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Epidemiological Review of Viral Hepatitis A in the West Bank

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Epidemiological Review of Viral Hepatitis A
in the West Bank

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Declaration

I certify that this thesis submitted to the degree of the master is the result of my own research, where otherwise acknowledged, this thesis or any of its parts has not been submitted to any other university or institution for a higher degree.

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Date: 20/8/2023

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وإلى جميع أساتذتي في جامعة القدس. إلى زملائي في الدراسة جميعا وأخص بالذكر الدكتور فهد طنينة والدكتور فراس حمامدة من كانوا سندا وعونا وأفضل رفقاء وآخر دعواهم أن الحمد والشكر لله.

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List of Abbreviations

ALT	Alanine Aminotransferase
HAV	Hepatitis A Virus
RT-PCR	Reverse Transcription Polymerase Chain Reaction
PeP	Post-exposure Prophylaxis
WHO	World Health Organization
MSM	Men who have Sex with Men
PWUD	People Who Use Drugs
SES	Socio-Economic Status
PCBS	Palestine Central Bureau of Statistics
MOH	Ministry of Health
RNA	Ribonucleic Acid
SES	Socioeconomic Status

Abstract

Hepatitis A Virus HAV has been a significant cause of infections among the children and adolescents of Palestine. The possibility of protection from HAV through vaccination made it necessary to identify the epidemiology changing of hepatitis A infection in Palestine and to understand the trends for HAV and possible age-specific prevalence transitions. This data-based cross-sectional study was conducted during the period April – July 2023 on 1,781 surveys from the records from the Preventive Medicine Department- Ministry of Health MoH in Palestine. The data collected were analyzed using SPSS against different variables (age, gender place of residents, environmental conditions, liver enzymes and HAV symptoms (Fever, chills, vomiting, Jaundice, and dark urine).

The high mean incidence rate in the 5 – 9 years age group suggests that individuals within this age range are particularly vulnerable to contracting HAV; which indicate an epidemiology changing of hepatitis A infection in Palestine

The study revealed the association of several risk factors for higher HAV incidence rates: (i) elder age groups; (ii) environmental and behavioral conditions.

This study provided strong evidence for continuous transition of HAV epidemiology towards intermediate endemicity in Palestine, with adolescents and adults most at risk. Following the World Health Organization (WHO) recommendations for countries with intermediate endemicity, vaccination strategy against hepatitis A is recommended for children in Palestine.

دراسة الوضع الوبائي لفايروس التهاب الكبد الوبائي(أ) في الضفة الغربية

إعداد الطالب: علاء الدين نور الدين عابد الشلالدة
إشراف: د. اسعد الرملاوي

الملخص:

يعتبر فيروس التهاب الكبد الوبائي (أ) سببًا مهمًا للعدوى بين الأطفال والمراهقين في فلسطين. إن إمكانية الحماية من فيروس التهاب الكبد A من خلال التطعيم جعلت من الضروري تحديد التغير الوبائي لعدوى التهاب الكبد A في فلسطين وفهم اتجاهات فيروس التهاب الكبد A والتحولات المحتملة لانتشاره حسب العمر. أجريت هذه الدراسة المقطعية المبنية على البيانات خلال الفترة من أبريل إلى يوليو 2023 على 1,781 مسحًا من سجلات دائرة الطب الوقائي بوزارة الصحة في فلسطين. تم تحليل البيانات التي تم جمعها باستخدام برنامج SPSS باعتماد متغيرات مختلفة (العمر، جنس مكان السكن، الظروف البيئية، إنزيمات الكبد وأعراض التهاب الكبد الوبائي (الحمى، القشعريرة، القيء، اليرقان، والبول الداكن).

يشير ارتفاع متوسط معدل الإصابة في الفئة العمرية 5 إلى 9 سنوات إلى أن الأفراد ضمن هذه الفئة العمرية معرضون بشكل خاص للإصابة بفيروس التهاب الكبد الوبائي. مما يشير إلى تغير وبائي في الإصابة بالتهاب الكبد الوبائي (أ) في فلسطين

وكشفت الدراسة عن وجود ارتباط بين عدة عوامل خطر تؤدي إلى ارتفاع معدلات الإصابة بفيروس التهاب الكبد الوبائي: (1) الفئات العمرية الأكبر سناً؛ (2) الظروف البيئية والسلوكية.

قدمت هذه الدراسة دليلا قويا على التحول المستمر في وبائيات فيروس التهاب الكبد الوبائي نحو التوطن المتوسط في فلسطين، مع وجود المراهقين والبالغين الأكثر عرضة للإصابة. في أعقاب توصيات منظمة الصحة العالمية (WHO) للدول ذات التوطن المتوسط، يوصى باستراتيجية التطعيم ضد التهاب الكبد A للأطفال في فلسطين.

Chapter One:

Introduction

1.1 Introduction

The World Health Organization (WHO) states that the Hepatitis A Virus (HAV) is one of the most pervasive illnesses. Approximately 1.5 million cases are being reported annually (WHO, 2010).

There are three possible HAV epidemiological patterns in most societies: the first is a high prevalence of antibodies in the population from an early age, as is the case in most developing countries; the second is a significantly low incidence level that may rise gradually with age, as is typically the case in developed countries; and the third is a very low incidence level (Schwartz, 1997).

1.2 Hepatitis A Virus

HAV is a positive sense, linear, Ribonucleic acid (RNA) single-stranded virus classified as hepatotropic and belongs to the family Picornaviridae, genus Hepatovirus. The ability of HAV to resist temperature and acid inactivation, which allows HAV to live in the environment as well as in food, sewage, and human skin, may be a result of its protein characteristic; that is folded in a very different way from other viruses of the Picornaviridae family. This has benefits for fecal-oral viral transmission (Lemon SM, 2017).

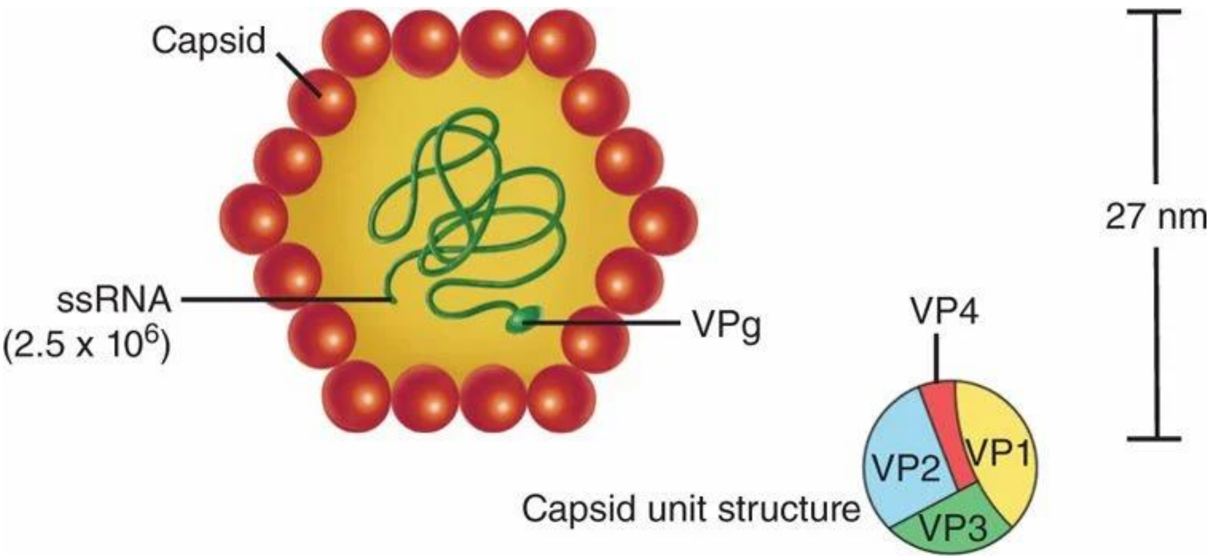

Figure 2.1: Structure of Viral Hepatitis A (HAV)

1.3 Transmission

Most frequently, transmission happens when the virus is ingested through fecal-oral transmission, either through consuming tainted food or drink or through direct contact with another person. Due to the virus' ability to withstand acidity and temperature stress, food- and water-borne transmission, either directly or through the mediation of food-handlers, is frequent. Person-to-person transmission involves very personal contact and frequently takes place in homes and schools. It also includes sexual transmission, which is mostly linked to high-risk sexual behaviors. Even though it requires a far lower infectious dose than oral transmission, parenteral transmission through contaminated syringes, blood components, or other human-derived materials has only occasionally been documented (Vaughan G, 2014).

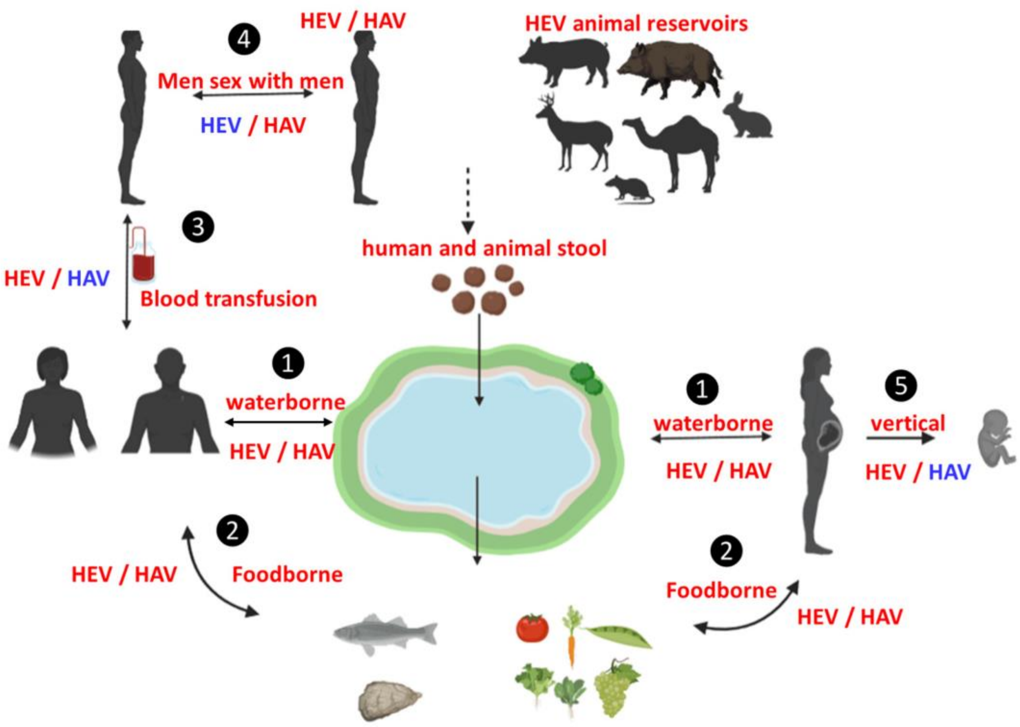

Figure 2.2: Possible routes of HAV dual infection

1.4 Study Justification

This study investigated the epidemiology of HAV infection in the general population in the West Bank. According to the published HAV infection incidence rates, there has been a rise in overt clinical cases since 1995 and a change in the peak age of infection from childhood to adults. Numerous parts of the world have reported on this altering epidemiology. It is hypothesized that this will be accompanied by a decrease in the community's general incidence rate of HAV infection. As a result, the need for a vaccination campaign is being proposed. The study examined the HAV incidence levels in Palestine overtime and investigated whether there should be a vaccination program or HAV incidence levels are remain within the same range that the vaccination policy recommendation is not justified.

1.5 Theoretical Background

Most HAV infections occur before age 5, and most of them are asymptomatic, in the nations where HAV is most endemic. As a result, these nations have low reported disease rates, and disease outbreaks are seldom. In contrast, it came to light that seroprevalences were less than 5% in several industrialized nations. In these nations, infection is typically contracted during adolescence and the early stages of adulthood and is accompanied with severe morbidity (CDC, 2021).

The no-vaccination alternative or policy may be valid under the assumptions; that there are no further deteriorations will occur in the level of hygiene (environment) in the future, and that natural vaccinations (occurring form usual incidence) will protect most of the growing population in Palestine, and that infections from external transmission of HAV will be less probable -no risk group that may bring HAV into Palestine.

In many underdeveloped sections of the Palestine, including villages, refugee camps, and a sizeable portion of the Gaza Strip, where contaminated water and unchecked sewage issues are becoming serious public health concerns, such a scenario is becoming more likely. Additionally, there has been a dramatic decline in all socioeconomic indicators and a worsening of people's living situations (Daghra, 2008).

The Palestinian environment has increasingly been deteriorating because of several internal and external factors especially regarding Refugee Camps areas, water resources and sanitation. According to the Palestinian Central Bureau of Statistics (PCBS) “More than 97% of the water pumped from the Coastal Aquifer does not meet the standards of the World Health Organization” (PCBS, 2022)

As the dangers of HAV infection are related to the age of the individual. Infection in children less than 6 years old will most likely have passes unnoticed in most cases with no health complications; it is estimated that 70% of infections in this age are asymptomatic; this means that it is typically not accompanied by jaundice. On the other hand, older people are more likely to have health complication. Persons with chronic liver disease are at an increased risk for acute liver failure when infected with HAV (CDC, 2021).

Incidence rates were calculated as the sum of all episodes of illness of HAV in each perspective year divided by the size of population at risk in that given year.

1.6 Research Questions

1.6.1 Study Main Question

- Is Palestine experiencing an epidemiology changing of HAV?

1.6.2 Study Sub-Questions

- What population is most affected by hepatitis A?
- What are the sex differences in hepatitis A incidence rates?
- What age group is more likely to be hospitalized?
- What age group is more likely to have HAV disease symptoms (Fever, chills, vomiting, Abd pain, Jaundice, dark urine)?
- Does the geographic location affect HAV incidence rates?
- What are the environmental conditions for the patients of this study?
- Has the HAV infection been confirmed through lab testing?
- What effects of the values of liver enzymes have on HAV disease symptoms?

1.7 Study Aim

The aim of this study is to investigate the need for a vaccination program against HAV in the Palestine.

1.8 Study Objectives

- The main objective of this study is to describe the HAV epidemiology in Palestine during the period (2015- 2022). Examine how the incidence of Hepatitis A have changed over time, identifying any significant increases or decreases.
- Determine the incidence and distribution of Hepatitis A cases in the West Bank during the period (2015- 2022).
- Investigate demographic factors such as age, gender, and geographic location that might be associated with higher rates of Hepatitis A infection.
- Identify potential risk factors for Hepatitis A transmission, such as exposure to contaminated water and sanitation practices.
- Analyse healthcare hospitalizations related to Hepatitis A cases.

1.9 Study Hypothesis

- First Hypothesis: "There exists no statistically significant reduction in patient hospitalization rates with respect to varying age groups".
- Second Hypothesis: "There exists no statistically significant relationship between patient age and the occurrence of HAV symptoms (Fever, chills, vomiting, Jaundice, dark urine)".
- Third Hypothesis: " There exists no statistically significant relationship between liver enzyme values and the occurrence of HAV symptoms (fever, chills, vomiting, jaundice, dark urine)".

1.10 Study Overview

This study contains five chapters. The literature review chapter review some of the most recent researches on HAV. Chapter three describes the methodology and the design of the research. In Chapter four results from data analysis are presented and discussed. Conclusion and recommendations are in Chapter five.

Chapter Two

Literature Review/ Theoretical Framework

2.1 Immune Response

HAV has a peculiar life cycle that is currently not entirely clear. Following ingestion, HAV enters the gut mucosa as a naked virus and travels to the liver as a quasi-enveloped virus, most likely via the portal circulation. This may be due to an initial, mild extra-hepatic replication taking place in the intestinal epithelium. Primary replication takes place in the hepatocytes once within the liver (Shouval D, 2014).

About a week after intravenous vaccination and for the five weeks that follow, HAV shedding in feces can be seen. A similar period of time sees the onset of viremia, which lasts for two to three weeks. In the hepatocyte, where it persists for a longer period of time and where HVA RNA is still detectable months after inoculation, HAV takes longer to be found (after about three weeks from inoculation). Although this could explain the clinical signs of recurrent hepatitis and the persistence of HAV antibodies, the presence of HAV RNA does not imply continued virus replication. Clinical signs and hepatitis emerged in the same animal models three to five weeks after inoculation, but anti-HAV specific antibodies (IgM) first showed three to four weeks later (Lanford RE, 2014).

Hepatic interferon responses appear to be one way that HAV can reduce innate host immunity. Only after HAV replication in the hepatocyte does the cellular immune response to HAV manifest. Anti-HAV IgM can be seen at the beginning of the increase in alanine aminotransferase (ALT), a few days prior to the onset of symptoms, whereas anti-HAV IgG and IgA show a few days later. About three and four weeks, respectively, following infection, asymptomatic patients can show signs of IgM and IgG production. IgG, which predominates the immune response, persists for many years, possibly for the rest of one's life, and protects against reinfection while IgM are only detectable for around four months (World Health Organization, 2019).

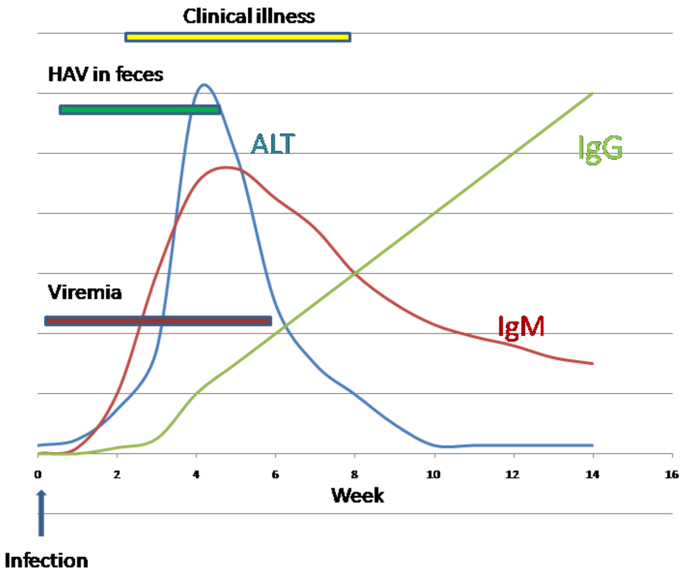

Figure 2.3: Clinical course of HAV infection- Antibody response of HAV infection (serum IgG, IgM), and ALT level is plotted

2.2 Clinical Presentation

Most kids under the age of five have no symptoms from HAV infection. The infection is frequently asymptomatic or just mildly symptomatic in older children and young adults, and both the incidence and the severity of clinical symptoms rise with age. Elderly people frequently have serious illnesses and may require hospitalization. After an incubation period of around four weeks, ranging from two to seven weeks, non-specific symptoms such as lethargy, vomiting, anorexia, diarrhea, and fever as well as specific signs such as dark urine, clay-colored urine, and jaundice manifest in symptomatic patients. Jaundice affects roughly 10% of children under the age of five and 70% of patients in adults, as was previously indicated, while practically all patients experience a notable increase in ALT and bilirubin blood levels. Vasculitis, acute renal injury, pancreatitis, meningo-encephalitis, and Guillain-Barré syndrome are only a few of the uncommon atypical and extra-hepatic symptoms that have been recorded (Jeong SH, 2010).

A highly serious consequence of hepatitis A that affects less than 1% of individuals is acute liver failure (fulminant hepatitis). A higher risk of acute liver failure is linked to aging, chronic liver disease, concurrent viral infections, including various hepatitis viruses and perhaps human immunodeficiency virus HIV. The host's genetic variants might possibly be involved. HAV infection is one of the leading causes of fulminant hepatitis in children in India, the Republic of Korea, Argentina, Brazil, and other South American nations. If a liver transplant is not an option, the case-fatality rate for pediatric and adult patients with acute liver failure is approximately 75%. Acute liver failure may recover on its own or necessitate liver transplantation (Shepherd RW, 2003).

Pregnant women are more likely to experience maternal problems and preterm labor if infected during the third trimester of pregnancy. Results for the mother and fetus are often positive. There have not been any reports of mother-to-child transmission. Anti-HAV antibodies are transmitted to offspring from seropositive mothers and last for six months to a year after birth. Hepatitis A case fatality estimates range from 0.1% in children under the age of 15 to around 5% in individuals over the age of 50. Recent figures, however, are sparse, and they might overestimate the number of hepatitis A cases that result in fatalities right now (Lednar WM, 1985).

Within two months following the onset of symptoms, 90% of patients are in remission. Relapsing symptoms happen to three to twenty percent of patients. Following the resolution of the initial clinical episode, relapsing hepatitis is characterized by the recurrence of clinical symptoms, a fresh rise in ALT values, viraemia, and viral shedding in feces. Relapse symptoms typically develop six months or longer after the first onset and are milder than those linked to the primary disease. HAV infection does not result in chronic infection or chronic liver damage and confers lifelong immunity (Glikson M, 1992).

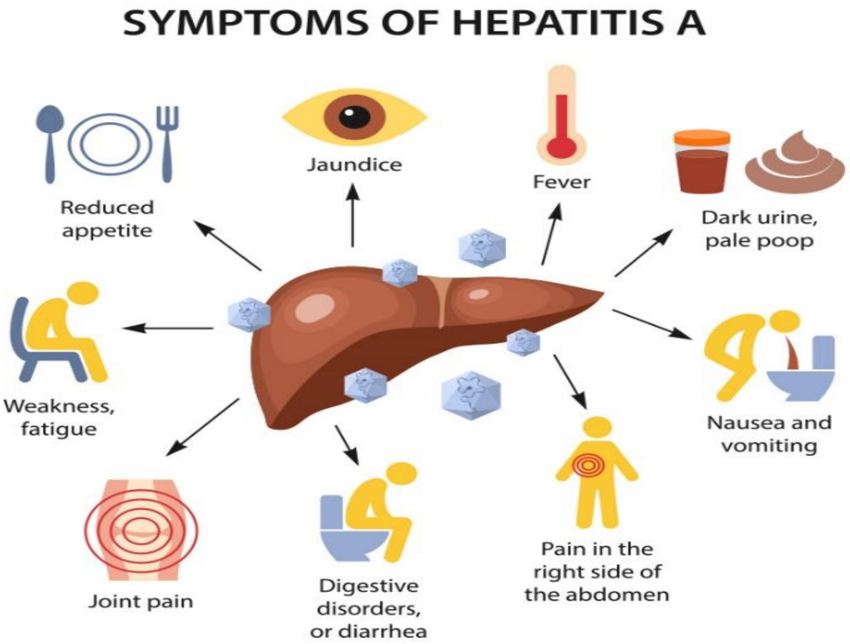

Figure 2.4: Symptoms-of-Hepatitis-A-Virus

2.3 Diagnosis and Diagnostics

Based on clinical symptoms and a history of risk factors for HAV infection, hepatitis A is diagnosed clinically. However, test confirmation is necessary since hepatitis A symptoms cannot be distinguished from those of other viral hepatitis. Traditionally, anti-HAV IgM in serum or plasma samples is detected serologically using enzyme immunoassay or other techniques for laboratory diagnosis. Anti-HAV IgG testing can also be done to increase the precision of the diagnosis. Due to the low anti-HAV IgM specificity, anti-HAV IgM testing has significant drawbacks that make it difficult to interpret ambiguous or low-level results in samples from asymptomatic or elderly persons. Anti-HAV IgG testing can be crucial to supporting result interpretation, together with the patient's clinical, biochemical, and vaccination information (Rycroft JA, 2022).

The ability to diagnose and track HAV infection, particularly in its early stages, has been demonstrated using RT-PCR to detect HAV RNA in serum, feces, and saliva samples. HAV can also be found in environmental samples using RT-PCR. Nucleic acid sequencing is used to characterize HAV and do phylogenetic research on purified PCR products produced from serum. Strain description, regional analysis, and support for public health investigations are all made possible by sequencing data combined with epidemiological information from the patients. Globally, numerous HAV genomic regions are the focus of various sequencing techniques (Enkirch T, 2019).

But during the past three decades, numerous distinct techniques have focused on various genomic regions, leading to a huge number of scattered fragments that differ in genomic position and length and partially or completely do not overlap. Due to this variation, only a portion of the genetic information contained in publicly accessible sequences may be compared. In terms of speed and sample turnaround, as well as a significant decline in technology costs, genomic sequencing is advancing quickly. For characterizing HAV strains, whole sequences offer the highest level of genetic resolution. As a result, advocates have pushed for the sequencing of all genomes. (Ramachandran S, 2021).

By looking for anti-HAV IgG in blood, plasma, or oral fluids, one can determine a person's history of spontaneous infection or immunization (and, thus, their immunity to HAV). Serology can be used to manage contacts of cases and, possibly, support investigation of clusters defining the direction of infection in household secondary transmissions, particularly when children are involved, in the absence of health records attesting history of infection or vaccination. There are highly sensitive immunological tests that can tell the difference between immunity from a natural illness and immunity from a vaccination, but they are not yet commercially accessible (Haywood B, 2019).

There are highly sensitive immunological tests that can tell the difference between immunity from a natural illness and immunity from a vaccination, but they are not yet commercially accessible. As soon as they are available, they will be helpful for interpreting seroprevalence data by differentiating between immunity from HAV infection and vaccination, clarifying the effect of vaccination on population immunity in the medium and long term, and directing vaccination policy (Rendi-Wagner P, 2007).

2.4 Treatment

Hepatitis A treatment is supportive because there is no specific therapy for the disease. Except in cases of severe vomiting, WHO does not advise the use of needless drugs such as acetaminophen or antiemetics. In the absence of abrupt liver failure or other serious consequences, hospitalization should also be avoided. The renal function should be assessed due to the possibility of acute kidney damage. When fulminant hepatitis is present, liver transplantation can significantly lower the risk of death in both pediatric and adult patients who need the procedure (Shepherd RW, 2003).

2.5 Endemicity and epidemiology

Levels of endemicity have been categorized based on seroprevalence as high (90% by age 10 years), intermediate (50% by age 15 years with 90% by age 10 years), low (50% by age 30 years with 50% by age 15), and very low (50% by age 30 years). This classification is in line with that used in the 2012 Hepatitis A Vaccine Position Paper (World Health Organization, 2012).

By the age of 10 years, >90% of children in areas with high endemicity are seropositive. Due to inadequate access to clean drinking water, food, and adequate sanitation, the virus is widely spread throughout the population. Most infections start early in life and show no symptoms. Because most infections are asymptomatic and because contextual surveillance systems have limitations, this generally leads to a modest number of reported hepatitis A cases. Low-income Sub-Saharan, northern, middle, and southern Asian nations are included in this category (World Health Organization, 2012).

Improvements in housing, food safety, sanitation, access to clean water, and immunization rates are just a few examples of the socioeconomic and human development advancements that have been made swiftly in many nations, both at the individual and communal levels. These nations are going through an epidemiological transition, going from having high or moderate levels of endemicity to having reduced levels (Cooksley WG, 2000).

In nations with intermediate endemicity, 90% of children by age 10 and 50% of children by age 15 are seropositive. In these environments, HAV circulation causes pockets of vulnerable adults who were spared infection as children to become the target of occasionally very big hepatitis A outbreaks. In contrast to other endemicity settings, the number of symptomatic cases as well as the number of clinically severe infections are significantly higher in adolescents and young adults because they more commonly have severe clinical symptoms than children. This category includes a few middle-income nations in northern Africa, the Middle East, southeast Asia, central and south America, and eastern Europe (World Health Organization, 2012).

50% of adults by age 30 and 50% of children by age 15 are seropositive in low endemicity nations. Except for those people who are more susceptible to infection, there is little virus circulation. Most instances are found in adolescents and young adults. This category includes a few middle-income nations in eastern Europe, east Asia, and central and south America (Cao G, 2021).

By the age of 30 in countries with very low endemicity, 50% of adults are seropositive. The virus is essentially nonexistent, and those that are susceptible have an extremely minimal probability of contracting it. In some nations, the annual incidence of hepatitis A can be as low as 1 case per 100,000 people (see Study 5). This category includes the majority of the high-income nations in North America, East Asia, Europe, and Oceania (World Health Organization, 2012).

Most cases in nations with very low or low endemicity are linked to either travel to endemic nations or foodborne illness in the place of origin. However, there are still population groupings where the HAV circulates continuously (or nearly continuously). Those are mostly members of racial or ethnic minorities, homeless persons, and groups of people who engage in high-risk sexual behaviors. People who participate in these organizations also interact with the general public, which is predisposed to HAV infection, leading to spillover events in the neighborhood, largely through contacts with households, nurseries, and schools, as well as through contaminated food handlers (Friesema IH, 2018).

2.6 Risk Groups

Groups at increased risk of infection and those at increased risk of a clinically severe disease (i.e., hospitalization, persistent illness, liver failure) can be distinguished in hepatitis A (World Health Organization, 2012).

In all endemicity settings, susceptible people who are in contact with an infected person and do not have access to strong public health infrastructures (such as potable water, sanitation, and suitable housing) are at an elevated risk of infection. Travelers to higher endemicity areas, MSM, PWUD, people experiencing homelessness, ethnic minorities, laboratory staff handling HAV, parents of recently adopted children, staff at children's nurseries, workers in contact with sewage waters, and frequent blood product recipients are among the groups at increased risk of infection in very low and low endemicity settings (Lemon SM, 2017).

Older adults and patients with underlying chronic liver disease are two groups who are more likely to experience a bad result. The inclusion of HIV patients in this group is controversial because their increased risk of a serious outcome seems to be linked to coexisting liver diseases (such as coinfection with HBV and HCV, liver damage from antiviral therapy, or alcohol abuse), and it goes away in patients who adhere to antiretroviral therapy (Migueres M, 2021).

2.7 Active and Passive Immunization

Active and passive immunization can both help prevent hepatitis A. Vaccination provides the first, whereas human immune serum globulin (Ig) provides the second. Hepatitis A vaccines are available in two forms: formaldehyde-inactivated, which is the type most commonly used worldwide, or live attenuated, which is mostly utilized in China and to a lesser extent in other Asian nations and Guatemala. All immunizations have a legal age limit of one year or older (Sun X, 2018).

When taken within two weeks of exposure, Ig, which contain human anti-HAV antibodies, have demonstrated 80 to 90% efficiency in preventing liver damage. Within hours after being administered intramuscularly, Ig become protective. After 2 to 5 months, their effects wear off and the person loses immunity. Despite being safe, Ig should not be given to people who have IgA deficiencies or are receiving live attenuated vaccines, such as the hepatitis A live attenuated vaccine. Ig have been used to prevent infection for a very long time, but during the past three decades, their use has drastically decreased for a variety of reasons. Cost, the emergence of less expensive vaccinations that can provide protection instantly and for decades, their limited supply, and the declining availability of human plasma pools with sufficient anti-HAV IgG are a few of these. They should be used as soon as feasible after exposure and for no more than 14 days in post-exposure prophylaxis (PeP) (World Health Organization, 2019).

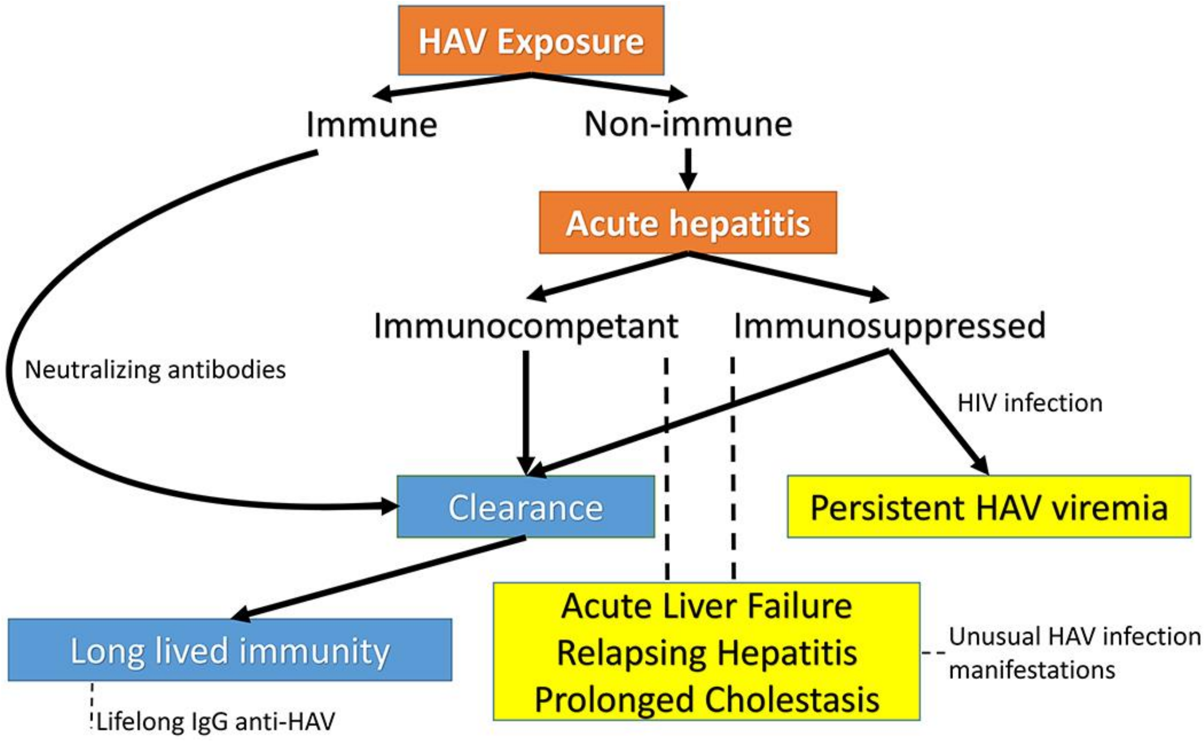

Figure 2.5: Immunization response

2.8 Immunization Strategies

The WHO developed immunization strategy guidelines based on country endemicity levels because they offer a reliable quick assessment tool to guide preventative programs. WHO does not advocate widespread hepatitis A immunization in nations with high endemicity. WHO advises universal hepatitis A vaccination for toddlers in countries with intermediate endemicity; such a policy should be considered after economic analyses and implemented along with improvements in hygiene and sanitation, as well as building up capacities for surveillance, outbreak response, and monitoring of vaccination impact (World Health

Organization, 2012). WHO advises targeted vaccination of people in low- and very-endemicity countries who are at higher risk of infection or a severe outcome, such as travelers to endemic regions, MSM, PWUD, workers who come into contact with human primates, patients who need ongoing transfusion therapy, or people with chronic liver disease (World Health Organization, 2012). The WHO recommends vaccination for additional groups, such as food handlers, daycare center employees, garbage and sewage workers, people who are homeless, the parents of adoptees who were born in HAV-endemic countries, and children of refugees and migrants from HAV-endemic countries, in the 2019 Immunological Basis for Immunization Series on Hepatitis A. While this thesis is being printed, an updated WHO position document on hepatitis A vaccines is anticipated to be released (World Health Organization, 2019).

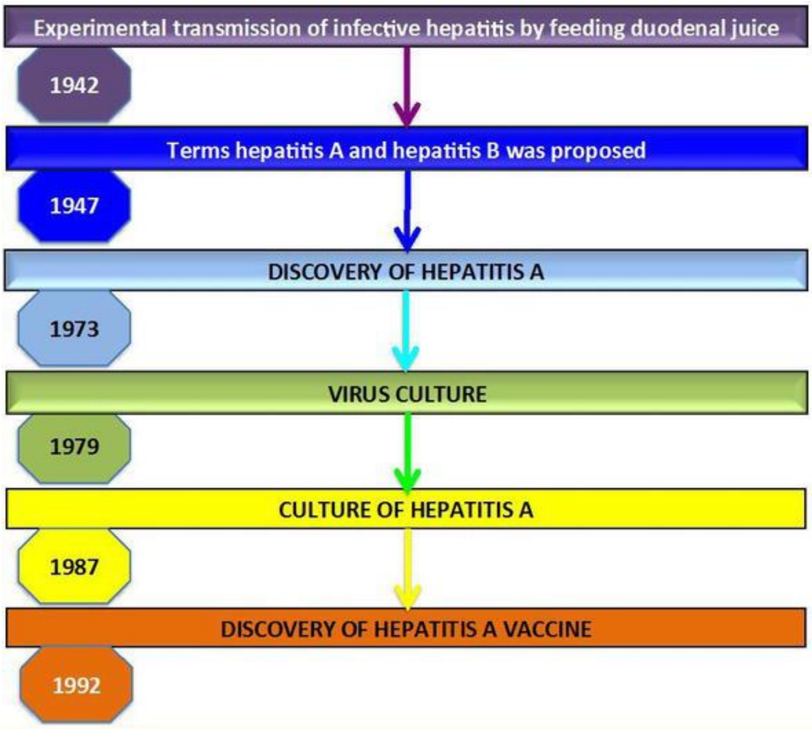

Figure 2.6: The timeline of Hepatitis A virus HAV

2.9 Situation in Palestine

Since 1995, the reported incidence of acute hepatitis A virus infection HAV infection has increased in Palestine. There have been concerns about whether the epidemiology of HAV has changed because overt clinical illness affects adults more frequently. A decline in the overall incidence rate and a shift in the mean age of infection towards adolescent and early adulthood are the typical characteristics of this. A significant section of the teenage and adult population may now be at risk of infection because of changes in HAV infection epidemiology brought on by improvements in the socioeconomic situation in the West Bank (Yassin et al., 2001).

A study done in the Gaza Strip in 2001 found that the prevalence of anti-HAV was 93.7 percent (95% CI: 91.3, 96.1%). Stratifying the prevalence by age revealed that 87.8% (95%CI: 78.6, 97%) of children aged 6 and under had HAV antibody positivity. Nearly 98% (95% CI: 92-7, 100%) of people were HAV antibody positive by the age of 14 (Yassin et al., 2001).

According to (Ramlawi et al., 2000), "The epidemiological survey of viral Hepatitis A showed that viral hepatitis A is endemic in Palestine, with the prevalence of viral hepatitis A among school students aged 6 to 15 years being about 86.1%, ranging from 68.3% for Bethlehem district to 98.6% for north Gaza district." The states that it typically manifests in early childhood, usually with minor symptoms.

The necessity for a vaccination campaign is currently being debated because of this shifting epidemiology, which has been documented in numerous parts of the world (Battegay et al., 1995). The bulk of HAV infections, according to the aforementioned study, continue to occur in young children, when they are typically asymptomatic and have minimal clinical impact. However, there is discussion concerning an epidemiology changing and the necessity for a vaccine campaign against HAV infection. Palestine is categorized by the WHO as a region with intermediate HAV endemicity. As many nations have seen considerable advancements in socioeconomic status (SES), sanitation, and access to clean water. The typical age of first exposure to and infection with HAV, as well as the prevalence of acute hepatitis A, are anticipated to change because of these advancements (Battegay et al., 1995).

Another study conducted by Sufyan Daghra, Awad Mataria and Khalid Abu- Khalid in 2008, entitled: Management of HAV in Countries under Conflict: Palestinian has concluded that the economic burden of HAV vaccination program is less that the economic burden required to deal with HAV cases. To compare savings to prospective costs, the article uses a Cost-Consequences analysis based on the Human Capital model, which takes productivity loss and lost school days into account. Analysis of Case as a Cost and Consequences Recent discussions about hepatitis A infections in Palestine raise the possibility that the epidemiology of the disease is changing in Palestine.

2.10 HAV Vaccination Policies in Israel

Between 1993 and 1998, Israel experienced a mean annual incidence of 50.4 cases of hepatitis A per 100 000 people (Dagan, 2005). The Israeli Ministry of Health launched a universal program of hepatitis A vaccine for infants 18 months and younger in July 1999. Wherein children receive two doses of the vaccine at 1.5 and 2 years old—two (Manfred, 2001). For several population groups, such as infants, travelers, and high-risk persons, the Israeli Ministry of Health advised routine vaccination against Hepatitis A. In Israel, the typical childhood vaccination schedule includes the hepatitis A vaccine. At 12 months of age, infants receive their first dose of the hepatitis A vaccine. At 18 months, they receive a booster shot. Travelers to nations with a higher risk of hepatitis A transmission, particularly developing nations, are advised to get vaccinated against the disease, according to the

Ministry of Health. The Hepatitis A vaccine may be advised for persons who have chronic liver illness or engage in high-risk activities such injectable drug use or MSM (Manfred, 2001).

In Israel, first dose vaccination coverage in 2001–2002 was 90%, and second dose vaccination coverage was 85%. Before 1999, the Jewish community's sickness rates decreased, but not those of the non-Jewish population. In all populations, there was a significant drop in disease rates following the start of the program. The 2.2 to 2.5 per 100 000 annual incidences between 2002 and 2004 represents a 95% or more reduction for each year compared to the mean incidence between 1993 and 1998 (P<001). In comparison to the pre-vaccination period, there was a 98.2% decrease in disease in children aged 1 to 4 years between 2002 and 2004 (P<001) (Dagan, 2005).

All other age groups (84.3% [<1 year], 96.5% [5-9 years], 95.2% [10-14 years], 91.3% [15-44 years], 90.6% [45-64 years], and 77.3% [≥65 years]) however, also saw a steep reduction. A more than 90% decrease in sickness was seen among the Jewish population of the Jerusalem district, where the active monitoring program was successfully carried out. 424 (97.9%) of the 433 cases reported countrywide between 2002 and 2004 in which the vaccination status could be determined were unvaccinated, and none had received two doses (Dagan, 2005). According to Dangan 2005, the universal toddler-only immunization program in Israel showed both strong herd immunity and excellent vaccination efficacy. Israel witnessed two outbreaks between 2007 and 2018. The first happened among an unvaccinated homeless population in the Tel Aviv district in 2012 and 2013. Beginning at the tail end of 2016, the second was likewise confined primarily to the Tel Aviv neighborhood. The most recent outbreak, in contrast to the earlier one, affected unvaccinated MSM, and like the MSM outbreaks in Europe, HAV was predominantly spread through sexual contact (Gozlan, 2021).

Chapter Three

Methodology

3.1 Introduction

This chapter describes the methodology used. Study design, study setting, study population, sampling frame, sample criteria, sampling process, and data collection procedures are all described. The study also addressed the various statistical methods and tests used in data processing.

3.2 Study Design

This research is a cross sectional study that use explanatory method, that aims to explain the relationship between the different variables in the data to test the research hypotheses. The data gathered and analyzed is quantitative in nature; hence, the relationship between variables is explained in numerical and statistical terms.

3.3 Sources of Data

Hepatitis A is a notifiable disease in Palestine. Since 2015, Hepatitis A has been reported separately from other types. Our data on the incidence of Hepatitis A between 2015 and 2022 were extracted from routine reports of the Ministry of Health, which contains documented patient's information; the information includes event date, registration date, occupation (career), patient address, patient age, patient district, patient locality, patient sex, patient symptoms, source of Water, patient hospitalization and patient Outcome. Data by population group was available for the period from 2015 to 2022. The rates for the population were computed using the annual average population as the denominator. Age and population group-specific rates were estimated using the corresponding specific annual average population sizes. The data was obtained through official channels; the researcher requested the data from MOH with a supporting document from Al-Quds University. The approval was granted, and the data were received accordingly.

3.4 Study Population and Sample

The target population of this study has represented all patients with viral hepatitis A in Palestine during 2015-2022, which included 1781 patients (Preventive Medicine Department-Ministry of Health MoH).

3.5 Study Variables

According to the study goals, some independent and other dependent variable are defined as follows:

- **Incidence rate** is a dependent variable represents the probability or risk of having a health problem in a population over a period of time. It is also the most common way of measuring and comparing the frequency of health problems in a population. The formula for calculating the incidence rate is measured by:

$$\frac{\textit{new cases occurring during a given time period}}{\textit{population at risk during the same time period}} \times 10^{n}$$

The researcher depends on the annual report of the Palestinian Central Bureau of Statistics (PCBS) to determine the population at risk. Table 3.1 represents the population at risk during 2015–2022.

Table 3.1: Population at Risk during 2015–2022

	Gender		Age categories							# of
Years	Male	Female	0-4	5-9	10-14	≥14	North	Middle	South	Population
2015	1,473,041	1,473,041	398,292	347,820	327,271	1,872,699	1133400	828718	936809	2,946,082
2016	1,510,377	1,461,692	403,891	355,781	331,455	1,880,942	1,160,641	848,543	962,885	2,972,069
2017	1,443,624	1,386,914	395,994	366,383	339,709	1,728,452	1,121,239	787,235	922,064	2,830,538
2018	1,505,853	1,448,090	387,243	359,471	332,814	1,874,415	1,163,416	834,366	956,161	2,953,943
2019	1,539,038	1,480,910	392,929	364,170	337,389	1,925,460	1,187,011	852,654	980,283	3,019,948
2020	1,572,632	1,514,184	398,831	368,766	341,989	1,977,230	1,210,993	871,096	1,004,727	3,086,816
2021	1,606,571	1,547,847	404,971	373,124	346,642	2,029,681	1,235,294	889,653	1,029,471	3,154,418
2022	1,640,796	1,581,850	410,652	377,859	351,345	2,082,790	1,259,824	908,297	1,054,525	3,222,646

- **Gender** as independent variable contains two categories (male and female).
- **Age categories** as independent contains four categories (0-4 years, 5-9 years, 10-14 years, and more than 14 years).

3.6 Data Analysis

Data analysis were performed by using version 23 of the Statistical Package for Social Sciences (SPSS). In this study, to examine the hypotheses and questions, the researcher must use nonparametric statistical tools as follows:

- Significance level used is 0.05 (5%), when the p-value is greater than the significance level, the results are not considered statistically significant, and the null hypothesis is failed to be rejected.
- Frequencies and percentages to describe the sample's characteristics and the trend of the incidence rate of viral hepatitis A
- Mann-Whitney U test to examine the differences between the mean of the incidence rate with non-normal distributions or non-equal variance in two groups (e.g., gender).
- The Kruskal-Wallis test is the non-parametric alternative one-way analysis of variance (ANOVA), which is appropriate when there is a need to compare the mean incidence rate of more than two groups to determine if there is a significant difference between the tested groups or not (e.g., age categories).
- Fisher's exact test to examine the relationship between two quotative variables if the assumption of the chi-square test cannot be met. This test is commonly used in medical research where researchers need to analyse small categorical datasets for potential associations.

Chapter Four

Result and Discussion

4.1 Introduction

This chapter includes the presentation of data analysis and testing the research hypotheses by answering the research questions and reviewing the main results of the study reached through analyzing the various paragraphs. SPSS program was used to obtain the results of the research that will be presented and analyzed in this chapter. The researcher presents the study results to answer the questions that appeared, and which represent the problem of the study after collecting the data required. Several of the results were reached, and advice for future research is offered to researchers in the same field, both at universities and in any other organization.

4.2 Sample Characteristics

Through the study, the researcher observed certain demographic characteristics of patients that included four variables, as shown in Table 4.1, which contains the frequency and percentage for each variable listed according to the survey categories. According to the results in Table 4.1, of the 1781 patients in this study, 934 (52.6%) were males and 842 (47.4%) were females. In terms of age categories, the majority of patients (n = 718; 40.4%) were between 5 and 9 years old, 411 (23.1%) were between 10 and 14 years old, 373 (21%) were more than 14 years old, and 277 (15.6%) were less than four years old. However, more than half of the patients (n = 1,206; 67.7%) were students, and 211 (11.8%) were workers. In addition, 66.1% of the patient were living in urban, while 23.2% and 10.7% were living in a rural and camp respectively.

Table 4.1: Socio-Demographic Characteristics of Patients (N=*1781*)

Variable	Options	Frequency	Valid Present %	Missing
Gender	Female	842	47.4	5
	Male	934	52.6	
Age categories	0 – 4 years	277	15.6	2
	5 – 9 years	718	40.4	
	10 – 14 years	411	23.1	
	More than 14 years	377	21.0	
Professions	Student	1206	67.7	238
	Employee	4	0.2	
	Not work	12	0.8	
	Worker	211	11.8	
	Other	52	2.9	
	Wife house	58	3.3	
Place of residence	Urban	66.1	1172	10
	Rural	23.2	412	
	Camp	10.7	190	

4.3 HAV Incidence Rate for the West Bank during (2015–2022)

This section displays the descriptive statistics of the viral hepatitis A epidemiology incidence rate for the West Bank during the study period (2015–2022). According to the result in Figure 4.1, the incidence rate of viral hepatitis A clearly decreased during the study period (2015–2022). The incidence rate decreased by 60% from 2015 to 2017, followed by a slight increase of 1.3% in 2018. Since 2018, there has been a slow decrease from 7.01 to 1.77 per 100,000 at the end of the study.

Overall Trend: the data reveals that the West Bank incidence rate of viral hepatitis A decreased significantly from 2015 to 2022. The rate dropped by 60% in the first two years, then declined more slowly after that. After a minor rise in 2018, the incidence rate consistently fell until it reached its lowest position at the end of the period. Better sanitation and hygiene practices can reduce the spread of HAV, which is primarily transmitted through contaminated food and water. Improvements in water quality, sanitation infrastructure, and public health education might have played a role in the overall HAV incident rate. Taking into consideration that many HAV cases goes without detection.

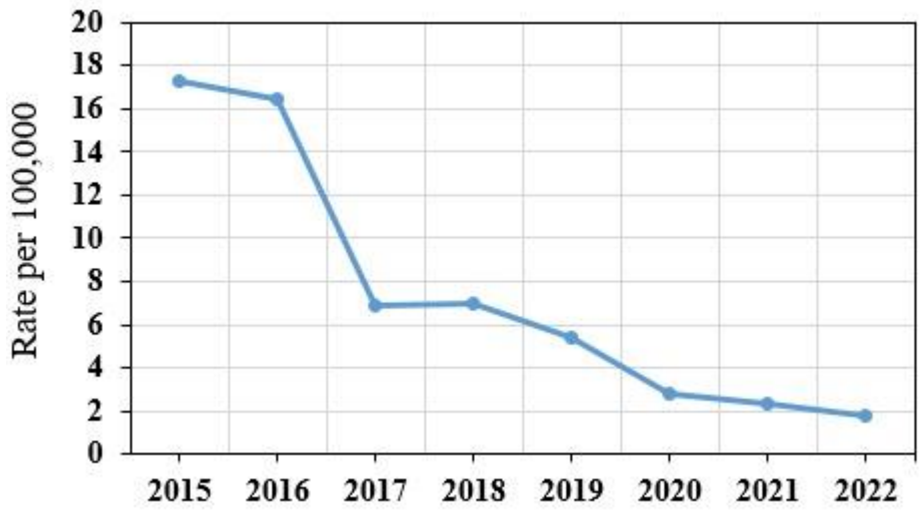

Figure 4.1: HAV Incidence of Viral Hepatitis A per 100,000/2015-2022

It is important to keep in mind though, that the COVID-19 pandemic has put a huge pressure on the world's healthcare systems due to the high number of COVID-19 cases. This greater demand on healthcare resources might have had an indirect effect on Hepatitis A reporting and surveillance systems. Health authorities might have had to put COVID-19 testing, treatment, and reporting at a higher priority in some areas, which might have had an impact on the reporting and monitoring of other infectious diseases like hepatitis A.

Additionally, COVID-19 pandemic preventive strategies like lockdowns and social isolation may have prevented the spread of Hepatitis A and other infectious diseases. For instance, practices such as consistent handwashing and improved sanitation may have reduced the spread of COVID-19 and Hepatitis A. As a result, the pandemic may have had an impact on the incidence of Hepatitis A cases.

4.3.1 Viral Hepatitis A Incidence Rate during (2015–2022) in Regards to Gender

The trend of the incidence rate declined through the study period in both the male and female populations. The incidence rate in both populations in the first two years most significant. For the male population, the trend declined and the incidence rate ranged between 1.65 and 18.13 per 100,000, while the trend generally declined and the incidence rate ranged between 1.71 and 16.5 per 100,000. Figure 4.2 display a comparison of the incidence rates between the male and female population groups. Until 2018, the incidence rates were consistently higher in the male population, and vice versa between 2018 and 2020 (the incidence rates were higher in the female population). Also, the gap began to narrow with time, the highest gap between the male and female population existed in 2016.

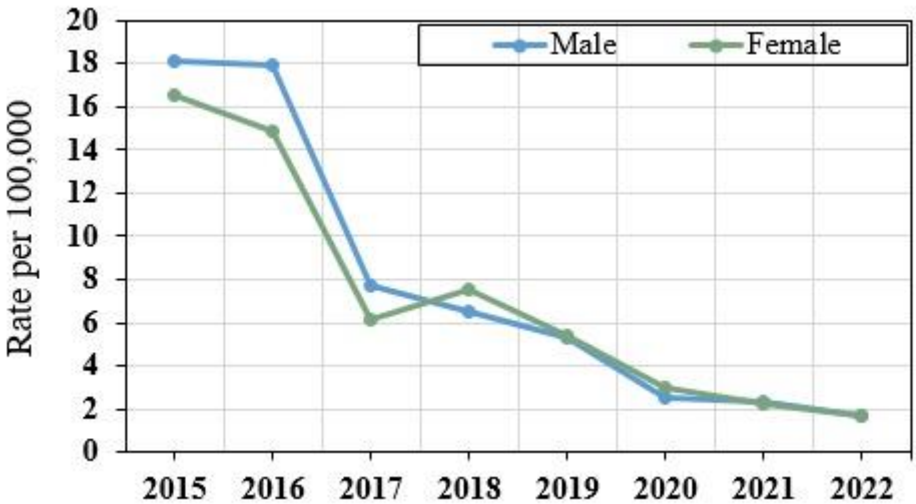

Figure 4.2: Incidence of viral hepatitis per 100,000 in regards to gender during 2015-2022

According to the results in Figure 4.2, there is no significant difference in the incidence rate mean between male and female groups since the p-value more than the significant level of

0.05. Furthermore, the mean incidence rate of the male group (7.77 per 100,000) was higher than the female group (7.72 per 100,000) in the study period (2015–2022).

Table 4.2: Result of Main Difference in HAV Incidence Rate Regarding Gender (2015-2022)

Option	**Mean ± SD (per 100,000)**	**Mean rank**	**Test statistic (z)**	**P-value**
Male	7.77 ± 6.68	8.75	30.00‡	0.834
Female	7.72 ± 5.64	8.25		

‡: Result obtained by Mann–Whitney U-test at p-value ≤0.05

In conclusion, the data demonstrates that both the male and female populations had a decrease in the condition's incidence rate during the study period. The relative incidence rates between the sexes fluctuated and changed, but there was no statistically discernible difference in the mean incidence rate between the male and female groups. Over time, the difference in incidence rates between the two groups also started to close, indicating a convergence in the effects of the illness on different genders.

4.3.2 HAV Incidence Rate During (2015–2022) Regarding Age

This section displays the descriptive statistics of the viral hepatitis A epidemiology incidence rate due to patient age during the study period (2015–2022). In Figure 4.3, the incidence rate for four different categories of age is displayed. The result indicates that the highest incidence rates were in children aged between 5 and 9 years with study time, where the incidence rate of this category ranged between 7.41 and 57.79 per 100,000, followed by 5–10 years, 0–4 years, and more than 14 years, respectively. The first two years (2015–2016) had the highest rates in each category compared to the others. Also, the gap began to narrow with time**,** the difference in incidence rates between the various age groups started to get smaller. This shows that as the study period went on, the incidence rates across different age groups converged.

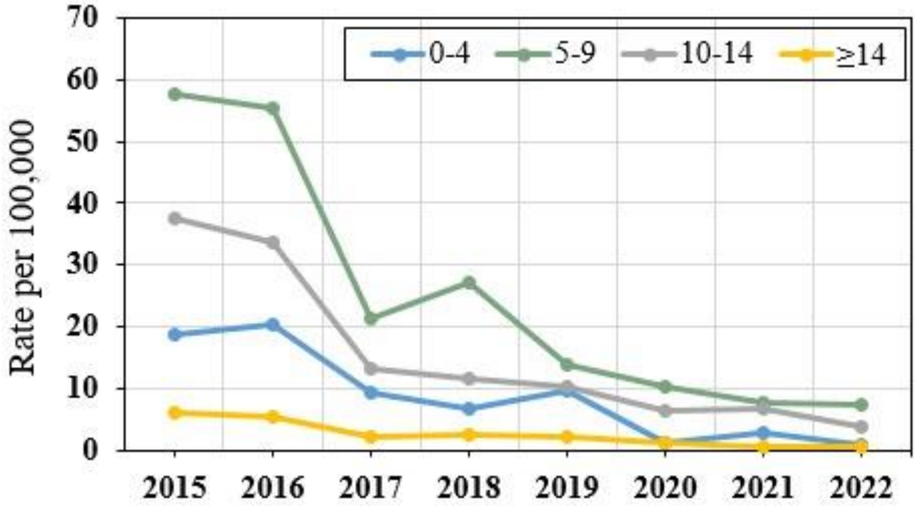

Figure 4.3: Incidence of HAV per 100,000 Regarding Age During 2015-2022

Furthermore, Kruskal–Wallis test revealed a statistically significant differences in the incidence rate mean due to patient age category, since the p-value is less than the significant level of 0.05. Also, the result confirmed that the highest mean of the incidence rate was in 5-9 category (25.08 per 100,000), followed by 10-14 years (15.40 per 100,000), less than 5 years (8.69 per 100,000) and more than 14 years (2.48 per 100,000) respectively.

Table 4.3: Result of Main Difference in HAV Incidence Rate in Regards to Age (2015-2022)

Option	**Mean ± SD (per 100,000)**	**Mean rank**	**Test statistic (χ^2)**	**P-value**
0 – 4 years	8.69 ± 7.45	15.00	30.00†	0.001
5 – 9 years	25.08 ± 20.58	24.38		
10 – 14 years	15.40 ± 12.85	20.25		
More than 14 years	2.48 ± 2.06	6.38		

†: Result obtained by Kruskal–Wallis test at p-value ≤0.05

The high mean incidence rate in the 5 – 9 years age group suggests that individuals within this age range are particularly vulnerable to contracting HAV. This age group might be more susceptible due to factors such as behavioral patterns, and exposure to contaminated environment. This might include the use of public toilets in schools, drinking un clean water and poor hygiene practices.

The high incidence rate in the 5 – 9 years age group indicates a public health concern, as it signifies a higher number of HAV cases in this specific age group. It can put a strain on the healthcare system, particularly in terms of diagnosing and treating the affected individuals. This age group's high incidence rate may lead to increased hospital admissions and outpatient visits related to HAV.

4.3.3 HAV Incidence Rate During (2015–2022) in Regards to Place of Residence

This section displays the descriptive statistics of the viral hepatitis A epidemiology incidence rate due to place of residence during the study period (2015–2022). In Figure 4.4, the incidence rate for three different areas was displayed. The result indicates that the highest incidence rates were in south area with study time except 2017, where the incidence rate of south area ranged between 3.69 and 26.69 per 100,000, followed by north and middle areas in the first tow year (2015 and 2016), in 2017 the highest incidence exist in south area, followed by north and middle respectively. From 2017 the gap of the incidence rate between middle and north began to narrow.

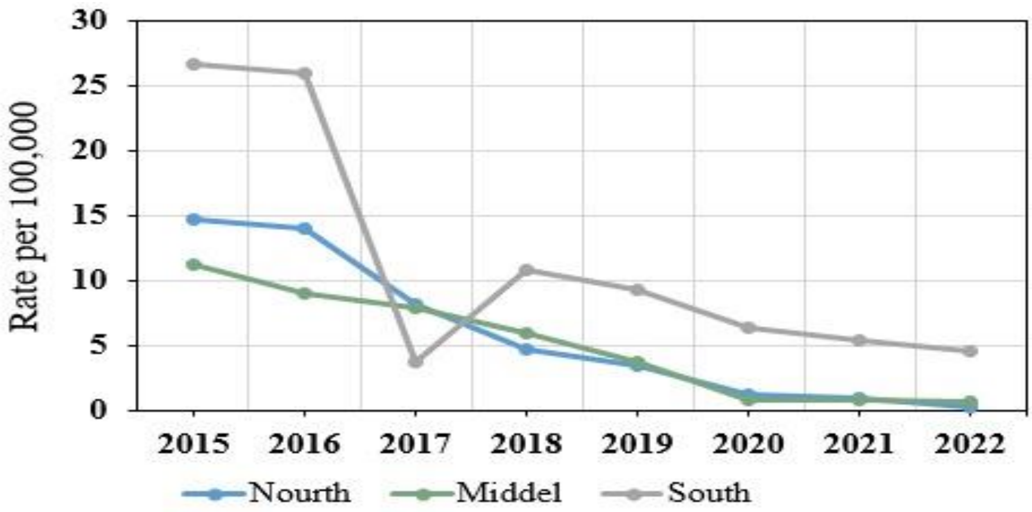

Figure 4.4: Incidence of HAV per 100,000 in Regards to Place of residence during 2015-2022

Furthermore, Kruskal–Wallis test revealed no statistically significant differences in the incidence rate mean due to place of residence, since the p-value is more than the significant level of 0.05. Also, the result confirmed that the highest mean of the incidence rate was in south (211.59 per 100,000), followed by north area (5.90 per 100,000) and middel area (4.99 per 100,000) respectively.

In conclusion, the study reveals significant variations in the mean HAV incidence rates among the three Palestinian regions. The Kruskal-Wallis test indicates that these differences are not statistically significant. Therefore, it cannot be said that the location of residence significantly affects the incidence of HAV in Palestine based on the data at hand.

Table 4.4: Difference in HAV Incidence Rate in Regards to place of Residence (2015-2022)

Option	**Mean ± SD (per 100,000)**	**Mean rank**	**Test statistic (χ^2)**	**P-value**
North	5.90± 5.82	11.13	3.215†	0.200
Middle	4.99± 4.14	10.25		
South	11.59± 9.39	16.13		

†: Result obtained by Kruskal–Wallis test at p-value ≤0.05

The examination of the incidence rate of the Hepatitis A Virus (HAV) in various regions may change, though, if we consider that the South of Palestine has substantially less water quantities. The amount of water can play a significant role in the spread of HAV. The fecal-oral route is the main way that hepatitis A is spread, and it is frequently through tainted food or drink. Due to the significantly decreased water availability in the South of Palestine, there may be a greater probability of using contaminated water sources or inadequate water sanitation, which may raise the risk of HAV transmission. The South's decreased water availability in certain locations could be viewed as a confounding variable.

Given this information, it may be necessary to revisit the analysis using a more thorough methodology, taking into account the potential influence of water availability on the incidence rate of HAV in various places.

Further research and data gathering on additional possible risk factors for HAV transmission, such as sanitation methods, hygiene, and food handling, may also contribute to a more accurate and thorough understanding of the situation in different Palestinian regions. This extra information would assist policymakers develop targeted initiatives to lessen the disease burden and enable a better understanding of the variables influencing the variations in HAV incidence rates between the regions.

4.3.4 Environmental Conditions of the Patients

This section displays the descriptive statistics of the environmental area of the patients including sources of water, hygiene environment and household hygiene. According to the result in table 4.3, 12.2% of patient used a rain water, 18.6% of them used a pipe, 0.8% used another source, 3.5% of the patient used both rain and pipes. The majority of patients (58.7%) were living in a good environmental hygiene, and 61.3% were living in a good household hygiene.

Table 4.5: Environmental Conditions of the Patients

Variables	Options	Frequency	Valid Present %
Sours of water	Pipes	331	18.6
	Rain	217	12.2
	Rain and pipes	63	3.5
	Other	14	0.8
	Unknown	1156	64.9
Environment hygiene	Good	1046	58.7
	Fair	534	30.0
	Bad	97	5.4
	Unknown	104	5.8
Household hygiene	Good	1092	61.3
	Fair	461	25.9
	Bad	48	2.7
	Unknown	180	10.1

A sizable part of patients utilized either rainwater or a pipe as their primary supply of water, whereas a lesser proportion used another source or a combination of pipes and rainwater. Understanding the potential causes of diseases or infections that may be transmitted by water can benefit from this information.

Most patients were said to be living in clean environments in terms of hygienic conditions. This implies that a sizeable fraction of the study population had access to sanitary living circumstances, which can be crucial in halting the spread of infectious diseases.

Like this, the vast majority of patients were said to maintain good housekeeping. This shows that a sizable portion of homes in the study group kept their living spaces clean and hygienic, which can improve overall health and slow the spread of infectious diseases.

To fully comprehend the implications of these findings and their possible influence on the prevalence of the illness under study, additional context and analysis would be required. A more thorough understanding of the environmental elements influencing the patients' health outcomes would also result from looking into additional pertinent aspects such sanitation practices, access to healthcare, and public health actions.

4.3.5 Confirmation of HAV Through Lab Testing for the Patients

According to the result in Figure 4.5, the majority of patients had a lab test at the time of study; all patients with the time had a lab test, while 93.7% of patients in 2015 had a lab test.

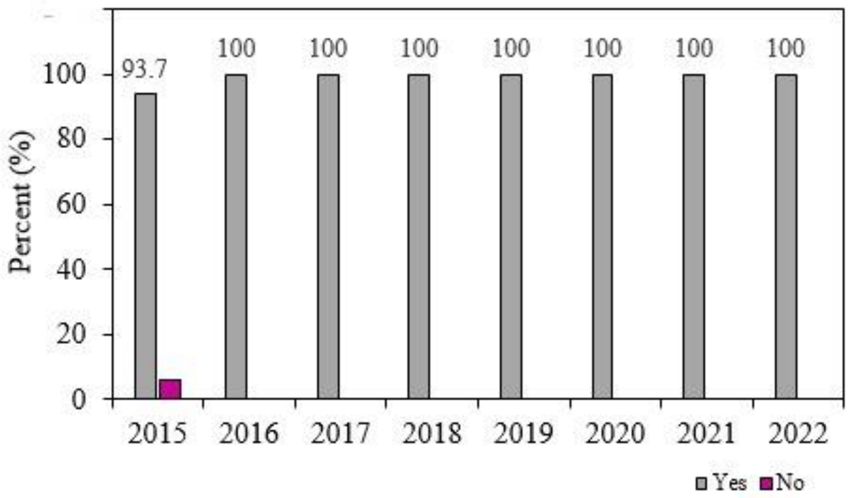

Figure 4.5: Confirmation of HAV through Lab Testing for the patients

4.4 Result of the Research Hypothesis

This section displays the result of the research hypotheses. To answer this hypothesis chi-square test and fisher's exact test were used.

4.4.1 Result of the First Hypothesis

This section displays the result of the first hypothesis, which states: “There **exists no statistically significant reduction in patient hospitalization rates with respect to varying age groups** ". The result of the chi-square test in Table 4.4 indicates there is a significant relation between patient hospitalization and their age, since the p-value (0.000) is less than the significant level of 0.05, which supports the first hypothesis. In addition, the result indicates that 20.4% of the patients whose ages are older than 14 years stay in the hospital, 12.2% of the patients whose ages are between 10 and 14 years stay in the hospital, and 9.7% and 7.9% of the patients whose ages are between 5 and 9 years and less than 4 years stay in the hospital, respectively.

Table 4.6: Result of the First Hypothesis

	Hospitalized stay		
Age categories	Non-stayed	Stayed	All patient
0 – 4 years	255 (92.1%)	22 (7.9%)	277 (100%)
5 – 9 years	644 (90.3%)	69 (9.7%)	713 (100%)
10 – 14 years	361 (87.8%)	50 (12.2%)	50 (100%)
More than 14 years	297 (79.6%)	76 (20.4%)	76 (100%)
Chi-square test= 32.123; p-value=0.000*			

*: Result significant at 5%.

In conclusion, the chi-square test and analysis of the descriptive statistics support the rejection of the null hypothesis and demonstrate a substantial association between patient age and hospitalization. Patients over the age of 14 had the highest percentage of hospital stays, with hospitalization rates rising with age. In other words, age affects the patient's stay in the hospital positively.

4.4.2 Result of the Second Hypothesis

This section displays the result of the second hypothesis, which states: "**There exists no statistically significant relationship between patient age and the occurrence of HAV symptoms (Fever, chills, vomiting, Jaundice, dark urine)**". The result of the Fisher's Exact Test in Table 4.7 indicates there is a significant relation between patient age and the presence of fever, chills, and vomiting symptoms, since the p-values (0.007, 0.010, and 0.034, respectively) of each of them are less than the significant level of 0.05. While the result indicates there is no significant relation between patient age and the presence of jaundice and dark urine symptoms.

In addition, the result indicates that 19.3% of the patients whose ages are older than 14 years, 15.9% of the patients whose ages are between 10 and 14 years, and 11.7% and 13.9% of the patients whose ages are between 5 and 9 years and less than 4 years have a fever. In terms of the chill's symptom, 13.6% of the patients whose ages are older than 14 years, 10.4% of the patients whose ages are between 10 and 14 years, and 7.1% and 9.1% of the patients whose ages are between 5 and 9 years and less than 4 years have a chill. However, 15.6% of the patients whose ages are older than 14 years, 19.4% of the patients whose ages are between 10 and 14 years.

Table 4.7: Result of the Second Hypothesis

Symptoms	**Age categories**				**P-value**
Fever	0 – 4 years	5 – 9 years	10 – 14 years	More than 14 years	
Not-exist	235 (86.1%)	614 (88.3%)	338 (84.1%)	296 (80.7%)	0.007*
Exist	38 (13.9%)	81 (11.7%)	64 (15.9%)	71 (19.3%)	
	273 (100%)	695 (100%)	402 (100%)	367 (100%)	
Chills					
Not-exist	241 (90.9%)	629 (29.9%)	352 (89.6%)	306 (86.4%)	0.010*
Exist	24 (9.1%)	48 (7.1%)	41 (10.4%)	48 (13.6%)	
	265 (100%)	677 (100%)	393 (100%)	354 (100%)	
Vomiting					
Not-exist	235 (88%)	602 (86.2%)	328 (80.6%)	303 (84.4%)	0.034*
Exist	32 (12%)	96 (13.8%)	79 (19.4%)	56 (15.6%)	
	267 (100%)	698 (100%)	407 (100%)	359 (100%)	
Jaundice					
Not-exist	220 (79.4%)	576 (80.9%)	321 (78.3%)	293 (79.4%)	0.755
Exist	57 (20.6%)	136 (19.1%)	89 (21.7%)	76 (20.6%)	
	277 (100%)	712 (100%)	410 (100%)	369 (100%)	
Dark urine					
Not-exist	226 (83.1%)	591 (84.4%)	326 (80.7%)	297 (81.8%)	0.416
Exist	46 (16.9%)	109 (15.6%)	78 (19.3%)	66 (18.2%)	
	272 (100%)	700 (100%)	404 (100%)	363 (100%)	

*: Result significant at 5%.

According to the findings of the Fisher's Exact Test, there is a substantial association between patient age and the occurrence of symptoms including fever, chills, and vomiting. This indicates that there are considerable differences in the likelihood of exhibiting these symptoms depending on the age group. Even though the statistics in this study indicated that the existence of jaundice and dark urine symptoms do not significantly associate with patient age; those finding cannot be accepted since the possibility of symptomatic illness from HAV infection is directly related to age, in older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients (CDC, 2021). The explanation of these findings might be that age group less than 5 years old involved in this study have shown symptomatic illness, and therefore the statistic differentiations were not obvious with regard to jaundice and dark urine.

In conclusion, Fisher's Exact Test and the analysis of the descriptive statistics show that the occurrence of fever, chills, and vomiting symptoms is substantially correlated with patient age, rejecting the null hypothesis for these symptoms.

4.4.3 Result of the Third Hypothesis

This section displays the result of the third hypothesis, which states: " **There exists no statistically significant relationship between liver enzyme values and the occurrence of HAV symptoms (fever, chills, vomiting, jaundice, dark urine)**". The result of the Fisher's Exact Test in Table 4.6 indicates there is a significant relation between the liver enzyme degree of the patient and the presence of vomiting and dark urine symptoms, since the p-values (0.003 and 0.044, respectively) of each of them are less than the significant level of 0.05, while the result indicates there is no significant relation between liver enzyme degree and the presence of fever, chills, and jaundice symptoms.

In addition, the result indicates that 20% of the patients with a degree of a liver enzyme greater than 3000 had a fever symptom, while 23.1% of them have dark urine, 19.2% of the patients with a degree of a liver enzyme between 1000-1999 had a fever symptom, and 20.6% of them have dark urine.

Table 4.8: Result of the Third Hypothesis

Symptoms	liver enzyme degree					P-value
Fever	<500	500 – 999	1000– 1999	2000– 2999	≤3000	
Not-exist	743 (87%)	300 (81.7%)	286 (86.1%)	114 (85.1%)	40 (80%)	0.129
Exist	111 (13%)	67 (18.3%)	46 (13.9%)	20 (14.9%)	10 (20%)	
	854 (100%)	367 (100%)	332 (100%)	134 (100%)	50 (100%)	
Chills						
Not-exist	762 (91.7%)	320 (89.6%)	291 (89.8%)	115 (89.1%)	40 (83.3%)	0.255
Exist	69 (8.3%)	37 (10.4%)	37 (10.2%)	14 (10.9%)	8 (16.7%)	
	831 (100%)	357 (100%)	324 (100%)	129 (100%)	48 (100%)	
Vomiting						
Not-exist	747 (88.2%)	300 (82.6%)	273 (80.8%)	108 (81.2%)	40 (80%)	0.003*
Exist	100 (11.8%)	36 (17.4%)	65 (19.2%)	25 (18.8%)	10 (20%)	
	847 (100%)	698 (100%)	338 (100%)	133 (100%)	50 (100%)	
Jaundice						
Not-exist	714 (82.4%)	286 (76.9%)	263 (76%)	107 (80.5%)	40 (78.4%)	0.062
Exist	152 (17.6%)	86 (23.1%)	83 (24%)	26 (19.5%)	11 (21.6%)	
	866 (100%)	372 (100%)	346 (100%)	133 (100%)	51 (100%)	
Dark urine						
Not-exist	730 (85.5%)	291 (80.6%)	270 (79.4%)	109 (82.6%)	40 (76.9%)	0.044*
Exist	124 (14.5%)	70 (19.4%)	70 (20.6%)	23 (17.4%)	12 (23.1%)	
	854 (100%)	361 (100%)	340 (100%)	132 (100%)	52 (100%)	

*: Result significant at 5%.

According to the results of the Fisher's Exact Test, there may be a connection between the level of liver enzymes and the occurrence of symptoms like vomiting and dark urine. This translates to a large variation in these symptoms' propensity to occur depending on the level of liver enzymes. The existence of fever, chills, and jaundice symptoms, however, do not significantly correlate with the level of liver enzymes, showing that the level of liver enzymes is not a significant factor determining the incidence of these symptoms.

The results of the Fisher's Exact Test and the analysis of the descriptive statistics support the rejection of the null hypothesis for the symptoms of vomiting and dark urine, showing that the level of liver enzymes is substantially correlated with their presence. Fever, chills, and jaundice symptoms, however, cannot be excluded from the null hypothesis, indicating that liver enzyme level has no appreciable impact on whether these symptoms occur.

Chapter Five

Conclusion & Recommendations

5.1 Conclusion

This study provides strong evidence that the incidence rate for HAV has been decreasing in the past five years in Palestine, with adolescents and adults most at risk; where students account for the most patients (67.7%). The high mean incidence rate in the 5 – 9 years age group suggests that individuals within this age range are particularly vulnerable to contracting HAV. The study confirmed that there is significant relation between patient's hospitalization and their age and demonstrate a substantial association between patient age and hospitalization. Patients over the age of 14 had the highest percentage of hospital stays, with hospitalization rates rising with age. Furthermore, the study shows that the occurrence of fever, chills, and vomiting symptoms is substantially associated with patient's age; also, the occurrence of fever, chills, vomiting, Jaundice, and dark urine correlated with the degree of liver enzyme (SGPT & SGOT).

The study was not able to stablish a relation between the location of residence and the incidence of HAV in Palestine based on the data at hand; however, it may be necessary to consider the potential influence of water availability on the incidence rate of HAV in various places of Palestine. Furthermore, there was no statistically discernible difference in the mean incidence rate between the male and female groups. Over time, the difference in incidence rates between the two groups also started to close, indicating a convergence in the effects of the illness on different genders.

Most of the patients were said to be living in clean environments in terms of hygienic conditions; additionally, most patients were said to maintain good housekeeping. However, additional context and analysis would be required to understand the environmental elements influencing the patients' health outcomes.

5.2 Recommendations

In regards to policy:

1. Water and food safety should be better controlled by the authorities to reduce morbidity of food- water borne diseases and special attention for schools' vulnerable people as well as remote areas.
2. Strengthening surveillance system for HAV by preventive medicine department in MoH, through other health providers involvement.
3. Periodical surveys are recommended to highlight any trend and age shifting.
4. HAV vaccine is recommended through the Palestinian vaccination program to improve health indicators and decrease disease burden.

In regards to community:

1. School health should increase teachers and students' awareness of oral-faecal diseases, highlighting HAV. Prevention through hygiene and sanitation.
2. WASH programs in schools should be strengthen and be provided political sport in general and in Jordan Vally and Bedouins areas in particular.
3. Promoting community educational campaign for hygiene and food-water safety.

In regards to research:

1. Identification of HAV prevalence in Palestine should be priority to identify the endemicity of the disease.

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