Helsinki Committee

Conditions:-

- Valid for 2 years from the date of approval to start.
- It is necessary to notify the committee in any change in the admitted study protocol.
- The committee appreciate receiving one copy of your final research when it is completed.

Gaza Etwam – Telefax 972-7-2878166

Annex No. (16)

Agreement of Ministry of Health

Annex No(16)

وزارة الصحة

كليـة الصحـة العامـة

School of Public Health

القدس - فلسطين

جامعة القدس

2006/12/23

الأخ/ د. علي قويدر المحترم

مدير عام الرعاية الأولية- وزارة الصحة

تحية طيبة وبعد،،،

الموضوع: مساعدة الطالب شحدة برهوم

يقوم الطالب المذكور أعلاه بإجراء بحث بعنوان:

"Evaluation of Hepatitis B Immunization Programme for Children in Gaza Governorate, Palestine,2007 "

كمتطلب للحصول على درجة الماجستير في الصحة العامة-مسار الوبائيات و الإحصاء الحيوي علماً بأن الطالب قد حصل على موافقة لجنة هلسنكي لأخلاقيات البحوث و ستكون المعلومات متوفرة لدى الباحث فقط. و عليه نرجو التكرم للإيعاز لمن ترونه مناسب لتسهيل مهمة الطالب في جمع البيانات الخاصة.

موافقتكم دعماً للمسيرة الأكاديمية

و تفضلوا بقبول فائق الاحترام ،،،

د. سوزان شعشاعه

عميد كلية الصحة العامة المساعد

كلية الصحة العامة / غزة
الرقم المسلسل: 151
التاريخ: 2006/12/23

نسخة: الملف

Annex No. (17)

Agreement of UNRWA

Annex No. (17)

وزارة الصحة

كليـة الصحـة العامـة

School of Public Health

القدس - فلسطين

جامعة القدس

2006/12/23

24.12.06

الأخ/ د. أيوب العالم المحترم

مدير برامج الصحة -وكالة الغوث

تحية طيبة وبعد،،،

الموضوع: مساعدة الطالب شحدة برهوم

يقوم الطالب المذكور أعلاه بإجراء بحث بعنوان:

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كلية الصحة العامة / غزة
رقم الصادر: 152
تاريخ الصادر: 2006/12/23

نسخة: الملف

Annex No. (18)

التاريخ: 1 / 1 / 2007

السلام عليكم و رحمة الله و بركاته

أنا الطالب: شحدة خليل برهوم بكلية الصحة العامة – جامعة القدس

أقوم بعمل بحث تخرج لدرجة الماجستير بعنوان تقييم برنامج تطعيم الأطفال لمرض التهاب الكبد الوبائي (ب) في غزة لمواليد عام 2001، و تم اختيار اسم طفلكم عشوائيا ضمن مجموعة البحث.

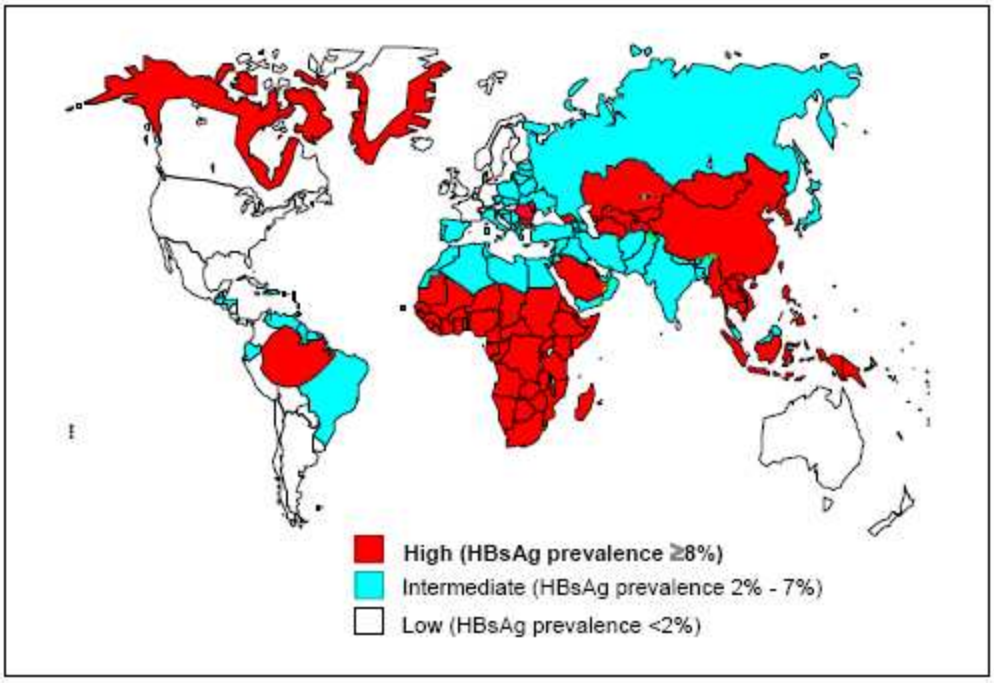
و نود أن نسألكم بعض الأسئلة المتعلقة بصحة طفلكم خلال السنة الأولى من التطعيم و كذلك الاطلاع على كرت التطعيم الخاص بالطفل، مع العلم أن المقابلة ستستغرق 15 دقيقة تقريبا. في حال أن الوقت غير مناسب الرجاء تحديد موعد آخر يناسبكم.

مشاركتكم تطوعية يمكنكم رفض الإجابة على أي سؤال و أرغب أن أؤكد لكم أن المعلومات التي تذكروها ستكون مصدر ثقة و سرية و ستستخدم فقط لغرض البحث العلمي و لتحسين برنامج التطعيم للأطفال و بدون ذكر الأسماء و لذا أرجو أن تكون الإجابات دقيقة.

و إذا كنت ترغب في معرفة المزيد عن الدراسة أو كان لديك خوف من وقوع أي ضرر يمكنك الاتصال بعميد كلية الصحة العامة في غزة / د. سوزان شعشاعة على تليفون المكتب 2878177

وشكرا على حسن تعاونكم

Annex No. 19



Global distribution of HBV

www.who.Int/vaccines-documents/ WHO/V&B/01.31(Accessed at24.10.2006)