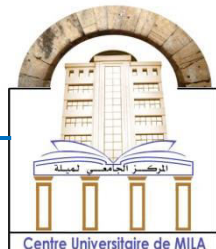


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Special Appreciation

In the name of Allah, the most graceful and most merciful.

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Abstract

In order to determine the epidemiological and clinical profile of hepatitis in the Mila region, we collected the data from this retrospective analytical descriptive study at the level of the infectious diseases service of the Department of Prevention and Epidemiology within Chelghoum Laid, Tadjenanet, Ferdjioua and Mila, and the central laboratory service, serology unit of a public hospital establishment Houari Boumedien, Chelghoum Laid, during a period extending from January 2020 to December 2024 and a prospective study lasting three months (from January to May 2025), 684 cases were reported. The descriptive analytical study showed that among the reported cases 55.84% were male and 44.15% were female. Patients between (10 - 14 years old) are the most exposed to the disease, followed by patients between (5 - 9 years old). The years 2023 and 2024 recorded the highest infection rates with 35.38% and 39.18% respectively. The predominance of this virus is noted during the autumn season. The highest number of infected cases was noted in the region of Mila, followed by Chelghoum Laid. Hepatitis A is the most common type with a percentage of 55.76%. Hepatitis B affects little more of female individuals than males, and the age group of [45 - 64]. Hepatitis C affects the age group over 65 and predominates during the winter and autumn seasons. Climatic conditions in the city of Mila including ambient humidity and precipitation are believed to be the cause of the increase in the hepatitis index, especially for hepatitis

Our prospective study during the first five months in the serology laboratory at the level of Department of Prevention and Epidemiology within Ferdjioua confirms our retrospective analytical study because we obtained the same results concerning the effect of sex and age on the distribution of hepatitis.

Keywords: Hepatitis, epidemiology, prospective study, hepatitis A, hepatitis B, hepatitis C, Mila, Chelghoum Laid, Tadjnanet, Ferdjioua, descriptive study

Résumé

Afin de déterminer le profil épidémiologique et clinique des hépatites dans la région de Mila, nous avons collecté les données de cette étude descriptive analytique rétrospective au niveau du service des maladies infectieuses de la direction de la prévention et de l'épidémiologie au sein de Chelghoum Laid, Tadjenanet, Ferdjioua et Mila, et du service du laboratoire central, unité de sérologie d'un établissement public hospitalier Houari Boumedien, Chelghoum Laid, durant une période s'étendant de janvier 2020 à décembre 2024 et d'une étude prospective d'une durée de trois mois (de Janvier à Mai 2025), 684 cas ont été déclarés que l'étude analytique descriptive a montré que parmi les cas rapportés, 55,84% étaient des hommes et 44,15% des femmes. Les patients âgés de 10 à 14 ans sont les plus exposés à la maladie, suivis des patients âgés de 5 à 9 ans. Les années 2023 et 2024 ont enregistré les taux d'infection les plus élevés avec respectivement 35,38% et 39,18%. La prédominance de ce virus est observée pendant la saison automnale. Le plus grand nombre de cas infectés a été noté dans la région de Mila, suivie de Chelghoum Laid. L'hépatite A est le type le plus fréquent avec un pourcentage de 55,76%. L'hépatite B touche un peu plus les femmes que les hommes, et la tranche d'âge [45 - 64]. L'hépatite C touche le groupe d'âge des plus de 65 ans et prédomine pendant les saisons d'hiver et d'automne. Les conditions climatiques dans la ville de Mila, notamment l'humidité et les précipitations seraient à l'origine de l'augmentation de l'indice d'hépatite, en particulier pour l'hépatite C et l'hépatite C.

Notre étude prospective durant les cinq premiers mois au niveau du laboratoire de sérologie de la Direction de la Prévention et de l'Epidémiologie de Ferdjioua confirme notre étude analytique rétrospective car nous avons obtenu les mêmes résultats concernant l'effet du sexe, de l'âge sur la répartition des hépatites.

Mots-clés : Hépatite, épidémiologie, étude prospective, hépatite A, hépatite B, hépatite C, Mila, Chelghoum Laid, Tadjnanet, Ferdjioua, étude descriptive.

الملخص:

من أجل تحديد الملامح الوبائية والسرييرية لالتهاب الكبد الوبائي في منطقة ميله، قمنا بجمع بيانات هذه الدراسة الوصفية التحليلية بأثر رجعي على مستوى مصلحة الأمراض المعدية التابعة لمصلحة الوقاية وعلم الأوبئة داخل شلغوم العيد، تاجنانت، فرجيوة وميله ومصلحة المخبر المركزي، وحدة الأمصال بالمؤسسة العمومية الاستشفائية هواري بومدين بشلغوم العيد، خلال فترة تمتد من يناير 2020 إلى ديسمبر 2024 ودراسة مستقبلية استمرت ثلاثة أشهر (من جانفي إلى ماي 2025)، تم الإبلاغ عن 684 حالة.

أظهرت الدراسة الوصفية التحليلية الوصفية انه من بين الحالات المبلغ عنها 55,84% من الذكور و44,15% من الإناث. المرضى الذين تتراوح أعمارهم بين (10 - 14 سنة) هم الأكثر تعرضاً للمرض، يليهم المرضى الذين تتراوح أعمارهم بين (5 - 9 سنوات). سجل العامان 2023 و2024 أعلى معدلات الإصابة بنسبة 35,38% و39,18% على التوالي. لوحظ انتشار هذا الفيروس خلال فصل الخريف. ولوحظ أعلى عدد من الحالات المصابة في منطقة ميله، تليها شلغوم العيد. التهاب الكبد الوبائي أ هو النوع الأكثر شيوعاً بنسبة 55.76%. التهاب الكبد الوبائي ب يصيب الإناث أكثر بقليل من الذكور، والفئة العمرية من (45 - 64). يصيب الالتهاب الكبدي الوبائي سي الفئة العمرية التي تزيد عن 65 عاماً ويغلب خلال فصلي الشتاء والخريف. ان الظروف المناخية في مدينة ميله بما في ذلك درجة الحرارة المحيطة والرطوبة وضربات الشمس؛ وهطول الأمطار، هي السبب في زيادة مؤشر التهاب الكبد الوبائي خاصة بالنسبة لالتهاب الكبد الوبائي.

دراستنا الاستطلاعية خلال الأشهر الخمسة الأولى في مخبر الأمصال على مستوى مصلحة الوقاية وعلم الأوبئة داخل فرجيوة تؤكد دراستنا التحليلية الاسترجاعية لأننا حصلنا على نفس النتائج المتعلقة بتأثير الجنس، د العمر على توزيع التهاب الكبد الوبائي.

الكلمات المفتاحية: التهاب الكبد الوبائي، علم الأوبئة، دراسة استباقية، التهاب الكبد الوبائي أ، التهاب الكبد الوبائي ب، التهاب الكبد الوبائي ج، ميله، شلغوم العيد، تاجنانت، فرجيوة، دراسة وصفية

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INTRODUCTION

Hepatitis is considered as one of many international health issues, similar to transmissible disease like AIDS, tuberculosis. This disease is a liver inflammation caused by viruses commonly, and less commonly by toxic substances. Up until now, there are five viruses that cause it. Said viruses are identified by the letters A, B, C, D and E, and each one differ from the other by their genetic properties, transmission mode, and the severity of the infection each one causes. Hepatitis A and E are caused normally by ingesting water from sources contaminated by their respective viruses, while Hepatitis B, C and D are caused from transmitting blood from an infected individual to a healthy one, or through the vertical transmission from the mother to the infant. **(WHO, 2020)**

As soon as viruses reach the liver, they penetrate its cells, the hepatocytes, and multiply. The body's immune system then destroys the infected cells, causing inflammation of the liver. Typical symptoms of acute liver inflammation are eventually observed when infected by these viruses, and can last for several weeks: yellowing of the skin and eyes, dark urine, discolored stools, extreme fatigue, nausea, vomiting and abdominal pain. It is impossible to distinguish between the different forms of hepatitis on the basis of symptoms in the acute phase of the disease. Unlike hepatitis A, hepatitis B, C, and E viruses can lead to a chronic carrier state, meaning that the subject does not get rid of the virus and may develop the serious complications of chronic hepatitis many years later. **(Lavanchy, 2013)**

According to **WHO, 2022**, 254 million people worldwide live with HBV, while 50 million ones live with HCV, deaths caused by chronic HBV and HCV were 1.3 million and 240 thousand respectively. HDV could be involved among HBV's death cases due to it being an ineffective virus that needs the latter to exist. HAV's infection cases reach 1.3 million annually, while HEV's are 20 million yearly. Outbreaks of those two are highly common in regions that lack decent sanitary conditions like Africa, Central America, South America, and some regions of East Asia.

The Popular Democratic Republic of Algeria isn't safe from viral hepatitis either, thanks to the lack of awareness among Algerians, outbreaks of the disease have been ongoing for a while, resulting in an unpleasant burden in the public health of the country

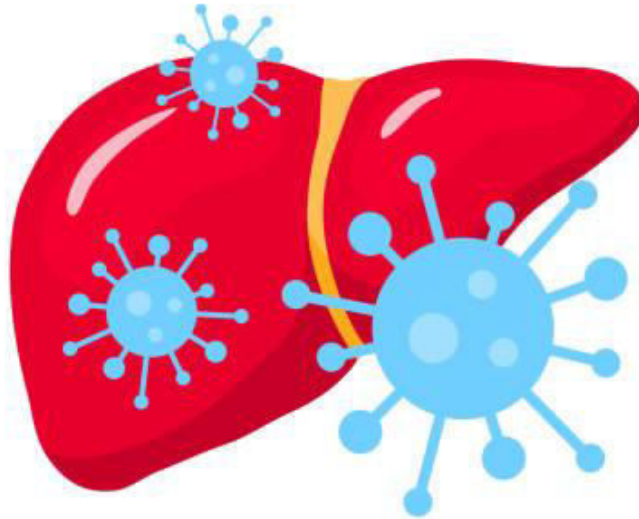
alongside severe cirrhosis cases that eventually evolved into a liver cancer in worse situations.

In Algeria, studies on hepatitis have mainly focused on the epidemiological profile of viral hepatitis A, B and C (**Mohamed Ykhlef, 2017**), and a retrospective study of hepatitis C in the Guelma region (**Babouri and Kaddour, 2013**), in the Wilaya of Mila very few studies are devoted to hepatitis. In 2017, Kamel Bouabdellaha reported that some thirty individuals, mainly children, contracted the hepatitis A virus in Rouached-Mila. In recent years, despite improvements in living standards and health conditions, Algeria has not been able to overcome this reality.

In this thesis, in order to understand the correlation between hepatitis' distribution and certain weather parameters, we traveled through four Dairas of Mila's region: Chelghoum Laid, Tadjenanet, Ferdjioua and Mila gathering data from each of their department of prevention and epidemiology facilities, with the objective of establishing the frequency of hepatitis A, B, and C in the region of Mila, as well as investigating the distribution of this viral disease according to sex rate, age groups, seasons, months and years.

This work was divided through four sections: Firstly, establishing a bibliographic review that focuses on all necessary information regarding the hepatitis and its five viral sources and the differences between each of them; genetic, transmit, and symptomatic and diagnostics' differences. Secondly, we shine a spotlight on our study area, the region of Mila, its climate and its natural resources. Thirdly, we investigate the methodology and the materials laboratories use to diagnose the disease. Thirdly, we showcase the results obtained from our research, providing a detailed interpretation of these findings, considering factors such as prevalence rates, demographic patterns, and any notable variations observed. And finally, we do a detailed discussion to determine how the weather parameters affect the prevalence of hepatitis in general.

VIRAL HEPATITIS



CHAPTER I: BIBLIOGRAPHIC ANALYSIS

1. BIBLIOGRAPHIC ANALYSIS

1. 1. History

A) Early observations to the hepatitis

The discovery of liver inflammation dates way back in time, with Hippocrates (460 – 375 BC) being the first to give a documentation regarding “epidemic jaundice” (Hepatitis B) that is still accurate to this day. He described the symptoms and what the infected patient went through during his observation, stating that “The patient became rave, soon became angry, started talking nonsense as if he was barking like a dog. His nails became red, and slowly lost his eyesight”. He stated that most patients did not live beyond 11 days, and very few survived. **(Ballière, 1844)**

A better observation of the viruses and their epidemiology was gained with a series of experiments done on human volunteers during World Wars. The first one was done by **(Lurman, 1885)** after an outbreak of jaundice that occurred in a Bremen factory among at least 190 of around 1200 to 1500 employees there few years before his documentation. In his book, Lurman concluded in his book that the reason for this sudden outbreak was most likely the revaccination of employees against small pox, while those who were vaccinated beforehand once were not infected. Later on 1943, **(Beeson, 1943)** documented 7 cases of hepatitis infections happened few months after a blood or possibly plasma transfusion.

Lastly, during World War II, a series of infections between soldiers in multiple military campaigns and locations got more specialists to look more into the nature of this disease, the following info is what was obtained from said observations and tests:

- In Dardanelles, Turkey, the disease took a benign course without mortality.
- In Palestine, according to data published by Cameron brought from studied volunteers, the minimum incubation period of epidemic jaundice was 32 days.
- **(Gutzeit, 1950)** used liver biopsies to observe and document progression of hepatitis to cirrhosis, and estimated during his studies that over 10 million individuals were affected by hepatitis during World War II
- In the United States, around 50000 cases of hepatitis were discovered among the Army due to yellow fever vaccinations that turned out to be contaminated by the Hepatitis virus, later noted by **(Seeff and al., 1987)** that all cases were caused by what is now known as HBV (Hepatitis B Virus).

B) Willowbrook experiments

Human experiments on viral hepatitis were most rewarding when (**Krugman and al ., 1967**) from New York University School of Medicine, NY, USA reported on his experiments carried out on children with intellectual disability located in the Willowbrook neighborhood on Staten Island in New York City. They admitted new entrants to the school in a special isolation facility and infected these with blood samples from patients of the school who had contracted hepatitis, and from there, they were able to come out with better information of the incubation period and severity of the infection of hepatitis through injecting two groups of patients with hepatitis with inoculums belonging to the same patient (Mir) With the first group (MS-1) getting the inoculums in a certain period, while the second group (MS-2) having the same one from the same patient 6 months after during the second attack of hepatitis.

Such experiment was riddled with controversy since it was highly unethical not only because the volunteers were purposefully infected, but they were children with special needs and the experiments were done in an unsanitary environment and despite Krugman arguing that the experiment was ethical in all sides, such thing was terminated for good. (**Goldby, 1971; Rothman, 1982**)

1. 2. Hepatitis virus study

1. 2. 1. Brief history

Despite the fact that the hepatitis was already being documented for a long time, the actual discovery of its cause; Hepatitis A, B, C, D and E, began in the middle of the XXth century:

- Hepatitis A was first described by Krugman after his controversial Willowbrook Experiment, and also detailed certain information regarding it (its resistance, its incubation period...). However, the specific identification of this virus and obtaining a full documentation of it was done by (**Feinstone and al., 1973**) whom were successful thanks to previous information regarding HAV from the 1930s, as well as their experiments on the stool of patients
- Hepatitis B and its antigen were discovered by (**Blumberg, 1965**) and his colleagues while studying genetic polymorphisms of serum proteins during his tenure at NIH, Bethesda, MD. They won the Nobel prize in 1977 thanks to their discovery, since it contained a detailed

morphologic and immunologic characteristic of Hepatitis B, which helped in the development of specific passive and active immunoprophylaxis of hepatitis B (**Gupta and al., 1957**)

- The search of Hepatitis C started when (**Alter and al ., 1975**) studied clinical and serological analysis of transfusion-associated hepatitis, the results of their tests revealed the hepatitis virus they were studying had a shorter incubation period, lower peak aminotransferase, and serum bilirubin in comparison to Hepatitis A and Hepatitis B, leading to theorize the existence of at least one Non-A Non-B virus within patients. It was until **1989** that it was fully documented by Houghton and his collaborators (**Gupta and al., 1957**)

-When it was thought to be a marker of a HBV antigen, Hepatitis D was discovered by Mario Rizzetto on 1980, whom collaborated with the National Institute of Health Bethesda, MD, USA and Georgetown University School of Medicine and Dentistry, Washington, USA, to do some experiments on chimpanzees. The results showed that HDV's antigen was not a component of HBV, instead it was a separate virus that required the latter's existence for its infection (**Rizzetto and al., 1980**)

-For nine years, in the period [1983-1990], investigators had a rather major setback and frustration in their research on Hepatitis E, the struggle was due to the fact that the samples (stool and sera) were lacking virus-like particles, not enough for cloning or sequencing. It was all solved in the hands of Dr. Bradley from CDC, Atlanta Georgia, USA, found enough VLPs in the stool of experimentally infected macaques, which later helped both **Reyes and al ., 1990** and **Tam and al ., 1991** clone the RNA sequences from them, leading to conclude the research by discovering HEV.

1. 2. 2. Hepatitis viruses' study

1. 2. 2. 1. Hepatitis A virus (HAV)

A- Definition

Also known as Hepatitis Alpha and "HAV", Hepatitis A virus is a single-strand RNA virus from the "*Picornaviridae*" family, it's known to withstand moderate temperatures and survive in the environment (**Martin and al., 2006**).

In comparison with the rest four viruses, HAV has the highest contagion rate, therefore it's the leading cause of acute hepatitis, and can even lead to liver failure in serious cases (**Win, 2019**).

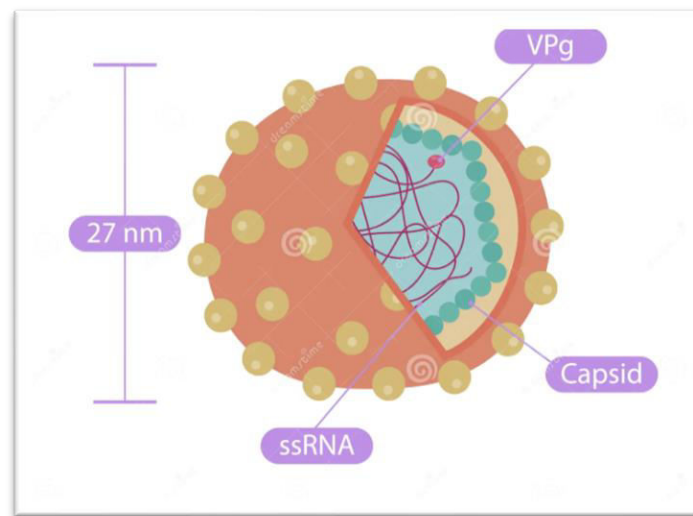


Fig. 01: HAV structure (Website 01)

B- Transmission and replication cycle

The main factor that plays in HAV's life cycle and spreading would be sanitary and socioeconomic, specifically the lack of clean water and poor sanitation since it can spread via oral-fecal contact, and there are frequent epidemics through nutrition. (Nelson, 2020).

It spreads through the orofecal route among children and adults, and it has different infection among both. For children, it occurs in less than 30% of cases with symptomatic hepatitis, while 80% of infected adults have a severe hepatitis with jaundice and a significant increase in transaminases. (Tong and al., 1995)

HAV usually causes short-term, self-limiting illnesses that go away without any long-term effects in 4–7 weeks. Dissimilar to HBV and HCV, HAV seems not to cause persistent liver damage. However, particularly in the elderly, severe fulminant hepatitis with possibly fatal liver failure may ensue. Transfusion transmission of HAV is exceedingly rare due to the short persistence of viremia throughout acute HAV infection (approximately 10–50 days. Symptoms may recur in up to 10 percent of patients after recovery, causing the disease to last for weeks or months (Ndumbi, 2018; Tejada-Strop, 2018)

HAV is also known to have a rather quick replication cycle within the hepatocytes cells in infected patients' livers in comparison with the other viruses, taking from 1 to 3 weeks replicating within the cells. How it happens is that the virus begins by penetrating the host cells by interacting with cell surface molecules, particularly sialic acid and ganglioside, and

then uncoating and delivering viral RNA from endosomes to the cytoplasm. The viral polyprotein is synthesized into distinct structural and nonstructural proteins under the supervision of an IRES. HAV then uses cellular membranes to build organelle-like structures in which the viral genome is replicated. When the freshly synthesized genomes are packed, newly synthesized HAV leaves the cells in the quasienvveloped virion forms. (Kulsuptrakul, 2020)

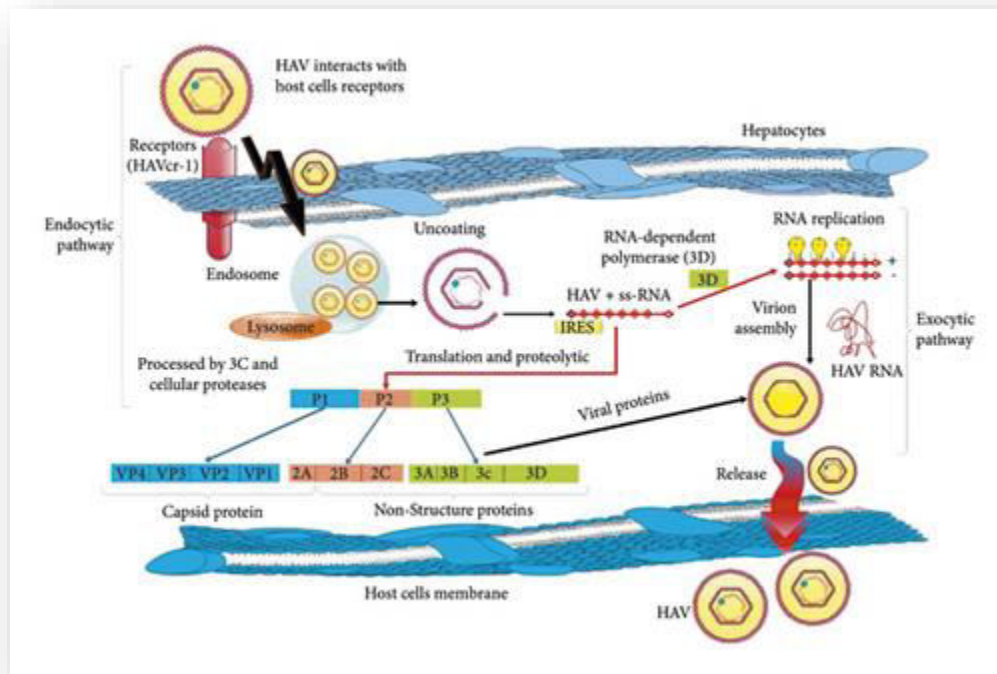


Fig. 02: HAV's life cycle (Costafreda *and al.*, 2018)

1. 2. 2. 2. Hepatitis B virus (HBV)

A- Definition

HBV is a hepatotropic virus from the "*Hepadnaviridae*" family, and is considered a highly dangerous virus since it can lead to both acute and chronic liver infections, with higher chance of mortality caused by this virus in comparison with HCV. HBV is the only Hepatitis virus that contains DNA, since the others have RNA. Its DNA consists of 3200 nucleotides. (Brechot and Pol, 1993).

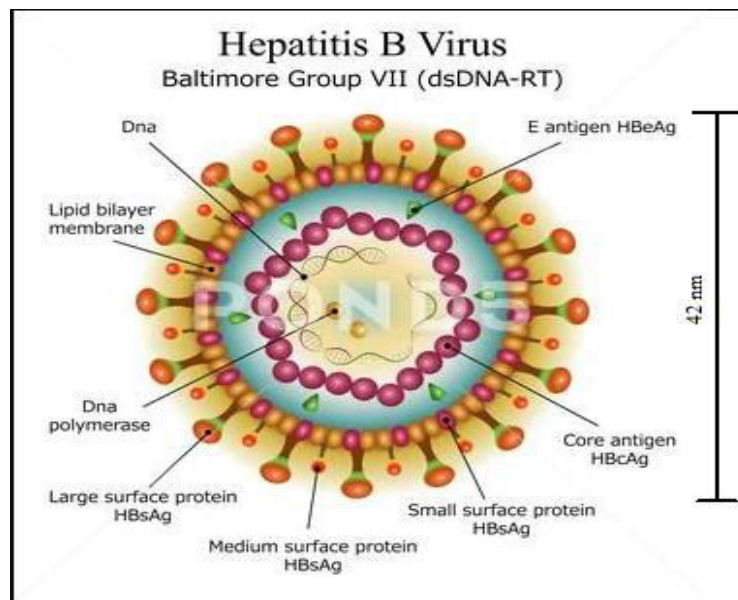


Fig. 03: HBV structure (Website 02)

HBV virus infection can lead to either acute hepatitis (fulminant hepatic failure) to chronic hepatitis, cirrhosis, and HCC. Most adults whom get infected with it recover, but between 5 to 10% of them don't fully recover and eventually develop chronic infection. Said infection range between mild liver disease with little to no long-term morbidity/mortality, up to critical liver diseases (cirrhosis and liver cancer). (Hyams *and al.*, 1995)

B- Transmission and replication cycle

HBV can be transmitted by several methods: the first method is through blood transfusion (an infected patient's blood to a healthy patient), the second method is the prenatal transmission (from the mother to the newborn), and another known method is the sexual intercourses. HBV can also be transmitted through environment interactions; however it is low to occur in comparison with the previously mentioned methods. (Nelson *and al.*, 2016)

Once the virus reaches the liver, it attaches itself to the host's cells, and remains there between 4 to 7 weeks before it starts replicating through the following process: (Gerlich *and al.*, 2013)

- **Uncoating:** core and viral DNA are released by the HBV membrane into the cytoplasm.

- **cccDNA formation:** The pol. of the virus synthesizes the dsDNA and later causes the formation of cccDNA in nucleus.
- **Transcription:** Host RNA polymerase converts cccDNA into pregenomic and subgenomic
- **Translation and reverse transcription:** core, DNA pol. And reverse transcription, are translated using pregenomic RNA as a template. The pregenomic RNA's packaging signal interacts with the DNA polymerase to form a bond, and the two come together to form the capsid of the virion (core). Through the conversion of pregenomic mRNA to DNA, the HBV genome grows in the core particle.
- **DNA synthesis:** The nucleocapsid, which contains partially dsDNA, is produced following the synthesis of the (-) and (+) strands of DNA.
- **Assembly:** dsDNA consists of Hepatitis B surface antigen and nucleocapsid (virion).
- **Release:** The infected hepatocyte releases the mature infectious agent Dane particle/cccDNA amplification.

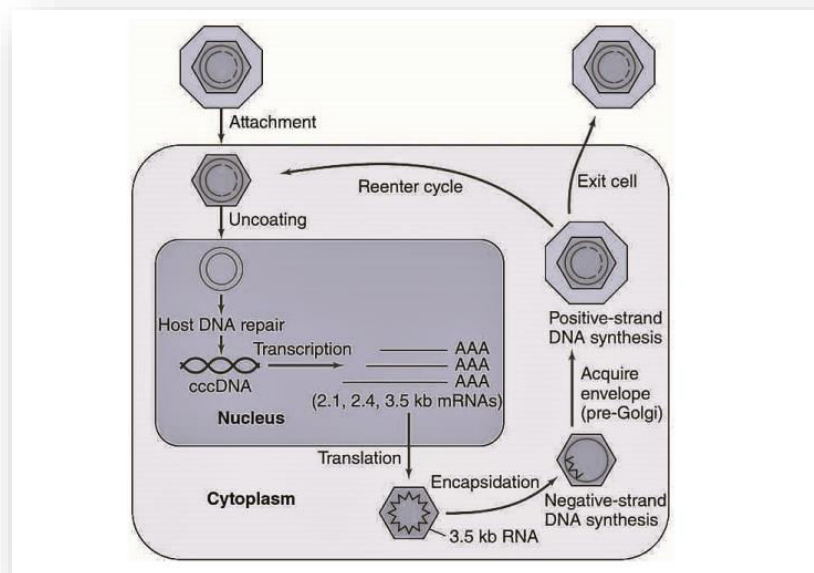


Fig. 04: HBV's replication cycle (Yang and Kao, 2000)

1. 2. 2. 3. Hepatitis C virus (HCV)

A- Definition

HCV virus is a small, enveloped, positive single-stranded RNA virus from the “*Flaviridae*” family and is the only member of genus “*Hepacivirus*”. The severity of HCV infection is not much different in comparison with HBV, however, the chance for patients

with HBV virus to reach chronic infection and even the mortality stage is higher in comparison with those with HCV. (Lauer, 2001)

It is possible for both HBV and HCV to co-exist and replicate within the same host's liver, however that requires the former to be a chronic infection for the latter's presence. This "superinfection" as described by (Jamma *and al.*, 2010) has a higher chance of developing chronic hepatitis and HCC, and is difficult to be diagnosed due to similarities in both antigens and mode of transmissions between the two. Fortunately, the chance for such phenomenon to occur is low (ranging from 1 to 15% globally) (Pol *and al.*, 2017).

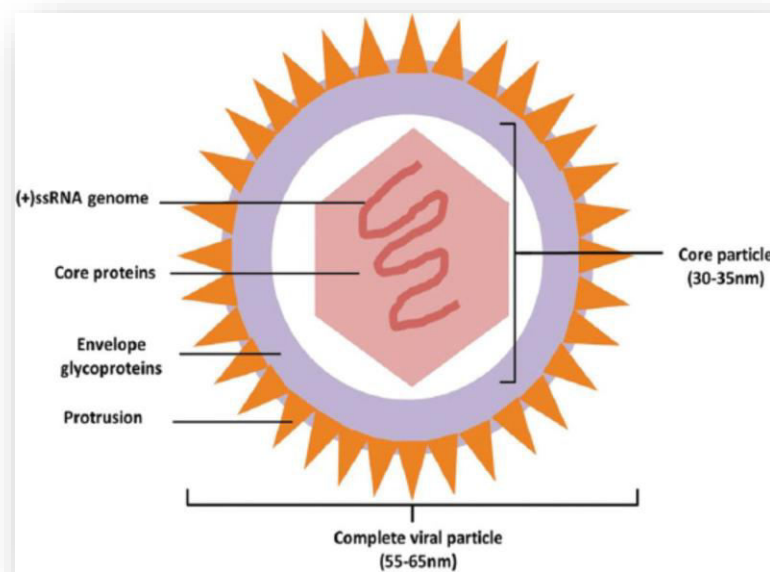


Fig. 05: HCV structure (Brass *and al.*, 2006).

B- Transmission and replication cycle

HBV and HCV viruses have the same transmission modes (blood transfusion, prenatal transmission, and sex intercourses), which could explain why it is possible for them to infect the same host in the "superinfection" phenomenon. (WHO, 2021)

And while both viruses share similarities in nature, they differ in their replication cycle, for HCV has been found to have a faster replication rate perhaps faster than any other hepatitis virus, and it produces new viruses more than its other counterparts starting from 1 week up to 6 months of incubating within the liver. (Hoofnagle, 1996).

This process of replication goes through 7 stages as follows (Barretto, 2014):

- **Attachment:** the viral particle, surrounded with lipoproteins, binds the target cells by interacting with several receptors some, most of which shown in figure, considered essential other accessory
- **Entry:** following attachment, the virus enters through clathrin-mediated endocytosis
- **Uncoating:** the cellular and viral membranes fuse and the capsid is disorganized with a process triggered by the low pH of the endosome. After uncoating the positive-strand RNA genome is released into the cytoplasm
- **Translation:** the genomic RNA is directly translated in a polyprotein precursor that is then cleaved into single proteins by both host and viral proteases
- **Replication:** the non-structural proteins and some host factors form a replication complex that synthesized multiple copies of the HCV RNA genome via a minus-strand replicative intermediate
- **Assembly and maturation:** packaging of viral progeny takes place in the endoplasmic reticulum from which the virion acquires the envelope with E1 and E2 glycoproteins. Maturation and association with endogenous lipoproteins to form lipoviral particles immediately follow
- **Release:** virions are released from the cells most likely by exocytosis or transmitted to other cells via a cell-free mechanism.

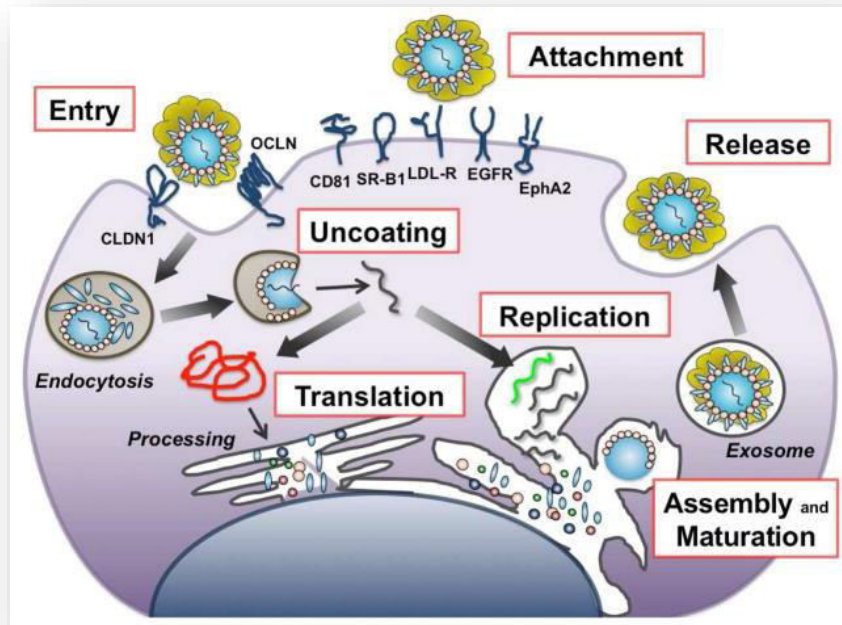


Fig. 06: HCV's replication cycle (Paul *and al.*, 2014)

1. 2. 2. 4. Hepatitis D virus (HDV)

A- Definition

HDV virus is a unique hepatitis virus from the “*Ribozyviria*” family, it consists of a circular, single-stranded minus RNA of about 1700 nucleotides enclosed in a particle coated by HBV's antigen “HBsAg” (HDV virion), with no nucleocapsid structure. (Taylor *and al.*, 2020).

Unlike the other hepatitis viruses, and despite it being the cause of Hepatitis D (which has more severe symptoms than the others), HDV is a defective virus, and cannot replicate or spread within the liver without the presence of HBV since the latter provides the former with the envelop protein needed to enter and exit the hepatocytes cells (Rizzetto, 2017). And despite such coexistence leading to suppressing HBV's replication, an HBV/HDV infection leads to liver diseases much more severe than what HBV can lead to independently (Romeo *and al.*, 2009).

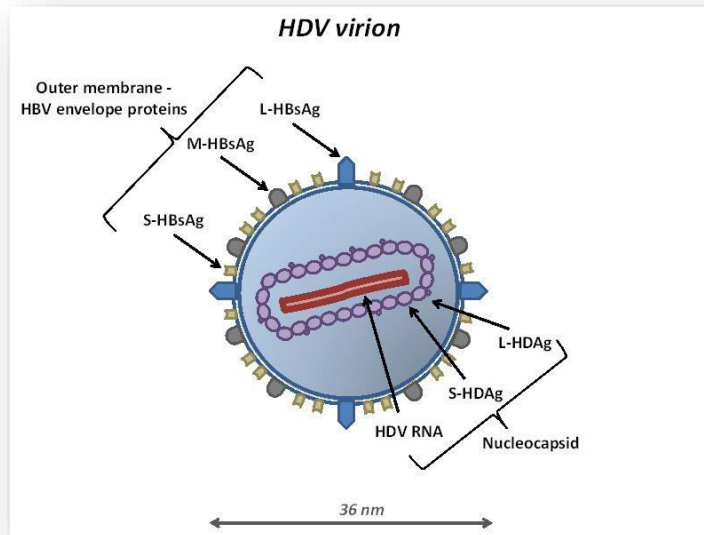


Fig. 07: HDV structures (Rizzetto and al., 1980)

B- Transmissions and replication cycle

The mode of transmission of HDV is a unique one, because it was found that it spreads while incased within not only the HBV and even HCV viruses, but also other viruses like vesiculovirus, arenavirus, metapneumovirus, and flaviviridae. Therefore, the way it enters the hosts depends on which virus it can attaches itself within. **(Perez-Vargas and al., 2019)**

As mentioned, HDV's life and replicating cycle cannot function properly without HBV's presence, while some studies showed that the virus can replicate without HBV, its rate would be low and its activity within the hepatocytes would be inefficient until HBV is introduced. Therefore, it requires the protein envelop of HBV to enter and exit the liver's cells through the following process: **(Engelke, 2006; Yan and al., 2012)**

- **Receptor binding:** HDV enters hepatocytes by binding to the carbohydrate side chains of heparin sulphate proteoglycan present on the surface of hepatocytes.
- **Entry:** The N-terminal aminoacids of the pre-S1 domain of L-HBsAg are thus obligatory to HDV entry into hepatocytes.
- **Uncoating:** After HDV enters the cell, the uncoating of viral particle occurs and HAD translocate the viral genome into the nucleus where RNA polymerases I and II are employed to replicate the genome
- **Transcription:** Polymerase I involves the transcription of antigenome from viral genome in the nucleolus, while polymerase II catalyzes genome replication from antigenome and transcription of mRNA in the nucleoplasm

- **Release:** When the process is complete, a new virus is released from the hepatocyte incased in an HBV envelope.

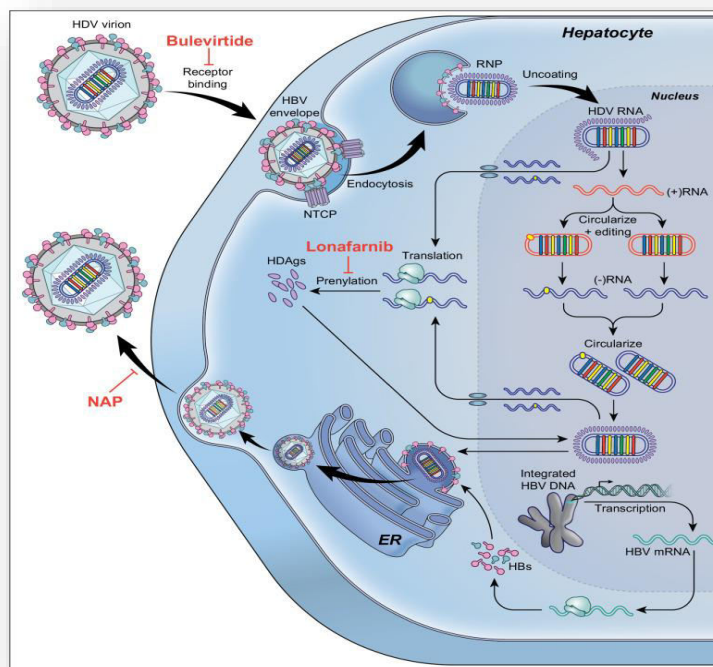


Fig. 08: HDV's replication cycle, which requires it to be incased within a HBV to function (Abdul Majeed *and al.*, 2023).

1. 2. 2. 5. Hepatitis E virus (HEV)

A- Definition

HEV virus is a small, single-stranded positive sense ribonucleic acid (RNA) genome, non-enveloped virus in the “*Hepeviridae*” family. Globally, HEV accounts for a significant proportion of liver disease, and is responsible for up to 70% of adult sporadic hepatitis cases in endemic regions. It is thought to be the most common etiology of acute viral hepatitis with an estimated incidence of 20 million cases yearly. (Petrik *and al.*, 2016).

HEV is the most common source of acute viral hepatitis worldwide, and the chances of it causing chronic diseases (leads to cirrhosis in most conditions) are significantly low unless the HEV infection coexists with HIV. (Kamar *and al.*, 2013).

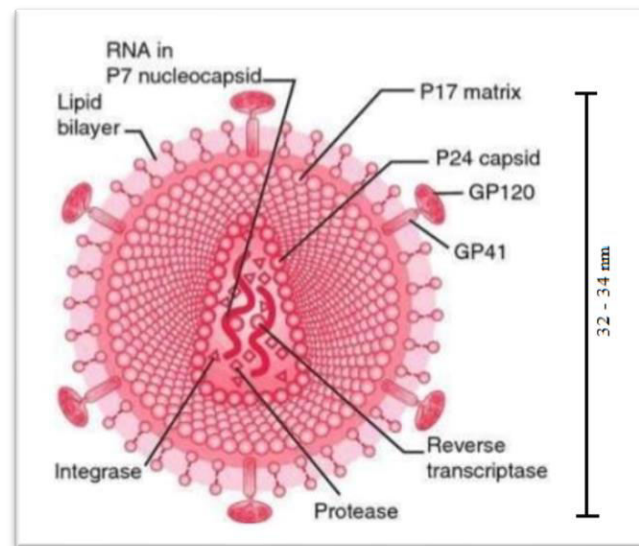


Fig. 09: HEV structure (Website 03)

B- Transmission and replication cycle

HEV is known to enter the body through contaminated water sources, and then it makes its way from the intestines to the liver where it starts its replication cycle.

Oddly enough, compared to the other four hepatitis viruses, HEV's replication method has little to no data about it. The only things known about it is that, while it does reproduce within the hepatocytes, the primary site of replication appears to be the intestinal tract (although it's not definitively identified to be the case). What is known about the virus' path after it enters the host's cells is that it reaches the liver via the portal vein, then attaches to the surface of hepatocytes via a yet unidentified receptor, enters these cells, and replicates in their cytoplasm (Krawczynski and Bradley, 1989).

1. 3. Hepatitis disease study

1. 3. 1. Definition of hepatitis (liver inflammation)

"Hepatitis" refers to the liver inflammation disease, it's commonly caused by five documented viruses, but other factors like drugs/alcohol and autoimmune diseases can cause hepatitis. Symptoms can last for weeks, and while it can resolve after a certain time period, it can progress to fibrosis, cirrhosis and liver cancer, and it can be life-threatening in worst cases. (WHO, 2013).

1. 3. 2. Epidemiology

1. 3. 2. 1. Hepatitis' types

To this day, five viruses have been discovered worldwide that cause the hepatitis disease, each one is different to the other in many ways. All can be summarized in the following table: **(Parth and Anil, 2020)**.

Table 01: Hepatitis viruses' properties.

Virus type	Incubation Period (Days)	Transmission modes	Symptoms	Prevention methods
HAV	~28	Fecal-oral route (Water, food and objects contaminated by infected feces)	Malaise, anorexia, nausea, vomiting, and jaundice.	- HAV vaccination - Washing hands properly before and after preparing and consuming edibles.
HBV	~84	Blood transfusion, prenatal transmission, and sexual intercourses.	Anorexia, malaise, and fatigue (Common), right upper quadrant pain (rare), fever, arthralgias, or rash. (Very low)	- HBV vaccination - Protected sexual interactions - Avoid sharing any item that can have blood in it (tooth brushes, shaving blades, clippers...)
HCV	~56	Blood transfusion, prenatal transmission, and sexual intercourses.	80% Asymptomatic, anorexia, malaise, and fatigue (During the acute infection)	- Avoid sharing any item that can have blood in it (tooth brushes, shaving blades, nail clippers...)
HDV	~91	Blood transfusion and sexual intercourses.	Similar to HBV's, can become much severe in case of HBV/HDV infection	- HBV vaccination - Protected sexual interactions. - Avoid sharing any item that can have blood in it (tooth brushes, shaving blades, nail clippers...)
HEV	14 - 70	Fecal-oral route (Water sources contaminated by infected feces.	Acute symptoms similar to HAV's. Severe symptoms' chances are rare.	- Washing hands properly before and after preparing and consuming edibles - Raise awareness for developing countries.

1. 3. 2. 2. Diagnosis methods

a) Physical exams

The physical exam allows identifying the symptoms of a possible hepatitis infection, part of the exam is asking the patients about symptoms like: fatigue, loss of appetite, weakness, nausea and vomiting. The second part is where doctors apply gentle presses in the abdomen to check for liver swelling, and then examines the skin and eyes' color for any yellow hue for possible jaundice. **(Website 04)**

b) Serological assays

This method is defined as blood tests done in laboratories to detect antigens, antibodies or both in blood samples of infected individuals. This diagnosis method is the first to be considered to pinpoint the exact type of disease a patient is experiencing. **(Wasley and al., 2006).**

How this method is executed is via collecting between 2 – 3.5ml of blood sample in a sterile, dry vial, then the serum needs to be extracted from the clotted blood within 4 hours of collection and stored in what can go as low as -70°C temperature. **(Longatti, 2015).**

The presence/absence of certain antibodies of viruses in serological assays may determine the infection period and whether the hepatitis disease is acute or chronic.

Table 02: Indicators of each Hepatitis virus infection in the serological test diagnosis
(De Paula, 2012; Runyon, 2004; Thornburn *and al.*, 2006; Huang *and al.*, 1998; Aggarwal, 2011).

Virus	Infection	Conditions
HAV	Acute	-Immunoglobulin M (IgM) antibody, test results for it are usually accompanied with a rise of ALT level - Immunoglobulin G (IgG) appears soon after IgM and persists for years - Presence of IgG accompanied by the absence of IgM indicates past infection rather than acute infection
HBV	Acute	- Presence of HBV's surface antigens (HBsAg), Core antibody (anti-HBc), and IgM anti-HBc indicates a previous or current acute Hepatitis B infection
	Chronic	- Presence of HBV's surface antigen (HBsAg) in high levels indicate either a chronic or acute infection, but can be confirmed to be a chronic one in the presence of anti-HBc antibody
HCV	Acute	- Presence of HCV's RNA with a negative antibody test means possible acute infection, more tests would be needed within 24 weeks after exposure to determine whether the infection is indeed acute or chronic
	Chronic	- A chronic HCV infection is determined once tests show positive antibody presence alongside the presence of HCV's RNA
HDV (can only be detected in "HBV-HDV" coinfection)	Acute	- The existence of both HDV's RNA and its antigen-IgG in the serum only indicates an acute infection if it does not persist long-term
	Chronic	- Presence of HDV's RNA + 10^5-10^7 copies/mL of antigen-IgG in a long term can indicate a chronic infection/coinfection - Presence of HDV's RNA in the liver
HEV	Acute	- HEV's RNA is the main factor to diagnose the presence of the virus, its presence in serum for short viremic phase (2 – 4 weeks in serum, 4-12 weeks in stool) pinpoints an acute infection
	Chronic	- Persistent detection of the RNA in serum and stool after a long period confirms a chronic HEV infection

c) Liver Function Test

The term “Liver function test” does not comment on the liver’s function, but rather pinpoint the source of the damage judging by any abnormal elevation in the liver’s enzymes. The main focus when it comes to diagnosing liver damage caused by hepatitis is the elevation of the following enzymes: “Alanine aminotransferase” (a specific marker for hepatocellular injury), and “Aspartate Aminotransferase”(may rise in conjunction with the previous enzyme to indicate the hepatocellular injury). **(Vagvala and Connor, 2018).**

The liver function test is performed on semi or fully automatic analyzers that are based on photometry (the measurement of light absorbed in the ultraviolet to visible to infrared range), which is used to determine the amount of an analyte in a solution or liquid. Photometers utilize a specific light source and detectors that convert light passed through a sample solution into a proportional electrical signal.**(Gowda and al., 2009).**

The specimens used in such method (plasma or serum specimens potentially positive for infectious agents) are required by laboratory workers to be prepared and handled carefully, especially as a precaution in cases of coinfections of HIV/HBV. Specimens need to be tested on immediately, and if not, they must be stored in 2°C to 8°C. for 48 hours max. And if it exceeds this period, samples must be frozen to what can reach -20°C. Frozen samples should be thawed **only once** for analysis. **(Lippi and al., 2019).**

d) Liver Biopsy

Liver biopsy is considered a golden standard for diagnosing a number of liver diseases, including chronic hepatitis. How it works is that patients are made to lie in a comfortable supine position, right arm placed under the head in a neutral position and kept calm, then the doctor uses certain needles (16- to 18-gauge needles are the most common to use), take a sample of a liver tissue, and used under the microscope to determine what disease the liver has. **(Website, 05)**

Liver biopsy has 4 techniques:

- **Percutaneous biopsy technique:** Performed with Palpation/percussion method; Imaging-guided; and Real-time image-guided. This biopsy technique is considered the most favorable one to identify hepatitis.

- **Transvenous biopsy technique:** Uses the transjugular/transfemoral approach. This technique is more favorable for patients who are high risk from possible complications from the percutaneous technique
- **Laparoscopic biopsy technique:** Uses needles for cutting and aspiration, and wedge biopsies. It's more recommended for patients with chronic liver disease.
- **Plugged biopsy technique:** Uses a biopsy tract that is plugged with gel foam. It's recommended if bigger liver samples are needed, and is safer than the first technique for patients with high risk of bleeding (ex: coagulopathy or thrombocytopenia).

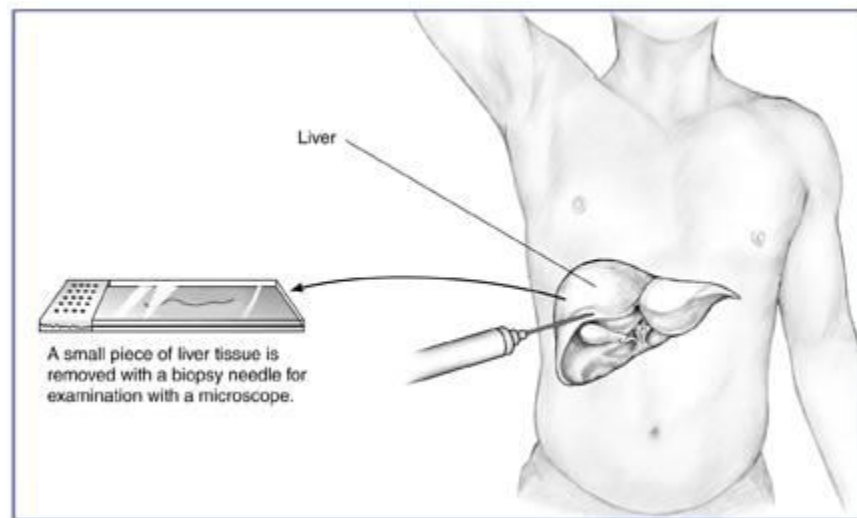


Fig. 10: Illustration of a simple liver biopsy (Website, 06).

e) Ultrasonography

This method of diagnosis can detect both acute and chronic hepatitis diseases using “The inverter”, which is a device that converts electrical signals into mechanical (ultrasonic vibrations), and vice versa. When activated inverter is leaned on the body, it emits an ultrasonic beam. Ultrasonic waves are focused by lenses, ultrasonic mirrors and by electronic means. (Markovic *and al.*, 1985).

It can be used to diagnose acute hepatitis caused by HAV and HEV within the gallbladder wall (Maurya *and al.*, 2019), and diagnose and differentiate between chronic hepatitis (mainly caused by HBV and HCV) and early-stage cirrhosis. Meanwhile, HDV cannot be diagnosed with ultrasounds (Gaiani *and al.*, 1997)

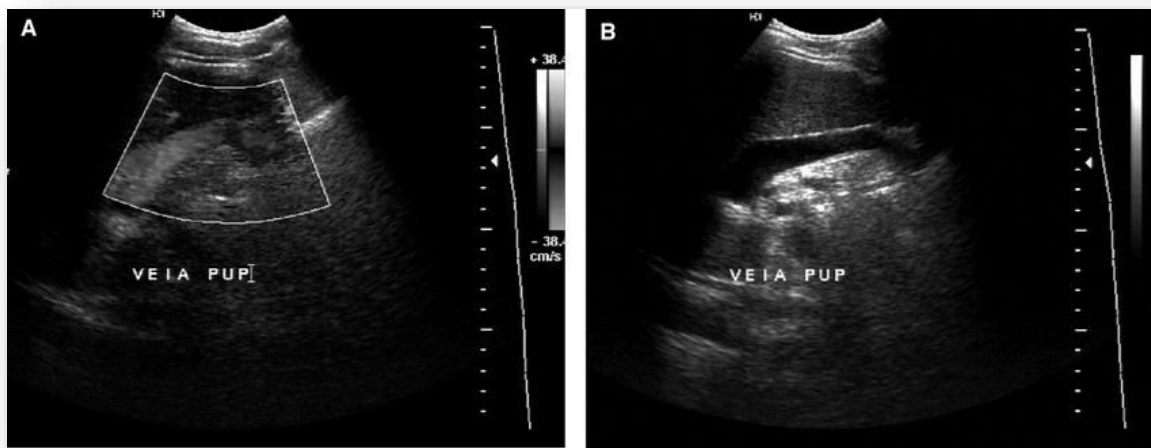


Fig. 11: An example of ultrasonography, the bright spots indicate an HCV infection in a liver vein (**Jorge and al., 2012**)

1. 3. 2. 3. Treatment And Prevention

Hepatitis has different treatment, which also varies depending on whether the liver disease is acute or chronic, and what type of virus caused what. In general, patients with hepatitis, specifically immunocompromised individuals and ones who experience nausea and vomiting get admitted and started on intravenous fluids to keep them hydrated. Patients who have complications like liver abscess, variceal bleed, or hepatic encephalopathy require admission and appropriate treatment. However, most of the patients can be safely monitored as an outpatient. Patients should avoid medications like acetaminophen or substances like alcohol that can be hepatotoxic. Patients with acute viral hepatitis infection take proper rest and avoid vigorous physical activities until the symptoms improve. If required, patients should obtain a referral to specialty services like gastroenterology or hepatology. (**Hutin and al., 2017**)

The following table summarizes available treatments and prevention methods for all hepatitis infections: (**Doshani and al., 2019; Rajbhandari and Chung, 2016; Murray and al., 2003; Brown, 2009; Yurdaydin, 2017; CCSEE, 2023**).

Table 03: Treatment and prevention against the five known hepatitis infection.

Type	Treatment	Prevention
HAV	-Limited to providing adequate supportive care for symptomatic cases since a specific treatment for HAV doesn't exist. Said care includes: using nutritional support, hydration, and using antiemetics (in case of vomiting)	- HAV vaccination starting from young age once every 5 years at least (a long-lasting vaccine to give immunity against HAV is yet to be discovered). - Sanitary precautions (drinking proper water, avoiding possibly contaminated products and water).
HBV	- Acute: Supportive care in regular infection. Usage of Oral Nucleotide Analogs for severe infections and coinfections with HCV or HDV - Chronic: Inhibiting the viral replication by suppressing the virus' DNA and forcing the loss of its antigen "HBeAg". Working on interfering with the infection to prevent its progression to possibly lethal infections (cirrhosis, hepatocellular carcinoma)	- Universal vaccination, including timely birth dose within 24 hours. - Post-exposure prophylaxis with hepatitis B immunoglobulin plus vaccination is effective in preventing mother-to-child transmission. - Safe injection practices and screening of blood products.
HCV	- Direct antiviral agents (DAA) are an effective HCV treatment due to it inhibiting the virus' replication cycle. This method works on both acute and chronic infection.	- HBV vaccination (preferably on birth). - Counseling for high-risk behavior (intercourse with multiple partners, and the use of drugs). - Avoid sharing equipment that can transmit the virus between individuals (blood transfer, tattooing, skin piercing...).
HDV	An exact treatment is still unknown, however the following methods has a decent efficacy: - HBV/HDV coinfection: the pegylated interferon (PEG-IFN). - HIV/HDV coinfection: Patients with this usually receive tenofovir therapy	Since HDV required HBV to cause an infection, the methods to prevent HDV infection is the same as HBV's
HEV	Only effective first-line drug is Ribavirin (RBV) that clears HEV's RNA and stabilizes the liver's enzymes. However, its use is rather limited due to teratogenicity and hemoglobin-lowering side effects. A more favorable treatment has not been discovered yet.	- Avoid possible source of infection (raw/undercooked meat, possibly contaminated water sources, dirty hands).

1. 3. 2. 4. Hepatitis' geographic distribution

A- Africa

Individuals in highly endemic regions of Africa, largely in sub-Saharan regions, develop an immunity to HAV, noting that Hepatitis A's epidemics are uncommon. **(Nelson, 2018)**. HBV is also present largely in the sub-Saharan regions, with 6.1% of Africa's population infected with the virus, and an estimated 18 million individuals in Africa struggle from chronic HCV infection. **(WHO, 2009)**. As for HEV, it's estimated, according to some studies to assess the damage caused by HEV past-infection, that Africa has the highest prevalence of the virus with around 21.76% on the whole continent. **(Kmush and al., 2013)**

B- Eastern mediterranean region

Instances of HAV infections in the Middle East and North Africa decreased over the last decades to an intermediate prevalence level **(Jacobsen, 2018)**. It was noted that 3.3% of the region's population are infected by HBV, and around 800 000 individuals suffering from HCV, with Egypt having the highest rate of HCV with 14.5 million being HCV positive, 7.8 million individuals from that developed chronic HCV. **(Esmat, 2013)**

HDV was noted to be highly present, and is mostly associated with patients infected with chronic HBV and HCC, with over 27.8% of the population in this region suffering from it. The infection cases are highly common specifically in Saudi Arabia and Egypt **(Pascarella and Negro, 2011)**. As for HEV, it was noted in high endemic regions like Somalia, Sudan and South Sudan due to the lack of sanitary water. **(Website, 07)**

C- South-East Asia

The majority of the region have Hepatitis A's seroprevalence at a high level, despite some recent data indicating a decline in it in India, and a low endemicity in East Asia **(David, 2004)**. HBV infections reach 100 million chronic infections, with an average of 5 million death yearly because of it. Surprisingly, the prevalence of Chronic hepatitis in South-East Asia is 30 times more than that of HIV, add to it around 10 million individuals carry HCV. Due to the lack of awareness regarding the hepatitis disease, 65% of HBV patients and 75% HCV patients are usually unaware of them. **(Mac Lachlan and Cowie, 2015; Giles-Vernic and al., 2016)**.

It's assumed that the cases of HCC and chronic HBV could be linked to HDV, and while the info regarding that is limited, some research estimated between 0.5% to 1.6% of the region's population being infected with Hepatitis D(Sy *and al.*, 1990). While HEV cases are estimated to be 12 million in South-East Asia alone every year, which accounts for more than half of the global cases. The true incidences are likely to be higher. (Scotto *and al.*, 2013)

D- Western Pacific Region (Include East Asia and Australia)

The mortality rate in the Western Pacific Region due to Viral Hepatitis is higher than HIV, tuberculosis and malaria together. Hepatitis A's prevalence is relatively low for high-income areas, and it's declining the more the economy in the other areas improves. (Yoon *and al.*, 2017)

Half of HBV's cases is located in the region with 350 million individuals, add to it 60 million cases of chronic HCV out of 150 million globally. The latter's prevalence in the region is low in East Asia (1 to 2%), and the highest one recorded was in Taiwan (4.4%) and Vietnam (2.9%) (Wiesen *and al.*, 2016)

There are no exact details regarding HDV and HEV's distribution in the region, although some studies speculate that 3% of deaths caused by chronic hepatitis is caused by HBV and HEV complications. As for HDV, the data related to it is limited in the Western Pacific Region for the moment.(Nur *and al.*, 2000)

E- Europe

The European region has a varied Hepatitis A's prevalence; in the western side, HAV transmission less more common among adults than children, and in the eastern side they have much less distribution of the virus but community wide outbreaks are not uncommon.(Lemon, 1994)

Hepatitis B and Hepatitis C's prevalences are low, however the infections cases are slowly rising, with numbers up to 1.4 million and 9 million cases of chronic HBV and chronic HCV respectively. The yearly death cases caused by each one is 36000 for HBV and 86000 for HCV.(Ishizaki *and al.*, 2017).

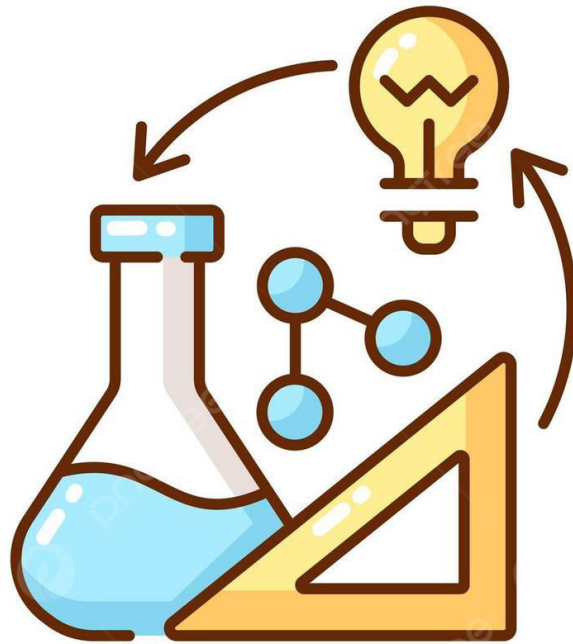
The presence of Hepatitis D in the region is rather low with around 3% of the population documented to have the virus.(Stockdale *and al.*, 2020) While Hepatitis E's prevalence was documented to be 9.31%.(Hartl *and al.*, 2016)

F- The Americas

Apart of high-income countries of North America, Hepatitis A's prevalence in Center and South America is rather high, and even though there was some noted reduction, outbreaks are still really common. HAV's symptomatic infection was noted to be higher among adolescents and adults than it was among children, fortunately almost half of the infected individuals gained immunity against the virus by the age of 15. **(Díez-Padriza *and al.*, 2013).**

The Americas, apart of Haiti, has the lowest Hepatitis B prevalence with 0.7% of the population having HBV infection. As for Hepatitis C, it's more noted in The Caribbean and Latin America countries with an average of 7 to 9 million individuals being anti-HCV positive.**(Díez-Padriza *and al.*, 2013).**

While the data is somewhat limited regarding Hepatitis D and E, it was noted that the estimated prevalence of HDV was 3.3% **(Mokdad *and al.*, 2014)**, while HEV's was 8.05% in the Northern side and 7.28% in the Southern side. **(Horvatits *and al.*, 2018).**



CHAPTER II: MATERIALS AND METHODS

2. Materials And Methods

2. 1. Presentation of Study Area – Mila’s Province

2. 1. 1. Geographic Location

Mila’s Province is located in the northeast side of Algeria, approximately 391km to the east from Algiers, and 50km to the northwest from Constantine. It’s located in what is named “Mila-Constantine basin” that covers a 3500km² zone. Located between latitude 244,591.01 and 263,859.46m North and longitude 4,027,529.17, 4,043,981.06m East (WGS 84 UTM 32), where the area of this municipality is 129.95 km² (**Bounemoeur and al., 2022**).

Mila is bordered by the following Provinces

- By Jijel in the North;
- By Constantine in the East;
- By Batna in the South;
- By Setif in the West;
- By Skikda in the North East;
- And By Oum El Bouaghi in the South East.



Fig. 12: Mila Province’s Map showcasing the borders between it and the other provinces (Website 09).

2. 1. 2. Administrative Aspect

The province of Mila was created during the last Algerian administrative division of 1984, with the city of Mila as the capital of wilaya 43. The province has 13 Daïras comprising 32 municipalities represents the administrative division of the Mila region.(Boularas and Kadjoudj, 2016)

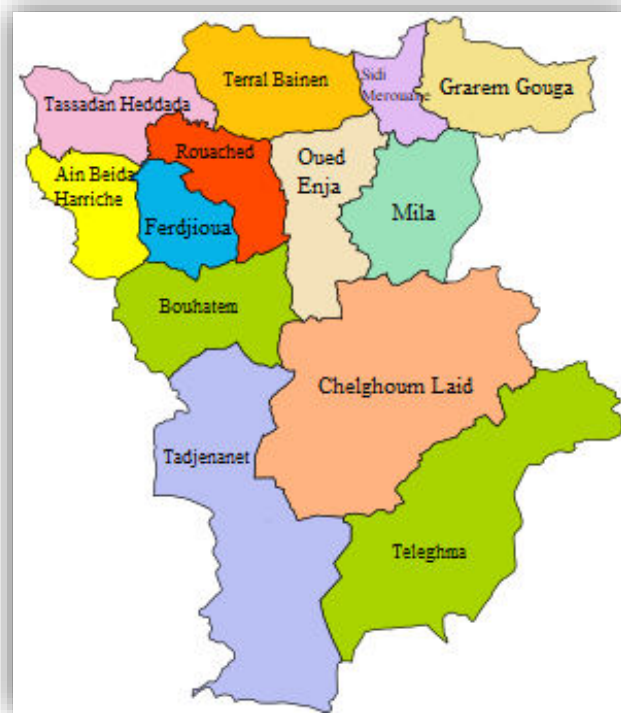


Fig. 13: Map of The Province's Daïras (Website 10)

Table 04: Administration division of the state (Mila) (Boularas and Kadjoudj, 2016)

Daïra	District	Surface (Km²)
Mila	Mila, Ain Tinn, Sidi Khelifa	212.56
Chelghoum Laid	Chelghoum Laid, Oued Athmania, Ain Mellouk	634.54
Ferdjioua	Ferdjioua, Yahia Ben Ghecha	109.07
Grarem Gouga	Grarem Gouga, Hamala	199.13
Oued Enja	Oued Enja, Ahmed Rachedi, Zeghaia	186.97
Rouached	Rouached, Tiberquent	145.82
Terrai Bainen	Terrai Bainen, Amira Arras, Tassala Lamtai	220.25
Tassadane Haddada	Tassadan Haddada, Minar Zarza	162.9
Ain Beida Harriche	Ain Beida Harriche, Elayadi Barbes	153.53
Sidi Merouane	Sidi Merouane, Chigara	86.52
Teleghma	Teleghma, Oued Seguene, M'Chira	484.85
Bouhatem	Bouhatem, Derradji Bousselah	233.34
Tadjenanet	Tadjenant, Ouled Khlouf, Benyahia Abderrahmane	577.52

2. 1. 3. Demographic data

2. 1. 3. 1. Population distribution by Daïras

The population in Mila was estimated to be 931 363 individuals distributed among 13 Daïras (32 districts in total).

Table 05: Population count in the districts and Daïras of Mila province.

Daïra	District	Population N°	Total
Mila	Mila	71147	86484
	Ain Tinn	9894	
	Sidi Khelifa	5443	
Chelghoum laid	Chelghoum Laid	102854	166848
	Oued Athmania	45454	
	Ain Melouk	18540	
Ferdjioua	Ferdjioua	58359	73372
	Yahia Ben Ghecha	15013	
Grarem Gouga	Grarem Gouga	48825	61866
	Hamala	13041	
Oued Enja	Oued Enja	24599	63943
	Ahmed Rachedi	18120	
	Zeghaia	21224	
Rouached	Rouached	29469	40703
	Tiberguent	11234	
Terrai Bainen	Terrai Bainen	28678	64279
	Amira Arras	18349	
	Tassala Lamtai	17252	
Tassadane Haddada	Tassadane Haddada	17781	44005
	Minar Zaraza	26224	
Ain Beida Harriche	Ain beida Harriche	25210	32258
	Elayadi Barbes	7048	
Sidi Merouane	Sidi Merouane	25481	42962
	Chigara	17481	
Teleghma	Teleghma	66521	95043
	Oued Seguene	14874	
	M'Chira	13648	
Bouhatem	Bouhatem	24962	37186
	Derradji Bouselah	12224	
Tadjenanet	Tadjenanet	96222	122408
	Ouled Khelouf	14537	
	Benyahia Abderrahmane	11649	

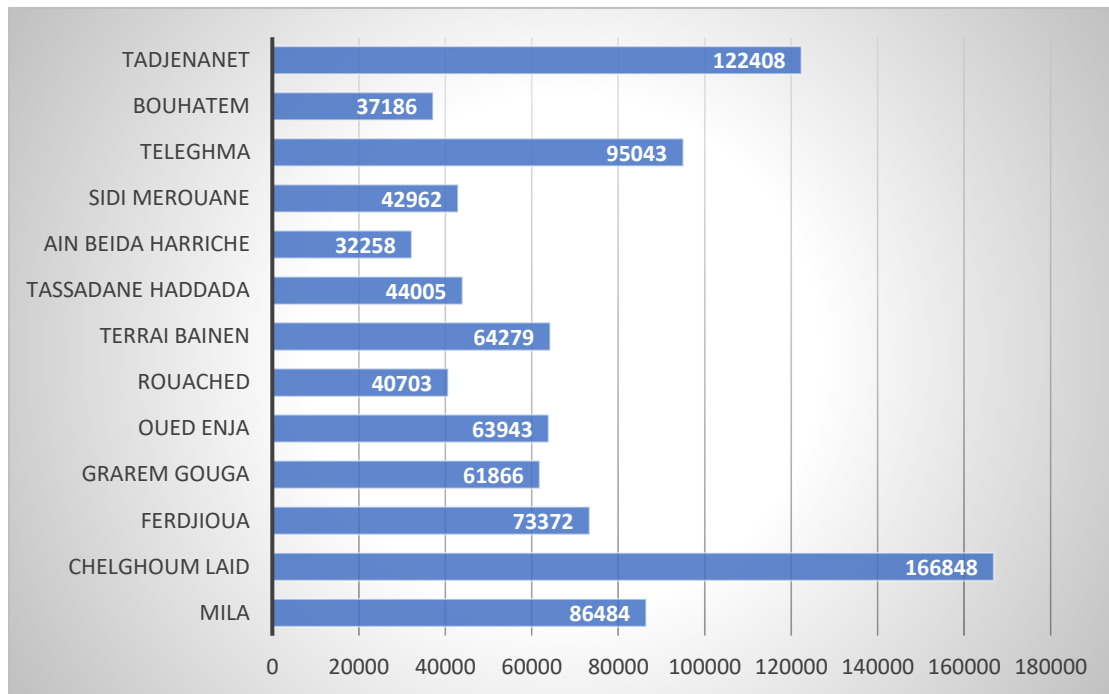


Fig. 14: Chart of population distribution in Mila Province's Daïras

2. 1. 3. 2. Population distribution by sex

The estimate population of Mila province by sex documented 468444 male inhabitants (~50.3%) and 462920 female inhabitants (~49.7%).

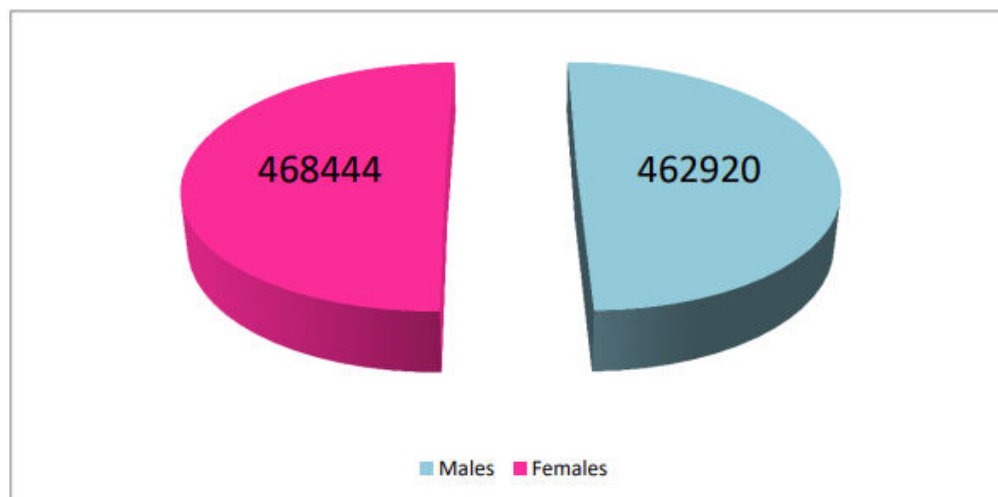


Fig. 15: Chart of population distribution by sex.

2. 1. 3. 3. Population distribution by age

The statistics from (DPSP Mila, 2023) indicates that the highest individuals count is in the age group of young adults (22 to 24), followed by teenagers (15 to 19).

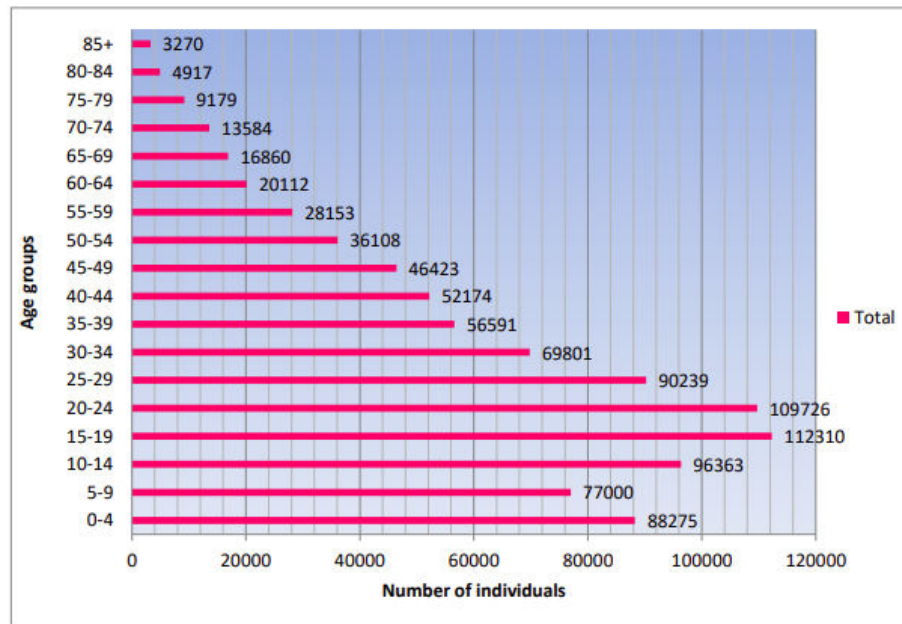


Fig. 16: Chart of population distribution by age groups

2. 1. 3. 4. Population distribution by economic activities

The total of active population is estimated to be 671,543 inhabitants, representing 66,74% of Mila's inhabitants, in which employed population in the state was determined to be 603,247. The activity rate determined to be 66,74%, noting public works also includes construction and hydraulics. (NAID, 2013)

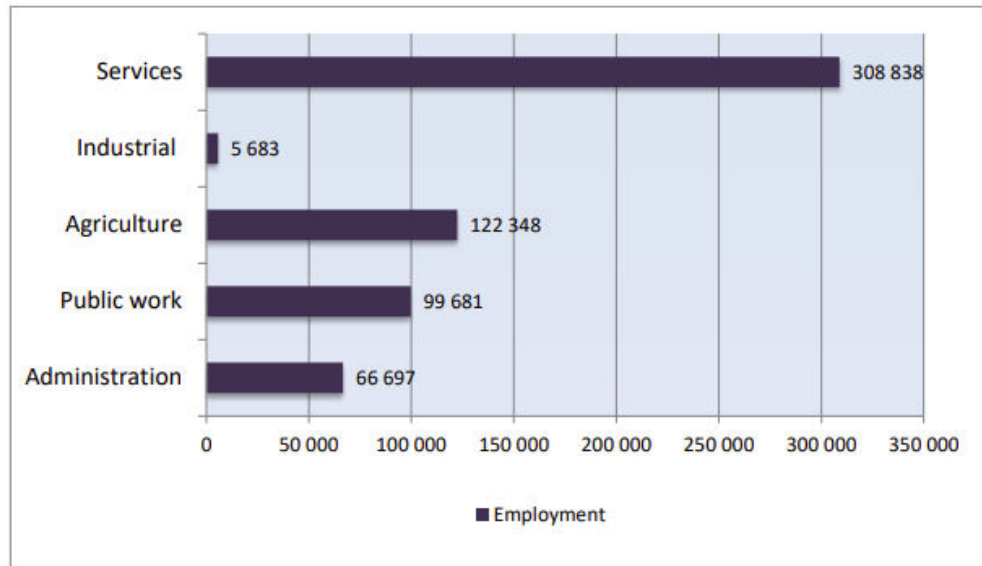


Fig.17: Chart representative of the population distribution by activity sector

Seeing that the industrial side has the highest number of employees, most of Mila's people reside in the urban areas than country side (**Fig. 18**).

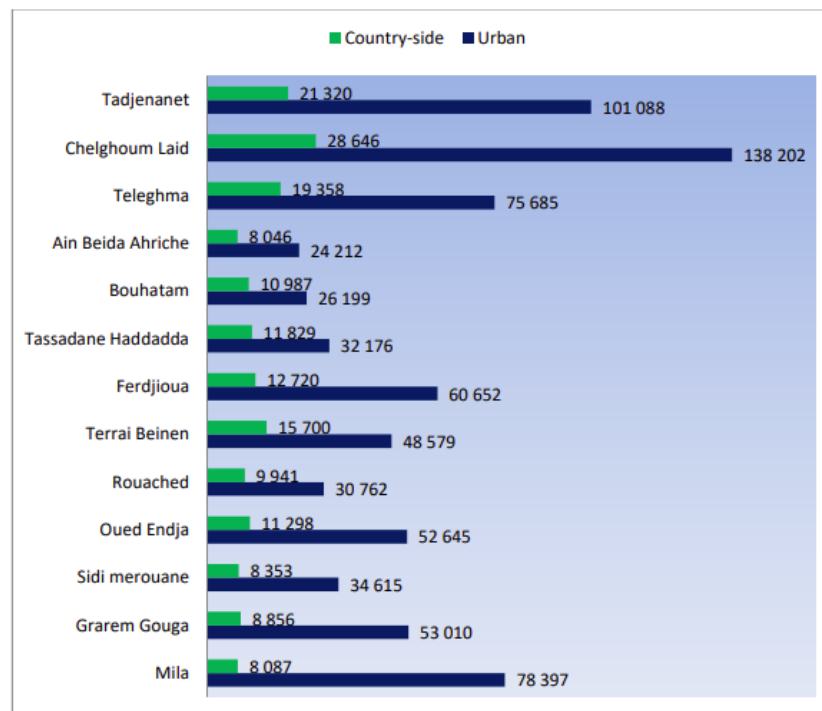


Fig. 18: Chart of population distribution in the urban/country-side zone.

2. 1. 4. Environmental characteristics

2. 1. 4. 1. Climate

Mila's region is characterized by a Mediterranean climate, which has cold and rainy winters, hot and dry summers, and receives a height of precipitation varying between 500 and 600 mm/year (**Bounemoeur and al., 2022**).

It's governed by three microclimates, which correspond to the arrangement of the three major morphological units (**NAID, 2013**):

- Humid for the mountainous reliefs of the North and the middle part, which extends from Bouhatem to Ain Tine;
- Semi-arid to sub-humid for the middle part of the province (its slopes);
- Semi-arid for the 'high plains'

2. 1. 4. 2. Natural potential

A- Agricultural potential

The total agricultural area is estimated at 315 745ha , 237 557ha (75.23%) of it are arable out of its total geographical area, which exceeds 3.48 thousand km². Of the total agricultural area, this area represents 90% of the area of the State, which is classified as an excellent peasant state.

Agricultural land is distributed according to the type and nature of exploitation for each municipality, as the municipalities located in the southern region of the upper plains contain the most significant percentage of agricultural land, in particular (Chelghoum Laid, Oued Athmania, Tadjenanet, Ouled Khelouf, M'Chira, Teleghema, and Oued Seguene) with a rate of more than 48%. Among the arable lands are the same municipalities that exploit the most irrigated areas. Meanwhile, the pastoral lands are concentrated in the municipalities of the north and the basins by way of allocation (Minar Zarza, Hamala, Ayadi Barbas, Tassala Lamtai, Shigara, Tassadane Hadada, Terai Bayane) where the pastoral lands in it constitute between 20 to 46% of the total agricultural lands for each municipality. However, they do not exceed 9% of the total arable lands. (**Bendjouad, 2023**).

B- Forest Cover

Out of Mila region's 340 684 ha area, 33 670 ha (9.80%) of it is covered by forests distributed in the following domains (**DAS, 2000**):

- **Natural forests:** Covering a 6 762ha area (20.08%), with the dominant species being cork oak "*Quercus suber*"
- **Reforestation:** Covering an 18 493ha area (54.92%), with the main species being Aleppo pine "*Pinus Halepensis*" and cypress "*Cupressus*"
- **Maquis:** Covering an 8,415ha area (25%), its main plants consist of holm oak "*Quercus Ilex*" and the Juniper "*Juniperus*"

C- Relief

1- In The Northern Region:

This region consists of mountainous area formed by a succession of mountain ranges (the Tellian massifs) stretching across the territories of the municipalities of Hamala, Chigara, Terrai Bainen, Amira Aress, Tassala Lemtai, Minar Zarza, and Tassadane Haddada. The highest points in this area are:

- "Djebel Tamezguida": 1600m; - "Djebel Zouagha" : 1300m;
- "Djebel M'cid Aicha": 1400m; - "Djebel Boufroun" : 1300m.

2- In The central region

A zone of foothills and hills constituting the central region of the southern Tellian foothills, which covers almost all of the districts of Ferdjioua, Oued Endja, and the municipality of Grarem Gouga. It comprises Intra-mountain plains in the Ferdjioua and Oued Endja regions with an average altitude of 400 m. Hills and foothills located in the eastern part of the province; they are bordered to the north by the mountainous region and form the southern boundary of the high plains.

The region of high foothills, which extends north westward as an extension of the Tellian reliefs, it encompasses the Ferdjioua and Oued Endja depression and extends from the municipality of Derrahi Bouslah to the reliefs of Sidi Khelifa and Ain Tine. The lowland of Mila formed by a set of low hills ranging from 500 to 600 m in altitude and isolated massifs such as Djebels Akhel, Boucharef, Ouakissen, and the Ahmed Rachedi massif.

3- In The southern region

In which a high plateau zone characterized by gentle slopes of less than 12.5% exists. It covers almost the entire district of Chelghoum Laid and the vast cereal plains of Tadjenanet and Teleghma. This region is also characterized with an average altitude generally ranging between 800 and 900 m that includes isolated mountainous massifs emerge, such as **Kef Lebiod** (1,408 m), **Djebel Tarioulet** (1,276 m), **Kef Lsserane** (1,276 m), **Djebel Gherouze** (1,271 m).

D- Water Resources

Mila's water sources, water reservoirs, and water flow, can be summed up in the following table:

Table 06: Mila Water Supplies' Data (DPSB/DAS, 2020)

Water Supply Units	Count	Water Flow/Capacity
Identified Water sources	330	7 804 812.16 m ³ /year
Identified Wells	40	1 814 942.16 m ³ /year
Boreholes	104	9 713 065.71 m ³ /year
Reservoirs	425	157 010 m ³
Water Towers	67	21 700 m ³
Hill Reservoirs	4	1 573 000 m ³

The irrigated area at the state level is estimated at 16030 ha or 6.7% of the arable area, which is a very weak percentage compared to the area irrigated by precipitation, despite the availability of a large dam that holds more than 1 000 000 000 m³. The precipitation rate is estimated at 700 mm/year in the northern mountainous regions and 350 mm/year in the southern regions. In comparison, in the central regions, it ranges between 400 and 600 mm per year, as the level of precipitation varies according to each season and from month to month, and is in constant changing lately due to the climate changes (**Bendjouad, 2023**).

Concerning groundwater, it is estimated at 56 million m³/year, and 36 by 46 wells exploit it, with a combined flow of 922301 L/sec. As for the unexploited explorations, their number is 15 explorations, of which eight (08) are in the municipality of Chelghoum Laid.

Three central valleys in the State flow continuously through the four seasons. Constantine, while the second is Oued Enja, whose length is 110 km, on a line parallel to the northern mountain range. Its most important tributaries are Oued Djemila, Oued Bousalah, Oued Radjas, and Oued Malah, which are 45 km long. On the other hand, there are three dams in the State, the great Beni Haroune Dam (960 million m³), Oued Athmania's Dam (35 million m³), and Guerouze Dam (41 million m³). All three dams are used for consumable water, in addition to partial exploitation for irrigation, especially for the southern extension line. Beni Haroune Dam towards Batna is used for irrigation at the municipality level of Teleghema (**Bendjouad, 2023**).

2. 1. 5. Mila's sanitary structure

The following data obtained from Nalira showcases the sanitary facilities/service (**table 07 and 08**) and the qualified human resources (**Fig. 19**) within Mila's province:

Table 07: Total facilities and services of the province (**Nalira, 2022**)

Facility/Service	Count
Hospitals	5 (835 beds capacity)
Polyclinics	40
Health centers	167
Maternity hospitals	9
Hygiene laboratories	3
Privat clinics	2

Table 08: Public sector healthcare establishments within the state of Mila (**Nalira, 2022**)

PSHE	Count	Region	Capacity
Psychiatric hospital	1	Oued Athmania	270 beds
Public hospital	5	Meghlaoui Mila	166 beds
		Tobal Mila	88 beds
		Ferdjioua	240 beds
		Chelghoum Laid	220 beds
		Oued Atmania	110 beds

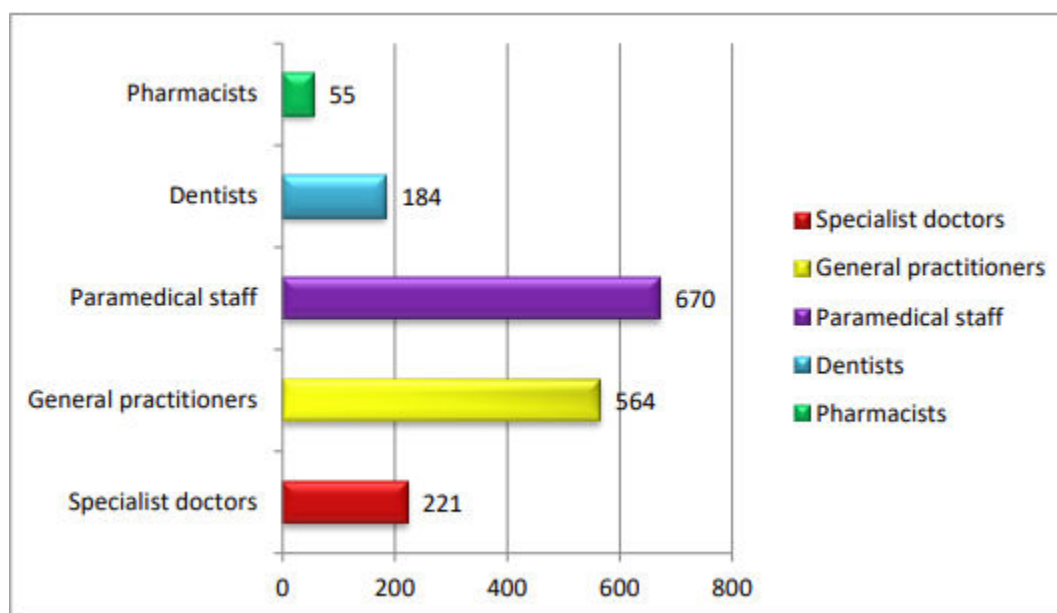


Fig. 19: Total qualified human resources of the province and their capacity (Nalira, 2022).

2. 2. Materials And Methods

2. 2. 1. Location, Type and Period of the survey

The descriptive epidemiological study of hepatitis, was done on four different hospital establishments within the state of Mila during the period (2020-2024).

- The central laboratory service, medical virology unit of the —Bentobal —public hospital establishment of Mila region
- The central laboratory service, medical virology unit of —Mohamed Meddahill public hospital establishment of Ferdjioua region
- The central laboratory service, medical virology unit of the || public hospital establishment of Tadjanet region
- The central laboratory service, medical parasitology and mycology unit of —Houari Boumadienell public hospital establishment of Chalhoun El-Aid region.

2. 2. 2. Patients of interest

From what I learned, patients who exhibit an abnormal expansion in their belly, a pain in the right side of their abdomen, nausea and sometimes vomiting get tested in private serological labs or within hospitals specializing in serological tests to diagnose what the cause of the issue is.

In this study, I noted the diagnosis of 684 patients across the 4 Dairas from 2020 to 2024. A majority of said patients are young kids and adolescents, nearly all had hepatitis A, which leads me to assume that wherever they live or whatever schools they attend are having some severe sanitary issues (unsanitary water and washrooms). While the other somewhat rare cases of Hepatitis B and C were mostly consisting from middle aged and senior individuals, and since HBV and HCV takes the serological path for transmission, it's safe to assume that activities and processes that included using syringes and needles are involved in how the viruses affected them (vaccinations, blood tests, tattoos).

2. 2. 3. Serologic analysis

In order to understand how serologic laboratories diagnose hepatitis within patients, all information of both the materials and method of analysis were obtained from the Analysis Laboratory of Dr. Doula, Tadjanet.

The lab uses what is called the ELISA test, which stands for “enzyme-linked immunosorbent assay” which is used to diagnose antibodies found within the patient's bloodstream using specific reagents. Said test is capable of diagnosing HAV, HBV and HCV.

2. 2. 3. 1. Materials

- Microplate
- Washer
- Microwells
- Incubation oven
- Micropipette
- Read
- Yellow tip



Fig. 20: All laboratory materials needed for diagnosis (personal photos).

2. 2. 3. 2. Reagents

- | | |
|-------------------------------|------------------------------|
| • Chromogen A | • HBV / HCV Negative control |
| • Chromogen B | • HBV / HCV Positive control |
| • HBV / HCV Biotin Conjugates | • Stop solution |
| • HBV / HCV HRP-Conjugates | • Wash buffer |

2. 2. 3. 3. Method of analysis

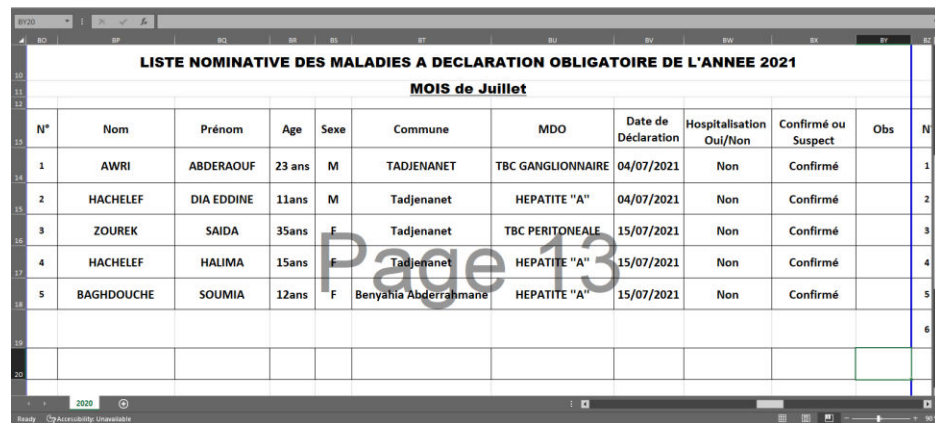
Measuring antibodies to the hepatitis virus is essential for diagnosis. These antibodies appear very early in the course of the disease, and can be detected as soon as the first clinical signs appear. IgM antibodies are present in the blood only during the initial infection with the hepatitis virus.

The following steps are how the ELISA test is done:

- 1) Mark 2 wells as positive and negative controls;
- 2) Add 50µm of the biotin conjugates to the other wells;
- 3) Add 50µm of sample to the other wells, each one of said wells represent a sample;
- 4) Place the wells in the incubator for 60 minutes;
- 5) Wash all wells 5 times using the washer;
- 6) Add 100µm of HRP conjugate;
- 7) Incubate the wells yet again for 30 minutes;
- 8) Add 50 µm stop solution to stop the enzymes' reaction;
- 9) Use a reader to read the plates and determine the type of infection/virus within the blood;

2. 2. 4. Collecting patients' data

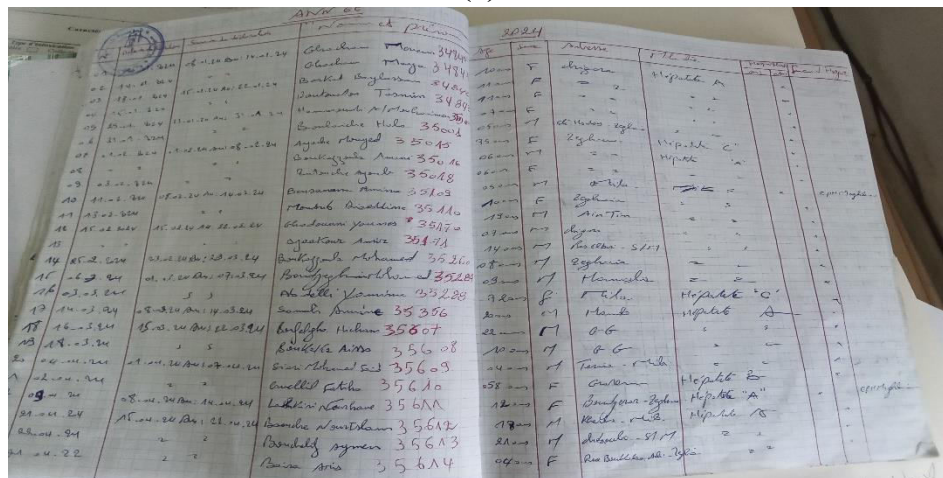
The data of patients that are diagnosed in laboratories are noted on a daily basis either on big register books or in computers in tabular softwares, with Excel being the most commonly used. Both methods document the patient's surname, first name, sex, age, date of diagnosis and the diagnosed disease.



The image shows an Excel spreadsheet titled "LISTE NOMINATIVE DES MALADIES A DECLARATION OBLIGATOIRE DE L'ANNEE 2021" with a subtitle "MOIS de Juillet". The table contains the following data:

N°	Nom	Prénom	Age	Sexe	Commune	MDO	Date de Déclaration	Hospitalisation Oui/Non	Confirmé ou Suspect	Obs
1	AWRI	ABDERAOUF	23 ans	M	TADJENANET	TBC GANGLIONNAIRE	04/07/2021	Non	Confirmé	
2	HACHELEF	DIA EDDINE	11ans	M	Tadjenanet	HEPATITE "A"	04/07/2021	Non	Confirmé	
3	ZOUREK	SAIDA	35ans	F	Tadjenanet	TBC PERITONEALE	15/07/2021	Non	Confirmé	
4	HACHELEF	HALIMA	15ans	F	Tadjenanet	HEPATITE "A"	15/07/2021	Non	Confirmé	
5	BAGHDOUCHE	SOUIMIA	12ans	F	Benyahia Abderrahmane	HEPATITE "A"	15/07/2021	Non	Confirmé	

(a)



The image shows a handwritten register book with columns for patient information and medical notes. The entries include names, ages, and dates, with some handwritten notes in French and Arabic. The text is written in cursive and includes details such as "Hépatite A", "Hépatite B", and "Hépatite C".

(b)

Fig. 21: Examples of archived data of hepatitis and other diseases. Chelghoum Laid and Mila provided register books (b) (Although they do have info saved in computers), while Tadjenanet and Ferdjioia provided tables in Excel (a).**(Personal images).**

2. 2. 5. Meteorologic data

The weather parameters' data needed for this study were all provided by the meteorologic station of Ain Tin, said parameters consist of the following:

- Average annual temperature;
- Average annual sunshine duration;
- Average annual precipitation;
- Average annual humidity;
- Average annual wind speed.

2. 2. 6. Data statistical analysis

The data underwent input and processing using Excel software, alongside SPSS (Statistical Package for the Social Sciences) Version 26 and prism GraphPad software. Descriptive statistics concerning sex, age groups, years, seasons, and months were depicted using graphs generated within R, which was utilized for all statistical analyses and graphical representations. Variations in each parameter across sex, age groups, months, seasons, years, and their interactions (sex $\times$ age groups) were assessed through one-way and two-way analysis of variance (ANOVA).

Subsequently,

Student's t-tests were performed to discern variability within each parameter group. Pearson correlation tests were then employed to explore the relationships among hepatitis dissemination parameters (including age, sex, months, seasons, years, and meteorological parameters), aiming to elucidate their behavior and interconnections under the meteorological conditions prevailing in the state of Mila.

The resultant correlation matrix was visualized through an interactive correlation diagram, employing the prism GraphPad software. Subsequently, utilizing 'SPSS', we implemented generalized linear mixed models to examine the relationships between hepatitis dissemination variation and the effects of temperature (T°), sunshine duration (Sun), precipitation (P), wind speed (WS), and humidity (H).

Statistical significance for all tests was established at $p < 0.05$, with a confidence interval of 95%.



CHAPTER III: RESULTS

3. RESULTS

This survey reveals cases of hepatitis diagnosed at the serological analysis laboratories of the state of Mila during the period from 2020 to 2024. According to the prescriptions of attending physicians, patients presenting with an abnormal expansion in their belly, a pain in the right side of their abdomen, nausea and sometimes vomiting were referred for serological tests. During this period, 684 patients were tested. The epidemiological study covers four areas within the Wilaya: Chelghoum Laid, Tadjanet, Ferdjioua and Mila.

3. 1. Overall prevalence of hepatitis during the descriptive study period (2020-2024)

3. 1. 1. Comprehensive state-wide retrospective analysis of the study population

3. 1. 1. 1. Distribution of patients according to sex during the descriptive study period (2020-2024)

The formula used within Excel to count the number of male and female individuals is the “COUNTIFS”, which count the number of “Ms” (male) and “Fs” (Female), after that, we count the percentage of each one using the fourth proportional as follows:

$$\text{Percentage (\%)} = \frac{(\text{N}^\circ \text{ of Male/Female individuals} * 100)}{\text{Total Individuals' N}^\circ}$$

What follows below are graphs obtained from the data we gathered from the period between 2020 to 2024 (**Refer to the annex section for the detailed tables**):

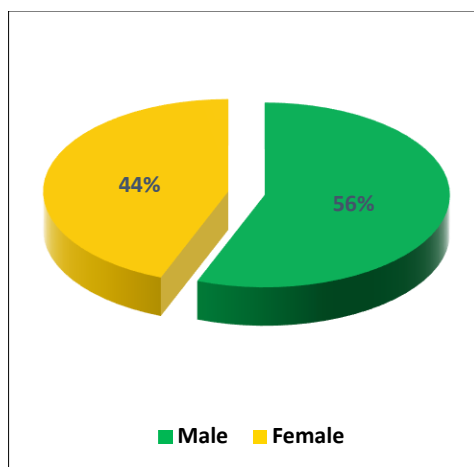


Fig.22: Distribution of hepatitis-infected patients by sex ratio during the period (2020 – 2024)

Our data from **Fig. 22** revealed that the majority of cases were found in male individuals ($n=382$) (56%) during this period (2020 – 2024). The results obtained showed highly statistically significant differences ($p < 0.001$) between sex ratio for hepatitis infection. One-way ANOVA reveals a not significant sex effect ($p > 0.05$).

3. 1. 1. 2. Distribution of infected patients according to age slices during the study period (2020-2024)

Using the same formula “COUNTIFS” but with specific conditions to sort individuals by an age domain, and the same fourth proportional formula stated earlier, we got the following results

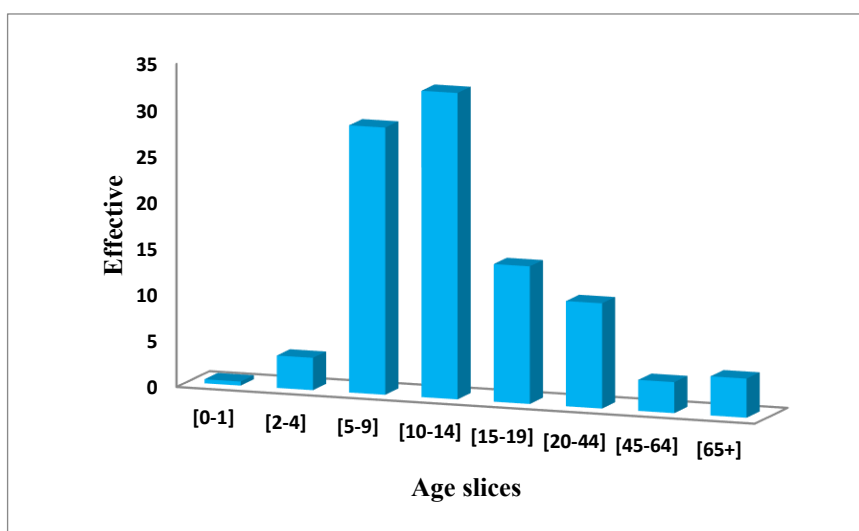


Fig. 23: Distribution of hepatitis-infected patients by age slices through the period (2020 – 2024)

According to the presented data, the most affected age group is [10-14] years, with 227 cases and a rate of (33, 19%). Followed by the categories, [5-9] age group which show 198 cases and a rate of (28, 95%), the category [0-1] years is the less representative group by 3 cases and a rate of 0, 44%. The results obtained showed highly statistically significant differences ($p < 0.001$) between sex ratio for hepatitis infection. One-way ANOVA reveals a significant age effect ($p < 0.05$).

3.1.1.3. Distribution of infected patients according to the months during the study period (2020-2024)

Following the same formula and mathematic equation mentioned earlier, this is the following results:

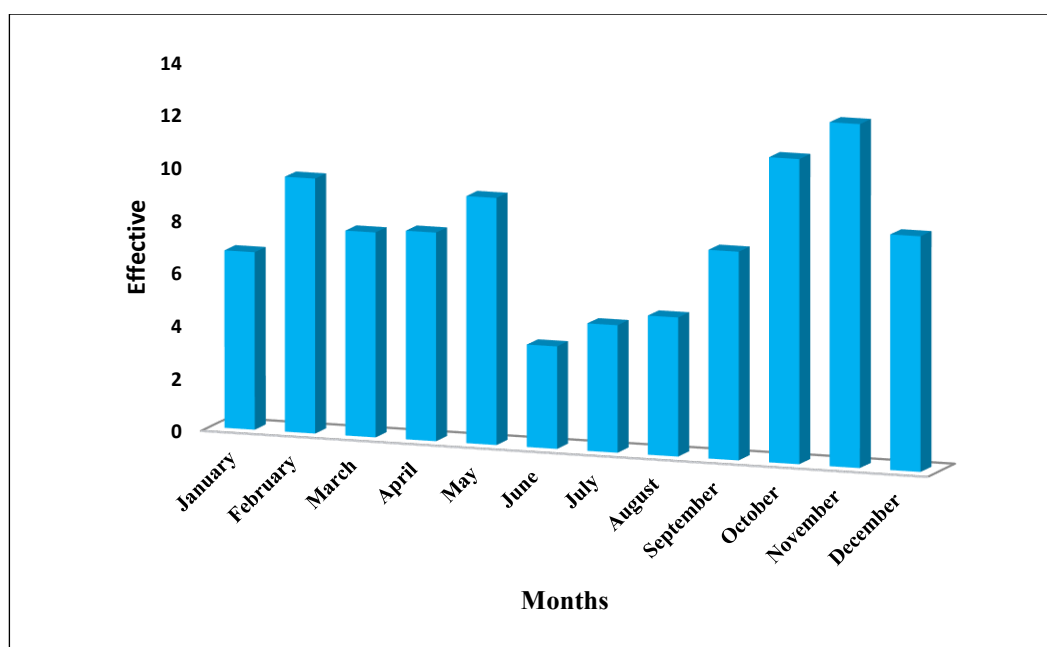


Fig. 24: Distribution of hepatitis-infected patients by month during the period (2020 – 2024)

It shows that the highest number of viral cases was recorded during the month of November at (~13.01%), followed by October at (~11.15%). The lowest percentages were detected in the months of June and July at a rate of (3,89%) and (4,84%), respectively over the study period. The results obtained showed highly statistically significant differences ($p < 0.001$) between months for hepatitis infection. One-way ANOVA reveals a significant month effect ($p < 0.05$).

3. 1. 1. 4. Distribution of infected patients according to the seasons during the study period (2020-2024)

Following the same formula and mathematic equation mentioned earlier, this is the following results:

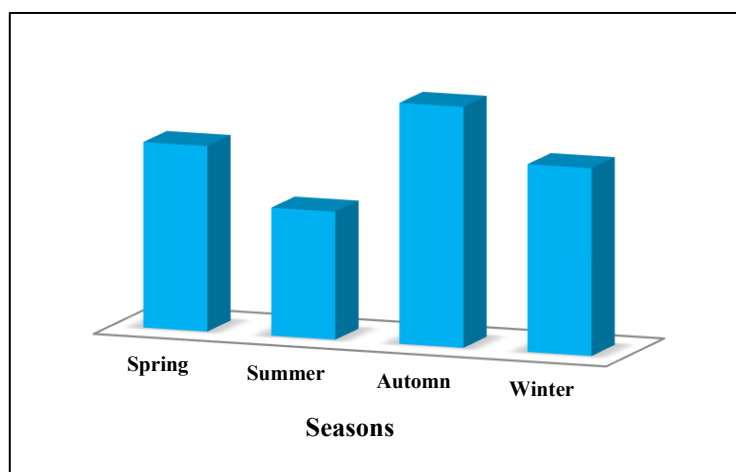


Fig. 25: Distribution of hepatitis-infected patients by seasons during the period (2020 – 2024) Our result shows that the highest number of infected cases was observed during the Autumn season, followed by the winter season, with a rate of (32,46%) and (25,29%), respectively. While the lowest number of cases was recorded during the summer season, with a rate of (17, 25%). The results obtained indicate statistically significant differences in hepatitis infection rates between seasons. The results obtained showed highly statistically significant differences ($p < 0.001$) between sex ratio for hepatitis infection. One-way ANOVA reveals a significant season effect ($p < 0.05$).

3. 1. 1. 5. Distribution of the infected patients according to the years during the study period (2020-2024)

The results were as followed:

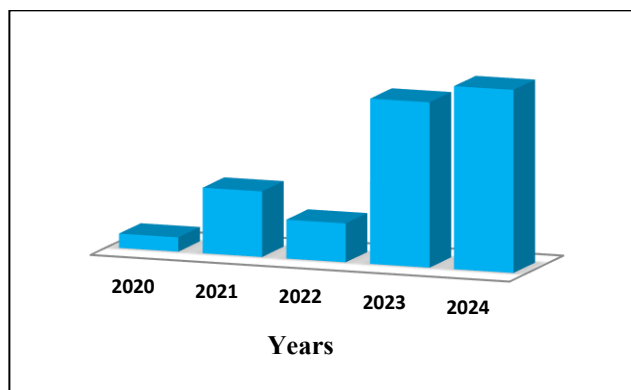


Fig. 26: Distribution of hepatitis-infected patients by years between 2020 and 2024.

The years 2024 and 2023 exhibited the highest rates of human hepatitis, registering a rate of (39.18%) and (35.38%), respectively, compared to other years. Conversely, the rates for human hepatitis ranged from (8.33%) to (3.07%) during the years 2022 and 2020, respectively. The results obtained showed highly statistically significant differences ($p < 0.001$) between years for hepatitis infection. One-way ANOVA reveals a significant year effect ($p < 0.05$). The analysis of data revealed a highly significant interaction between year and region ($p < 0.001$) (**Table in annex**).

3. 1. 1. 6. Distribution of the infected patients according to the type of hepatitis during the study period (2020-2024)

Our data we collected shows that the highest number of viral cases was recorded to hepatitis A at (~89.18%), followed by hepatitis B at (~7.01%). The lowest percentages were detected in the type C at a rate of (~3.08%) over the study period. The results obtained showed highly statistically significant differences ($p < 0.001$) between types of hepatitis for hepatitis infection. One-way ANOVA reveals a not significant type of hepatitis effect ($p > 0.05$).

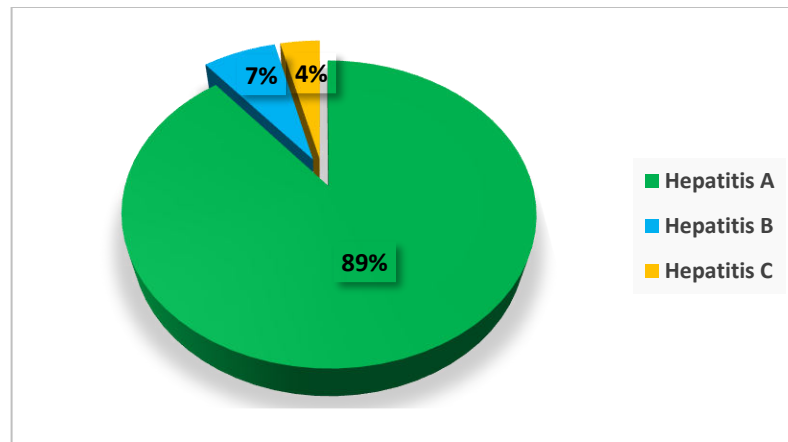


Fig. 27: Distribution of hepatitis-infected patients by types of hepatitis between 2020 and 2024.

3. 1. 2. Specific retrospective analysis of each region of the study area

3. 1. 2. 1. Distribution of patients according to the region during the descriptive study period (2020-2024)

Our data illustrates that during the study period (2020-2024), the Mila region recorded the highest number of patients, accounting for (36,07%) of the total. Following Mila, the Chelghoum Laid region and the Ferdjioua region recorded patient rates of (27,19%) and (24,56%), respectively. Then at last, the Tadjenanet region with a rate of (11,55%). The analysis of the data showed statistically a very highly significant difference between groups for region ($p < ,001$). One-way ANOVA reveals a highly significant region effect ($p < 0.001$). **(Refer to the tables in the Annex section)**

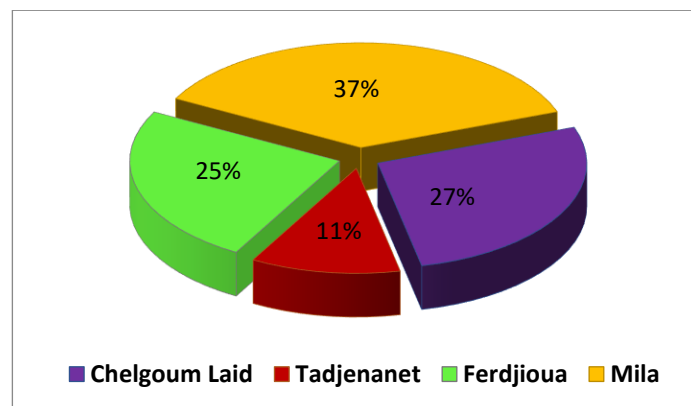


Fig. 28: Distribution of hepatitis-infected patients by region between 2020 and 2024.

3. 1. 2. 2. Distribution of patients according to sex ratio during the descriptive study period (2020-2024)

Our study revealed that the highest prevalence was along men in the regions of Mila, Ferdjioua and Chelghoum Laid at (57,77%), (57,49%), and (53,76%), respectively.

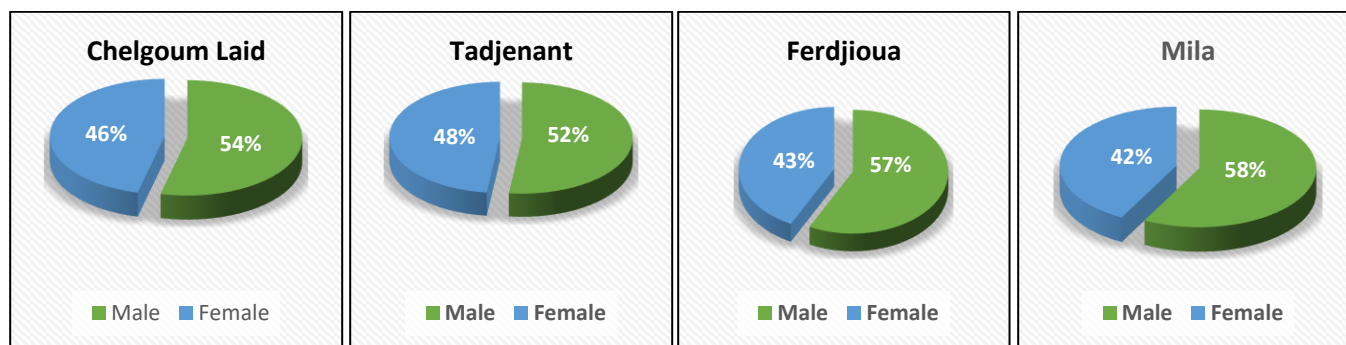
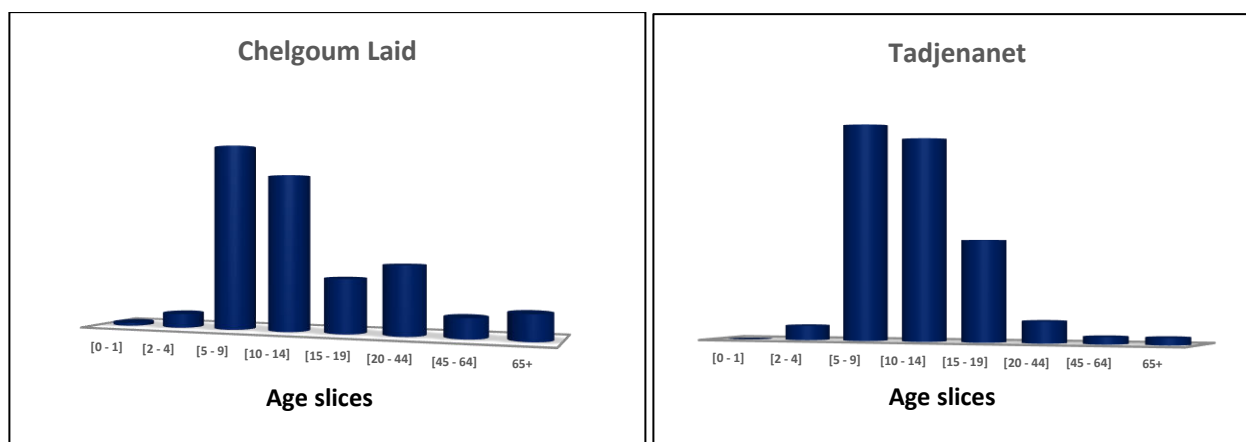


Fig. 29: Regional distribution of infected patients according to the sex ratio during the period (2020-2024).

3. 1. 2. 3. Distribution of infected patients according to age slices during the study period (2020-2024)

Based on our gathered data, we noted that the most affected age group within the four regions of the study is [10-14] years with 80 cases in Mila, 64 cases in Ferdjioua, Chelghoum laid 55 cases in and 28 cases in Tadjnanet, and infection rate of (31,87 %), (38,09 %), (29,56 %), (35,44 %), correspondingly. Conversely in Chelghoum Laid and Tadjnanet region the age slice [5-9] years is the most affected with 66 cases in Chelghoum Laid and 30 cases in Tadjnanet.



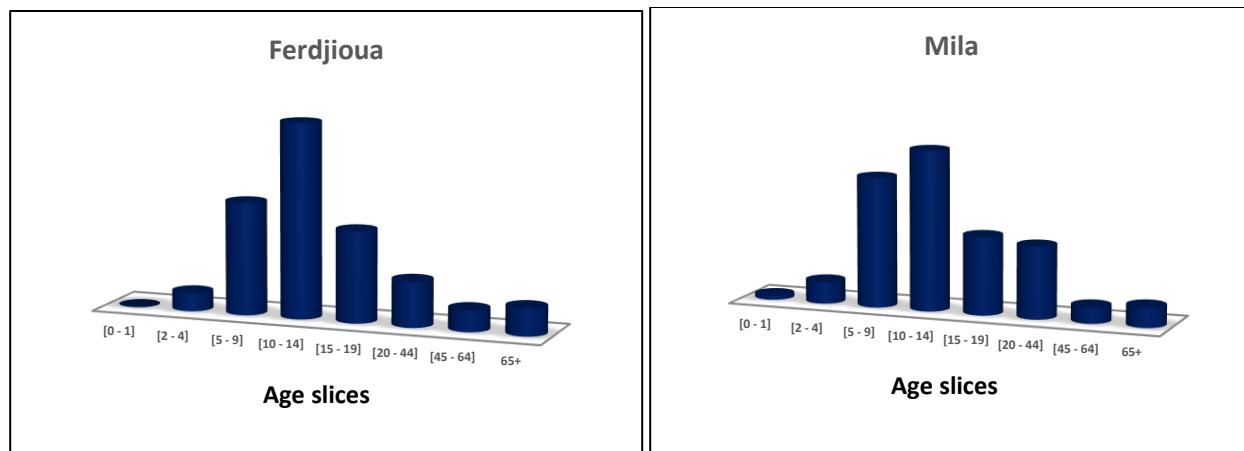
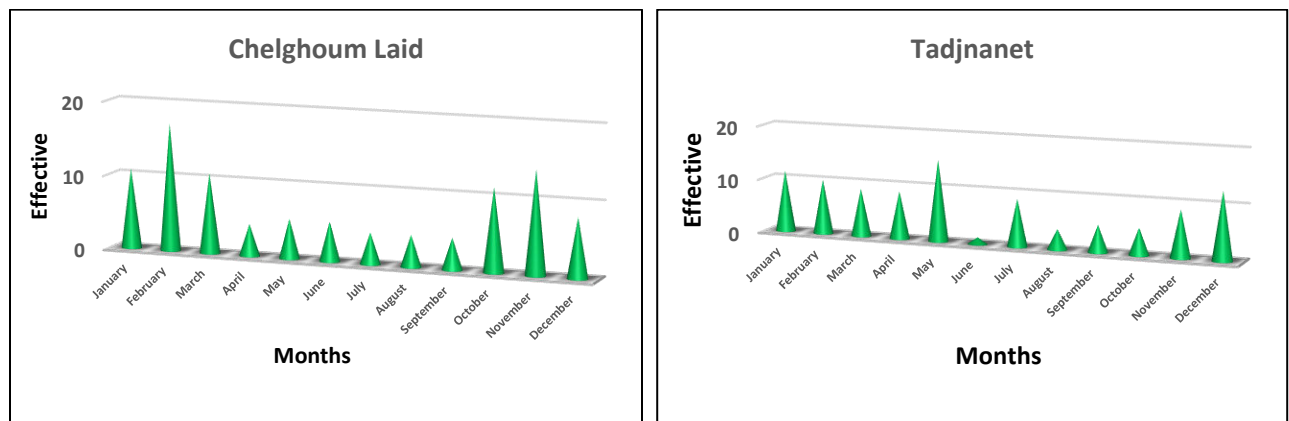


Fig. 30: Regional distribution of infected patients according to age slices during the period (2020-2024).

3. 1. 2. 4. Distribution of infected patients according to the months during the period (2020-2024)

It was indicated by our collected data that the region of Mila shared higher prevalence in April with a rate of (14,46%). While regions like Ferdjioua and Chelghoum Laid shared a high prevalence rate in October and February with a rate of (25%) and (17,2%), respectively. At last, a pattern was also noticed between the regions of Mila and Tadjanet, indicating a common high prevalence rate in May with a rate of (13,65%) and (15,19%), respectively.



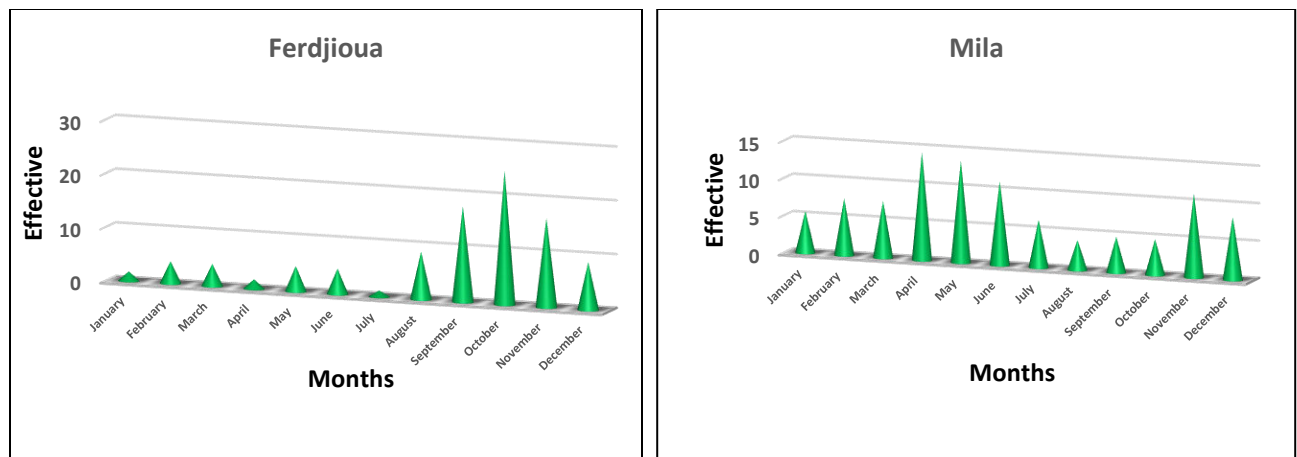


Fig. 31: Regional distribution of infected patients according to the months during the period (2020-2024).

3. 1. 2. 5. Distribution of infected patients according to the seasons during the period (2020-2024)

Based on our data, we noted that the most affected seasons within the four regions of the study is Winter year with 54 cases in Mila, 25 cases in Ferdjioua, Chelghoum laid 67 cases in and 27 cases in Tadjnanet, and infection rate of (21,51 %), (14,88 %), (36,02 %), (34,18 %), correspondingly. Conversely in Ferdjioua region the Autumn season is the most affected with 100 cases and infection rate of 59,52% .Also in Mila region Spring is the season with higher rate of infestation 35,46%.

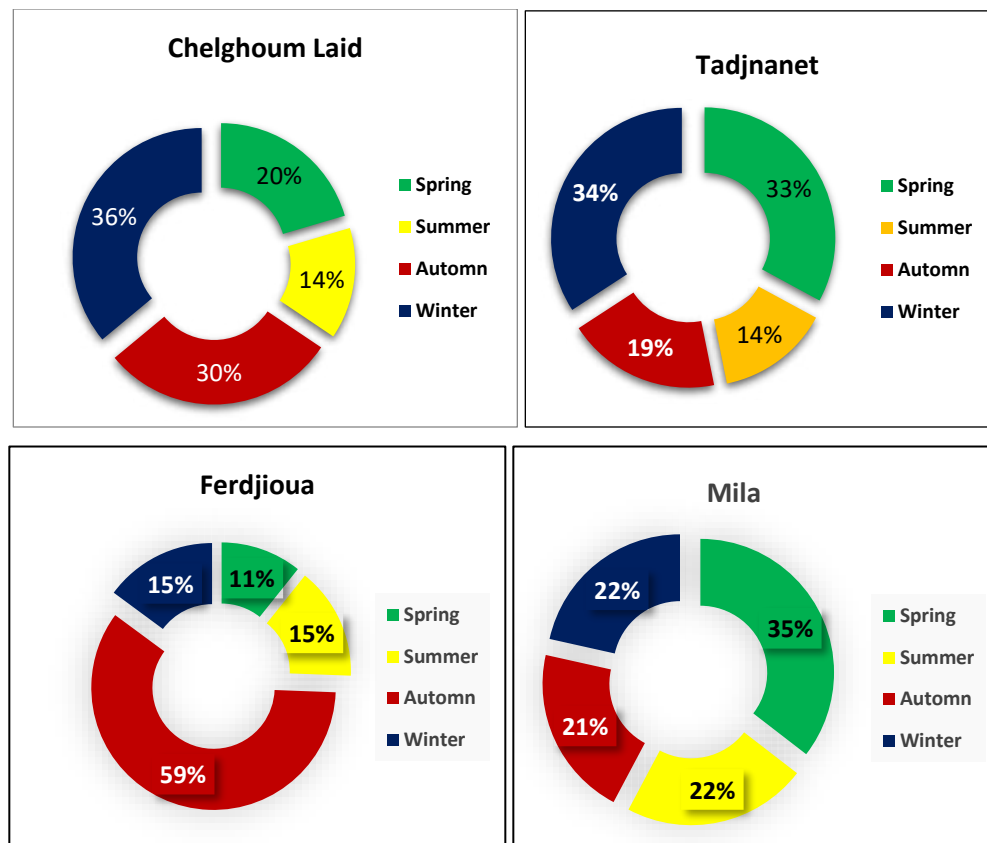


Fig. 32: Regional distribution of infected patients according to the seasons during the period (2020-2024).

3. 1. 2. 6. Distribution of infected patients according to the years during the period (2020-2024)

Based on the data we gathered, we noted that the most affected years within the four regions of the study is 2024 year with 104 cases in Mila, 46 cases in Ferdjioua, Chelghoum laid 79 cases in and 39 cases in Tadjanet, and infection rate of (41,43 %), (27,38 %), (42,77 %), (49,37 %), correspondingly. Conversely in Ferdjioua region the year 2023 is the most affected with 100 cases and infection rate of 59,52% .

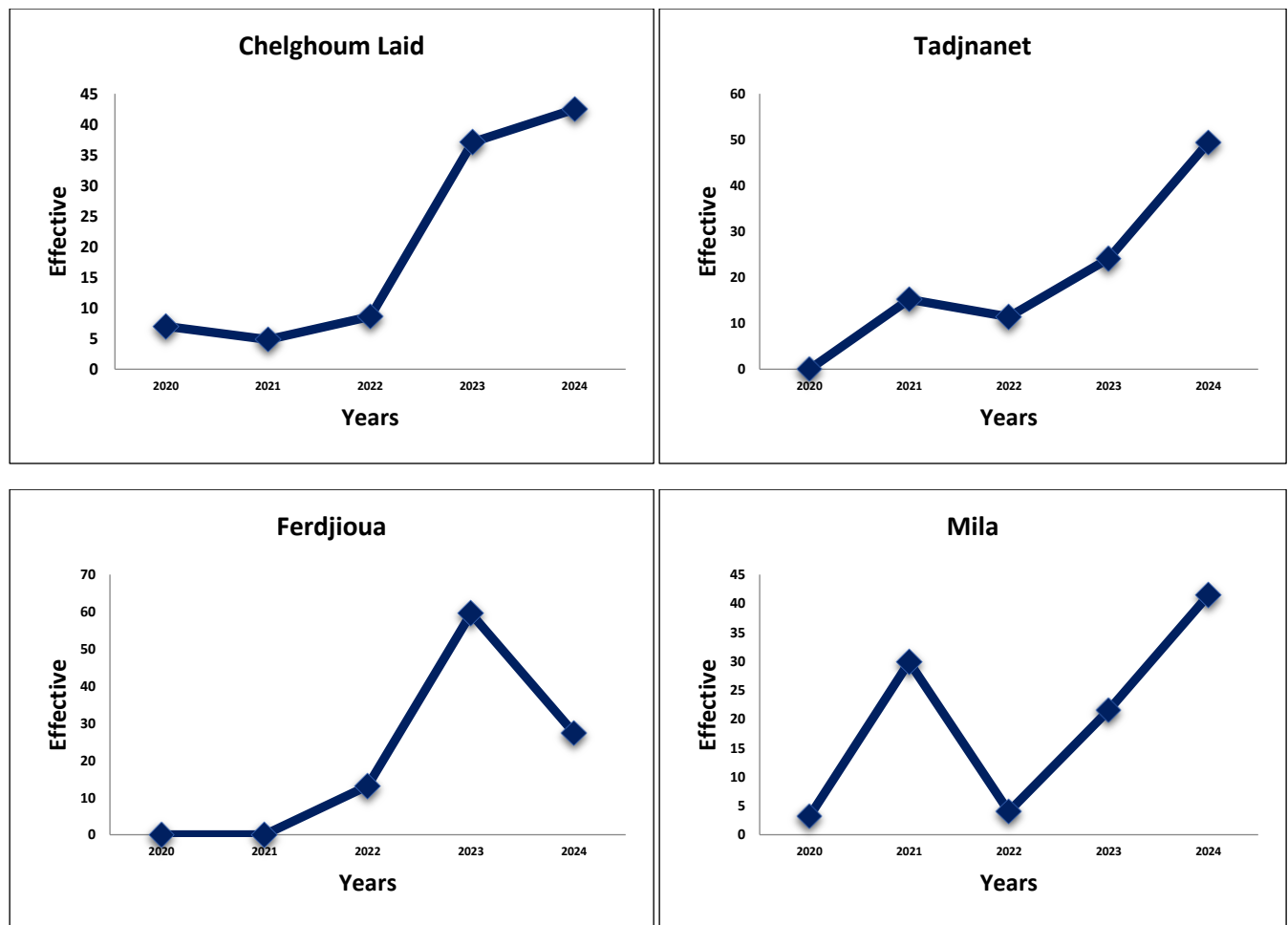


Fig. 33: Regional distribution of infected patients according to the years during the period (2020-2024).

3. 1. 2. 7. Distribution of infected patients according to the type of hepatitis during the period (2020-2024)

The obtained data demonstrates that the number of infected cases in the four regions of study, such as Mila, Tadjanet, Ferdjioua, and Chelghoum Laid, followed a pattern, with the highest infection rates occurring in hepatitis type A, with a rate of (90%) and (94%), (86%) and (88%) respectively.

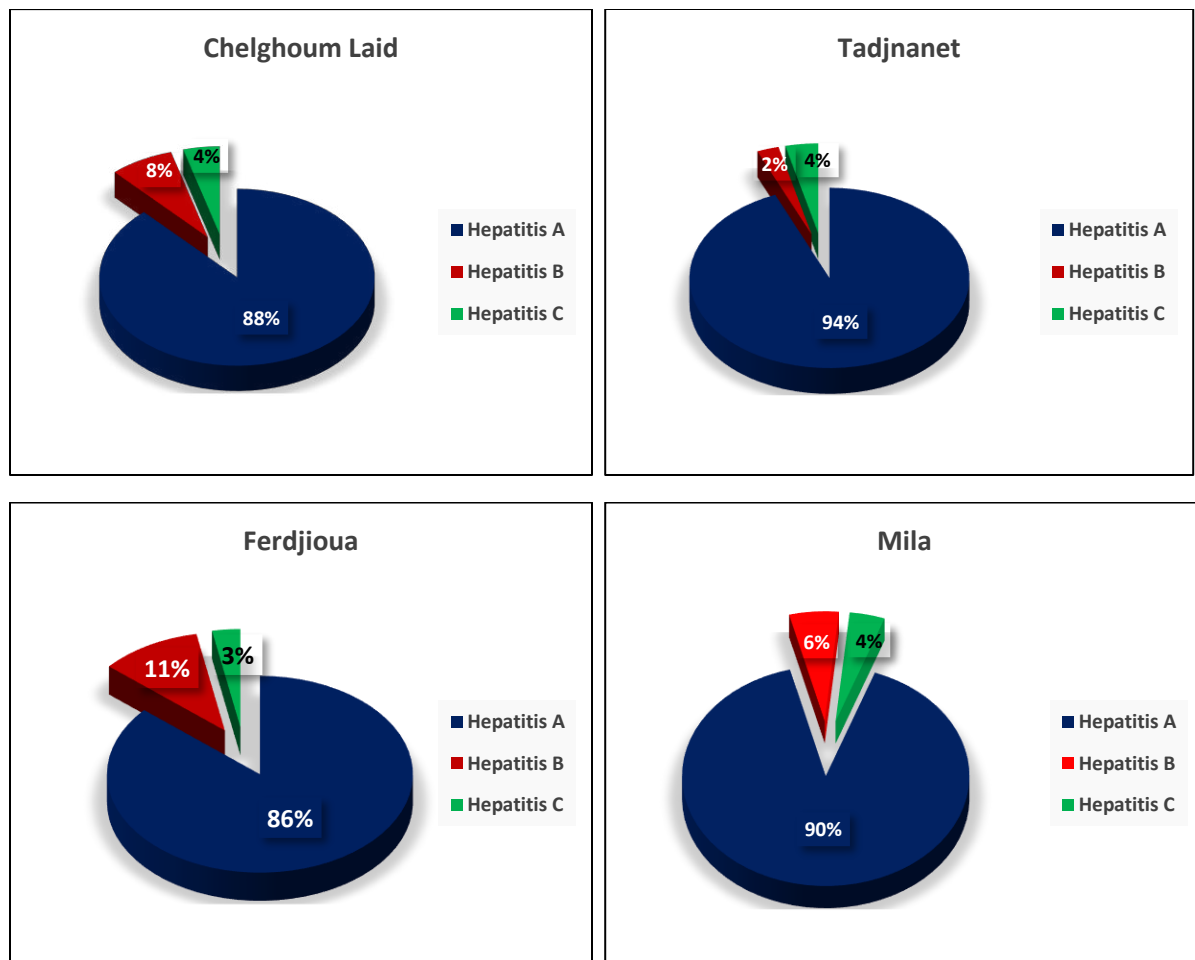


Fig. 34: Regional distribution of infected patients according to the types of hepatitis during the period (2020-2024).

3. 2. Overall prevalence of hepatitis during the prospective study period

Our prospective study was interested in 19 patients who were referred to a virology laboratory in Ferdjioua region during the first five months of 2025 and allows us to perform serologic examination of a sample in its fresh condition and can detect pathogenic Hepatitis virus.

3. 2. 1. Distribution of patients according to sex ratio during the period (January – May 2025)

The data from the figure and the annex table revealed that the most of infected cases were man with a prevalence rate of (58%).

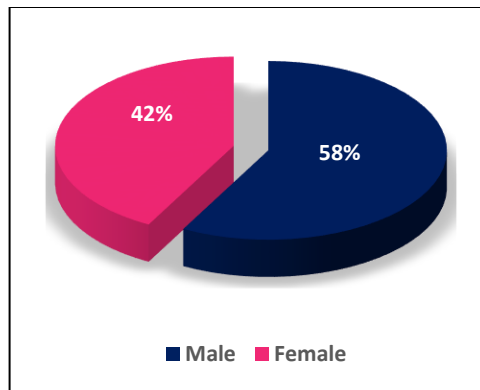


Fig.35: Distribution of hepatitis-infected patients by sex during the period (January – May 2025)

3. 2. 2. Distribution of patients according to age slices during the period (January – May 2025)

We notice that the age group [5-9] ,[15-19] and ≥ 65 years is the most affected with 21.05% followed by the age groups included between [20-44] years with a percentage of 15,79%.

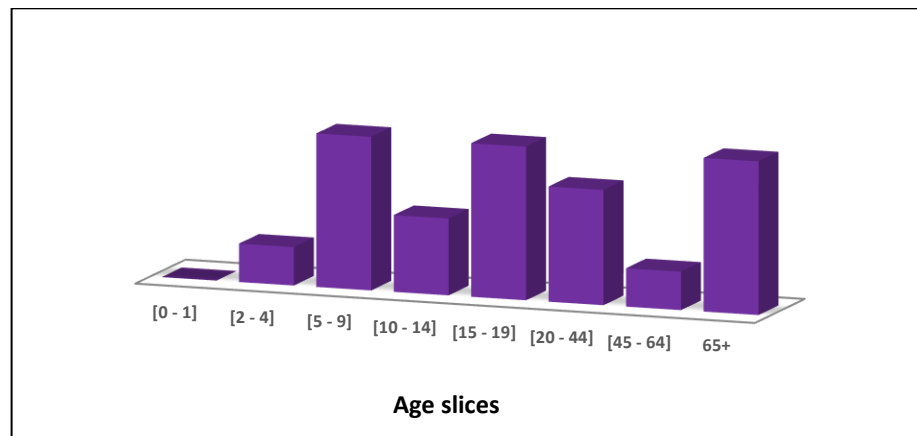


Fig.36: Distribution of hepatitis-infected patients by age slices during the period (January – May 2025).

3. 2. 3. Distribution of patients according to months during the period (January – May 2025)

Our data shows that the highest number of hepatitis cases was noted during the month of February 31, 58%, followed by the months of March and January with and 26,31% 21,05% during the period (January-May 2025).

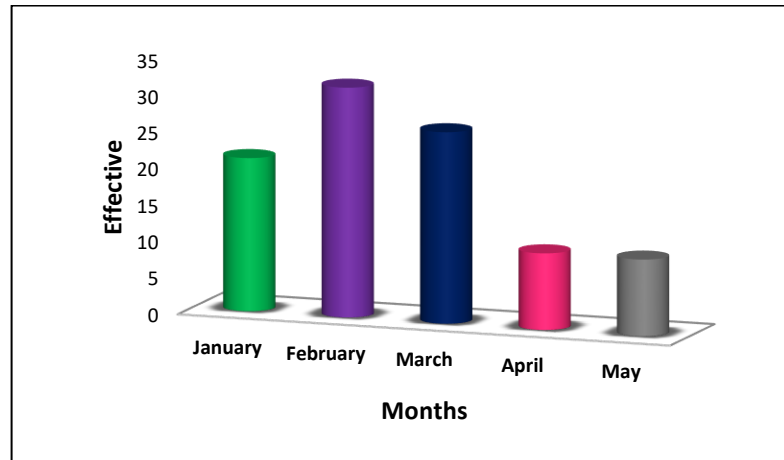


Fig.37: Distribution of hepatitis-infected patients by months during the period (January – May 2025).

3. 2. 4. Distribution of patients according to types of hepatitis during the period (January – May 2025)

According to the data presented, we note that the most affected type of hepatitis is type A with 14 cases and a rate of 73.68%, followed by the type B by 3 cases and a rate of 15,79%.

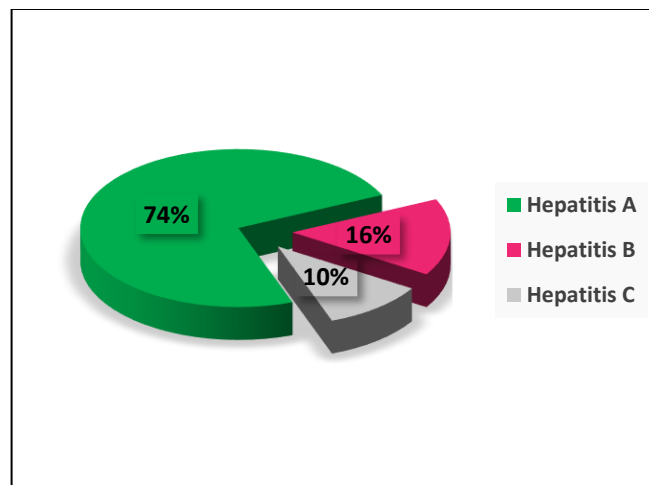


Fig.38: Distribution of hepatitis-infected patients by types of hepatitis during the period (January – May 2025).

3. 3. Correlation between the variation of metrological parameters and the propagation of hepatitis during the period (2020-2024)

To identify the relationship between meteorological parameters and the propagation of human hepatitis in the Mila region, we have used the model of diagram using the SPSS, we implanted generalized linear mixed models to following relationships: effects of T, Sun, P, WS and H on hepatitis dissemination variation. Pearson correlation will be used to clarify the correlation between the dissemination of hepatitis and the variation of different meteorological parameters.

3. 3. 1. The relationship between the variation of the average temperature and the number of infected cases during the period (2020 - 2024)

Linear regression and Pearson correlation analysis (**Fig. 40**) demonstrated that the number of infected patients decreases progressively with the increase in the average temperature. This indicates a very strong negative correlation between the variation in average temperature (°C) and the number of infected patients over the period from 2020 to 2024.

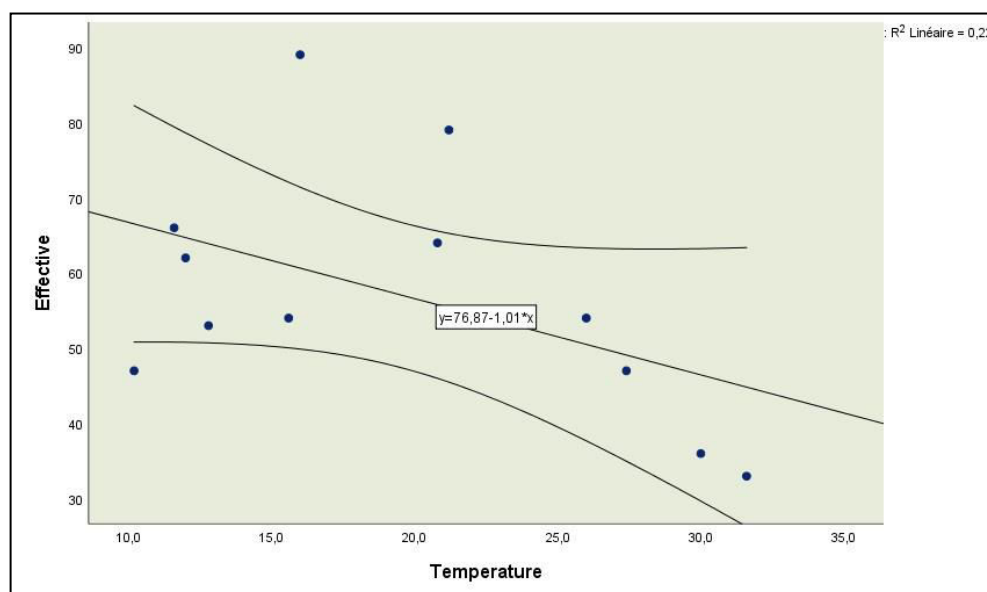


Fig. 39: The correlation between the average temperature (°C) and the number of infected patients according to the months and the season during the study period (2020-2024).

3. 3. 2. The relationship between the variation of the average precipitation and the number of infected cases during the period (2020-2024)

Linear regression and Pearson correlation (**Fig. 40**) showed that the number of infected patients increases progressively with the increase in mean precipitation, so there is a very strong positive

correlation between the variation in mean precipitation (mm) and the number of infected patients during the study period (2020-2024).

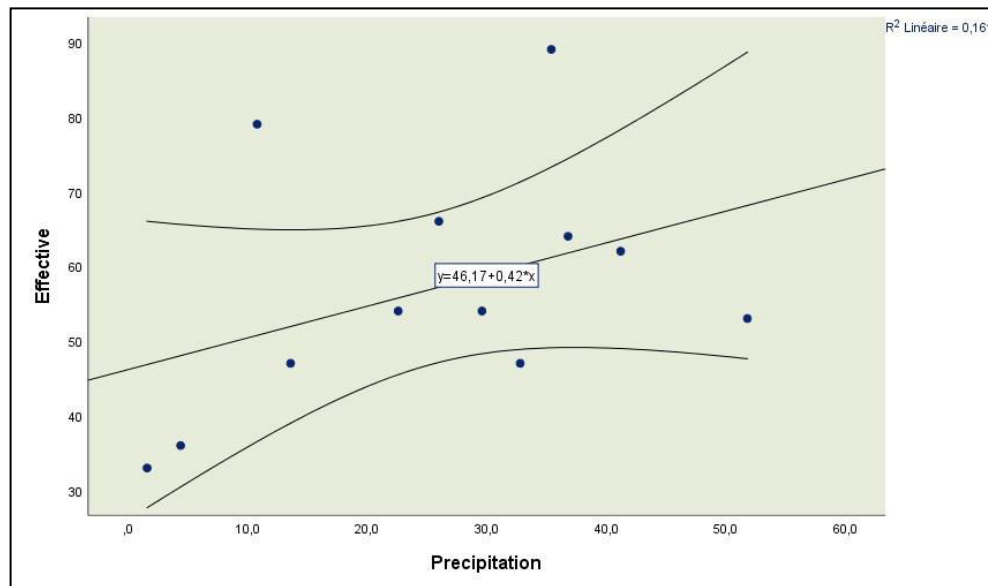


Fig. 40: The correlation between the average precipitation (mm) and the number of infected patients according to the months and the season during the study period (2020-2024).

3. 3. 3. The relationship between the variation of the average wind speed and the number of infected cases during the period (2020-2024)

Linear regression and Pearson correlation (**Fig. 41**) showed that the number of infected cases decreases progressively with the increase in mean wind speed so there is a strong negative correlation between the variation in mean wind speed (knots) and the number of infected patients during the period (2020-2024).

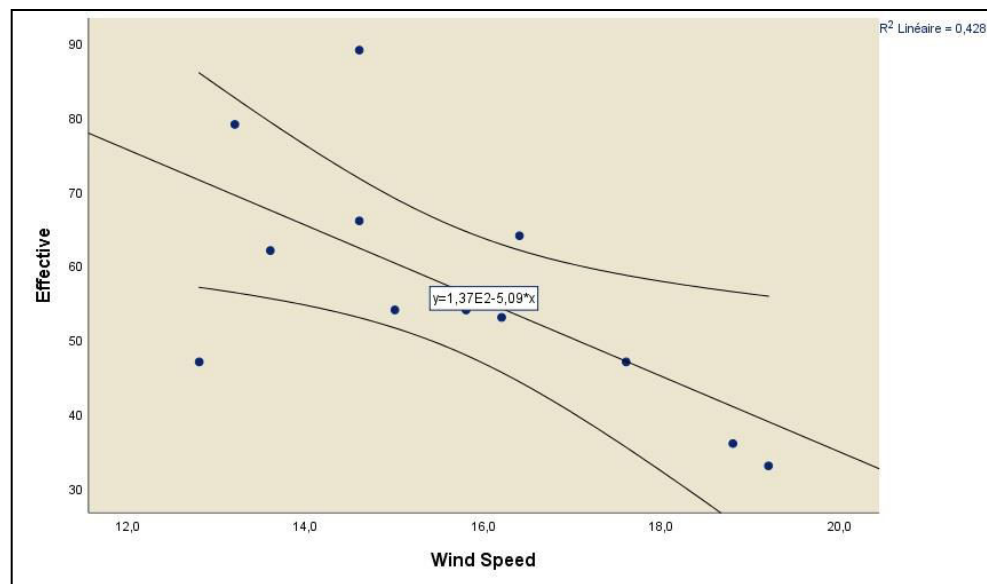


Fig. 41: The correlation between the average wind speed (Knots) and the number of infected patients according to the months and the season during the study period (2020-2024).

3. 3. 4. The relationship between the variation of the average humidity and the number of infected cases during the period (2020-2024)

Linear regression and Pearson correlation (**Fig. 42**) revealed that the number of infected patients increases progressively with increasing humidity, so there is a very strong positive correlation between the average humidity (g/m^3) and the number of infected patients during the study period (2020-2024).

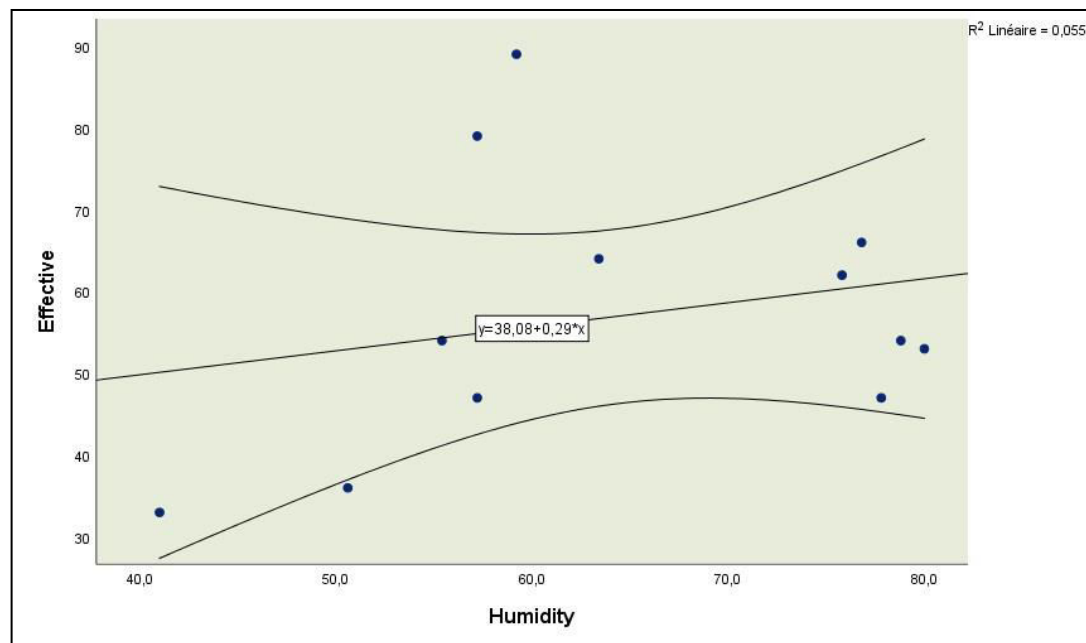


Fig. 42: The correlation between the average humidity (g/m3) and the number of infected patients according to the months and the season during the study period (2020 - 2024).

4.3.5. The relationship between the variation of the average sunshine duration and the number of infected cases during the period (2020-2024)

Linear regression (**Fig. 43**) showed that the number of infected patients decreases progressively with the increase in the average duration of sunshine (hours) so there is a strong negative correlation between the average duration of sunshine (hours) and the number of infected patients during the study period (2020-2024).

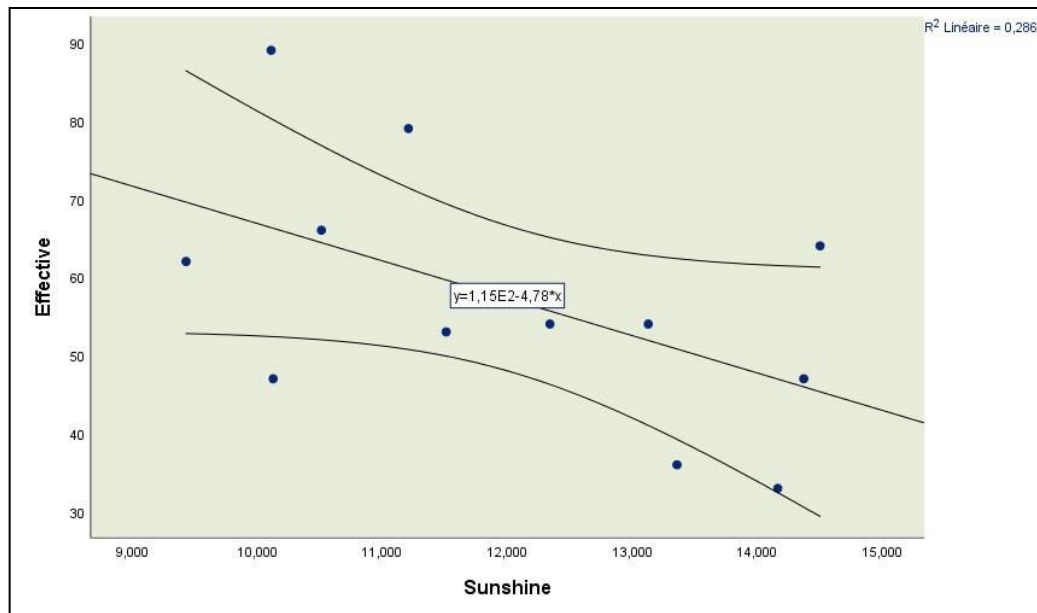


Fig. 43: The correlation between the average sunshine duration (hours) and the number of infected patients according to the months and the season during the study period (2020-2024).

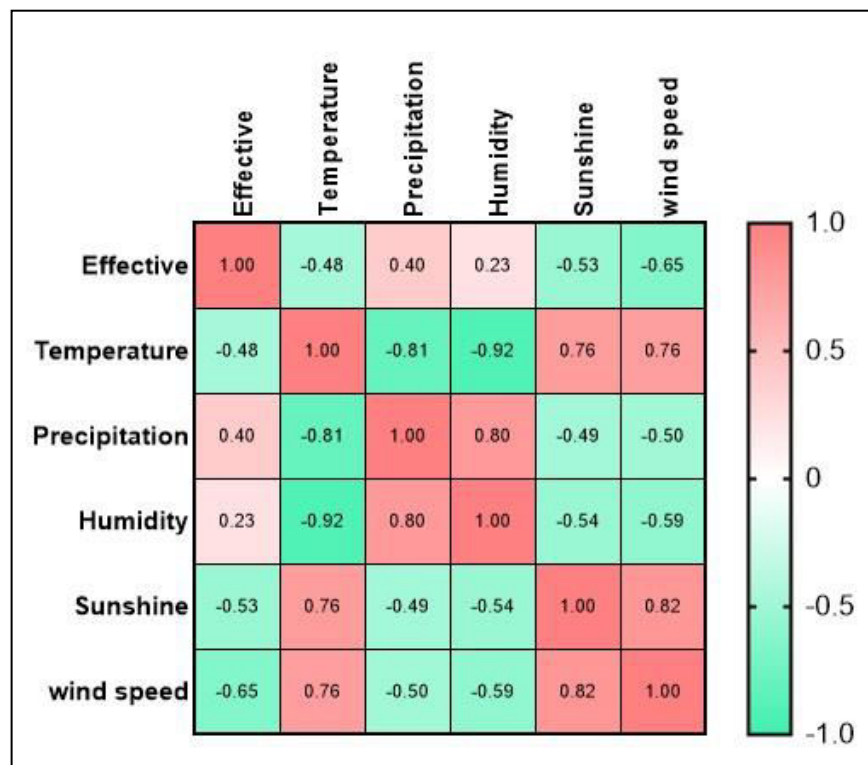


Fig. 44: Correlation matrix applied between meteorological parameters and number of cases of human hepatitis. Pearson correlation tests are given as correlation coefficients.



DISCUSSIONS

4. DISCUSSION

Viral hepatitis is the inflammation of the liver, it is caused by five different viruses named from A to E, and can be either acute or chronic depending on the virus that causes it and how long the infection is. An acute infection tends to be mild and self-resolving but can still be problematic and get as bad as causing fulminant liver failure, while the chronic infection is much more severe can cause fibrosis, cirrhosis, and even liver cancer, in worst cases it can lead to death. **(Dakhli, 2009; Ryder and Beckingham, 2001)**

Our research, alongside a comparison with previous similar ones, allowed us to identify the viral Hepatitis and highlight the relationships between viral propagation and various parameters such as patient age and sex, years, seasons, months, regions of study, and meteorological parameters. We took note of 684 cases of hepatitis from the four Daïras; Chelghoum Laid, Tadjenanet, Ferdjiousa, and Mila through a 5-year period from January 2020 to December 2024, and an additional period between January and May 2025 to confirm our results.

Hepatitis A was the most dominant among patients with an 89,18% (n= 610) out of 684 patients, followed by Hepatitis B with 7.01% (n= 48), and finally Hepatitis C with only 3,80% (n= 26) spread across the regions of study, confirming a previous study on the province that Hepatitis A is the highest spread viral hepatitis type in Mila's province. **(Benayache and al., 2020)**

Regarding the distribution of the disease among the two genders, the higher rate was among male patients (56%) than female patients (44%). The reason behind the infection rate being higher among males may be due to their involvement in outside interactions more frequently than females, commonly jobs and activities that involves coming in contact with contaminated edibles and blood-stained materials like blood transfusion, tattooing and barbering. Meanwhile, female individuals are more involved in household activities. Both cases can vary depending on social, cultural and religious preferences. That hypothesis is confirmed for HAV and HCV's cases were reported among male patients with a (56% and 62% respectively), and was also confirmed during a study done in Japan for an HAV outbreak where 65% of patients were males

(**Takahashi and al., 2006**), and another study in Taiwan related to the same virus which documented a much higher numbers of male patients with many of them getting hospitalized (**Chen and al., 2016**). Another example is from a study done in Egypt regarding HCV's cases where it was found out that 51.31% of 10 044 cases occurred for males than females. (**Soliman and al., 2019**)

Meanwhile HBV had an almost identical infection rate between male (48%) and female patients (52%), which is considered uncommon considering HBV was confirmed to be common among males in the majority of studies. We theorize the reason to be related to body piercings, pregnancy, and cosmetic-related activities female individuals engage in.

Looking into the age groups, HAV was found commonly among children of ages between 5 and 14, while HBV and HCV occurred among older individuals, commonly middle-aged and seniors. HAV's distribution occurs among children due to both interactions with the outside environment and their lack of immunity in comparison with adolescents and adults. The sanitary conditions of a country also plays a role, hence why low and middle-income countries have HAV outbreaks much higher than high-income ones (**Jacobsen, 2018**), confirming our study's results here. As for HBV and HCV's presence among much older patients, it could be either due to unprotected/unsupervised intercourses, procedures done with instruments that can have blood traces left on it if not properly cleaned or disposed (tattooing, vaccination, blood transfusion), or both, something studies done in Iran and Pakistan confirmed where HBV and HCV were found more among seniors above the age of 50 and adults between 20 and 34 respectively. (**Quershi and al., 2010; Zali and al., 1996**)

As for when said cases happen, it was evident that nearly all cases happened during both the autumn (32,46%) and the winter (25,29%) seasons, specifically during months from October to January, it was also during scholar period, which could explain our findings. Yearly-wise, 2023 and 2024 had most of reported cases; this is easily explainable with the fact that there was the COVID-19 pandemic going on world-wide during the period between 2020 and 2022, in which the lockdown limited interactions

between people and the outside environment, limiting the spread of all three hepatitis' viruses.

Onto the infection rate within each Daira, the infection rate was low depending on the count of infected patients and the total population of each Daira. Depending on the number of populations of each region plus how many documented hepatitis infection cases occurring during our period of study, Mila had the highest infection rate with 0,29%, followed by Ferdjioua (0,22%), then Chelghoum Laid (0,11%), and finally Tadjenanet (0,06%). Judging by the sanitary structure, water supplies, and perhaps the surroundings' cleanliness of the Mila Province, we could assume that the infection rate is linked to either some lacking of professional healthcare in some spaces, or that the sanitary condition in both the surroundings and work/school places may be very bad that it helped in spreading hepatitis among inhabitants.

Lastly, as previously stated regarding the season with more hepatitis cases alongside the infection rate within each region and the data given regarding the weather parameters during (2020 – 2024), there are four parameters that contribute to the prevalence of Viral Hepatitis A, B and C: Temperature, Sunshine, Humidity, and Precipitation. Wind Speed was excluded from this study for it doesn't have any correlation to HAV, HBV or HCV's spreading. HAV is more in correlation with the four weather parameters since it transmits through contaminated water/food and fecal-oral way, meanwhile HBV and HCV's transmission and spread is slightly affected by temperatures only given the fact that the two are blood-borne pathogens.



CONCLUSION

5. CONCLUSION

Our descriptive analytical study took place in the Public Organization for Neighborhood Health across each of the four regions of study in Mila's Province to study the data taken from the period of January 2020 to December 2024, add to it a five-month prospective study that took place in the same building in Ferdjioua from January to May 2025.

The low infection rate in each region confirms that the healthcare side may be even the hygiene one is slowly improving over time. Hepatitis was found more among male than female individuals, which may be due to the fact that males often interact with the outer world more than females, which can vary depending on the region's cultures, religion and social influence and preference.

Those that carried hepatitis A were children between 5 to 14 years old; meanwhile Hepatitis B and C were noted among middle-aged and senior patients, age from 45 to 65+ years old. Children are the most active individuals when it comes to outside interactions, add to it them not having the best immunity to HAV compared to their adult counterparts, and as for our other category of patients, HBV and HCV is common among that old age may be due to sharing equipment that could have a trace of blood contaminated with one of the viruses, mainly shaving tools, tattooing tools, needles, and so on.

Hepatitis A has the highest prevalence in the region with close to 90% of cases we studied.

Our prospective study from January to May 2025 corroborates findings from the retrospective analysis, reinforcing observations on seasonal and annual trends in hepatitis incidence. Moreover, our investigation highlighted the significant influence of climatic conditions, particularly in the Mila region. Decreased humidity and precipitation levels were associated with reduced dissemination of hepatitis. Conversely, higher average temperature, sunshine duration, and monthly wind speeds correlated with decreased virus indices.

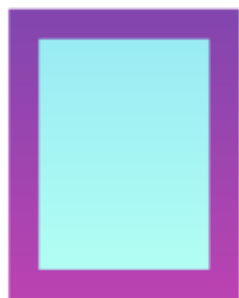
So, our study offers a comprehensive regional perspective on the epidemiology of hepatitis, emphasizing the complex interplay between environmental factors and disease transmission dynamics. These findings underscore the critical need for ongoing

surveillance and targeted interventions to mitigate the impact of climatic variability on public health in these regions.

These findings can be explained by several scientific reasons we made sure we discussed. These findings suggest that climatic conditions play a significant role in the epidemiology of hepatitis, influencing the survival, proliferation, and transmission of this virus in the environment.

The need to apply preventive measures is a policy of general and individual prophylaxis and an improvement in the social level in our country, such as rules of hygiene, vaccination against hepatitis A, B, and C, protected sexual relations, individual use of items that can be contaminated with blood (toothbrushes, razors, nail clippers, needles, drug snorting/smoking equipment), screening and treatment of infected subjects, will certainly lead to a considerable decrease in the prevalence of this disease.

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ANNEX

Table 09: Distribution of infected patients according to the sex ratio during the study period (2020-2024).

Sex	Effective	SVI%
Male	382	~55.84 (56)
Female	302	~44.15 (44)
Total	684	100

Table 10: Distribution of infected patients according to age slices during the period (2020-2024).

Age slices	Effective	SVI%
[0-1]	3	~0,44
[2-4]	24	~3,51
[5-9]	198	~28,95
[10-14]	227	~33,19
[15-19]	102	~14,91
[20-44]	78	~11,4
[45-64]	23	~3,36
[65+]	29	~4,24
Total	684	100

Table 11: Distribution of infected patients by months during the period (2020-2024).

Month	Effective	SVI%
January	47	6,87
February	66	9,65
March	53	7,75
April	54	7,89
May	64	9,36
June	47	6,87
July	33	4,82
August	36	5,26
September	54	7,9
October	79	11,55
November	89	13,01
December	62	9,07
Total	684	100

Table 12: Distribution of infected patients according to the season during the period (2020-2024).

Season	N° of individuals	SVI%
Spring	171	~25
Summer	118	~17,25
Autumn	222	~32,46
Winter	173	~25,29
Total	684	100

Table 13: Distribution of infected patients according to the years during the period (2020-2024).

Year	Effective	SVI%
2020	21	3,07
2021	96	14,04
2022	57	8,33
2023	242	35,38
2024	268	39,18
Total	684	100

Table 14: Distribution of patients according to the type of hepatitis during the descriptive study period (2020-2024).

Type	Effective	SVI%
Hepatitis A	610	89,1813
Hepatitis B	48	7,01754
Hepatitis C	26	3,80117
Total	684	100

Table 15: Distribution of patients according to the region during the descriptive study period (2020-2024).

Region	Effective	SVI%
Chelghoum laid	186	27,19
Ferdjioua	168	24,56
Mila	251	36,7
Tadjenanet	79	11,55
Total	684	100

Table 16: Regional distribution of patients according to the sex ratio of each region during the study period (2020-2024).

Mila

Sex	Count	%	~
Male	145	57,76892	57,77
Female	106	42,23108	42,23
Total	251	100	100

Chelghoum Laid

Sex	Count	%	~
Male	100	53,76344	53,76
Female	86	46,23656	46,24
Total	186	100	100

Tadjenanet

Sex	Count	%	~
Male	41	51,89873	51,9
Female	38	48,10127	48,1
Total	79	100	100

Ferdjioua

Sex	Count	%	~
Male	96	57,48503	57,49
Female	72	42,51497	42,51
Total	168	100	100

Table 17: Regional distribution of patients according to age groups of each region during the study period (2020-2024).**Mila**

Age Group	Count	%	~
[0 - 1]	2	0,796813	0,8
[2 - 4]	11	4,38247	4,38
[5 - 9]	65	25,89641	25,9
[10 - 14]	80	31,87251	31,87
[15 - 19]	39	15,53785	15,54
[20 - 44]	36	14,34263	14,34
[45 - 64]	8	3,187251	3,19
65+	10	3,984064	3,98
Total	251	100	100

Ferdjioua

Age Group	Count	%	~
[0 - 1]	0	0	0
[2 - 4]	6	3,571429	3,57
[5 - 9]	37	22,02381	22,02
[10 - 14]	64	38,09524	38,1
[15 - 19]	30	17,85714	17,86
[20 - 44]	15	8,928571	8,92
[45 - 64]	7	4,166667	4,17
65+	9	5,357143	5,36
Total	168	100	100

Tadjenanet

Age Group	Count	%	~
[0 - 1]	0	0	0
[2 - 4]	2	2,531646	2,53
[5 - 9]	30	37,97468	37,97
[10 - 14]	28	35,44304	35,44
[15 - 19]	14	17,72152	17,72
[20 - 44]	3	3,797468	3,8
[45 - 64]	1	1,265823	1,27
65+	1	1,265823	1,27
Total	79	100	100

Chelghoum Laid

Age Group	Count	%	~
[0 - 1]	1	0,537634	0,54
[2 - 4]	5	2,688172	2,69
[5 - 9]	66	35,48387	35,48
[10 - 14]	55	29,56989	29,57
[15 - 19]	19	10,21505	10,22
[20 - 44]	24	12,90323	12,9
[45 - 64]	7	3,763441	3,76
65+	9	4,83871	4,84
Total	186	100	100

Table 18: Regional distribution of patients according to the months of each region during the study period (2020-2024).**Chelghoum Laid**

Month	Count	%	~
January	20	10,75269	10,75
February	32	17,2043	17,2
March	20	10,75269	10,75
April	8	4,301075	4,3
May	10	5,376344	5,38
June	10	5,376344	5,38
July	8	4,301075	4,3
August	8	4,301075	4,3
September	8	4,301075	4,3
October	21	11,29032	11,29
November	26	13,97849	13,98
December	15	8,064516	8,07
Total	186	100	100

Tadjenanet

Month	Count	%	~
January	9	11,39241	11,39
February	8	10,12658	10,13
March	7	8,860759	8,86
April	7	8,860759	8,86
May	12	15,18987	15,19
June	1	1,265823	1,27
July	7	8,860759	8,86
August	3	3,797468	3,8
September	4	5,063291	5,06
October	4	5,063291	5,06
November	7	8,860759	8,86
December	10	12,65823	12,66
Total	79	100	100

Ferdjioua

Month	Count	%	~
January	3	1,785714	1,78
February	7	4,166667	4,17
March	7	4,166667	4,17
April	3	1,785714	1,78
May	8	4,761905	4,76
June	8	4,761905	4,76
July	2	1,190476	1,19
August	15	8,928571	8,93
September	30	17,85714	17,86
October	42	25	25
November	28	16,66667	16,67
December	15	8,928571	8,93
Total	168	100	100

Mila

Month	Count	%	~
January	14	5,62249	5,62
February	19	7,630522	7,63
March	19	7,630522	7,63
April	36	14,45783	14,46
May	34	13,65462	13,65
June	28	11,24498	11,25
July	16	6,425703	6,43
August	10	4,016064	4,02
September	12	4,819277	4,82
October	12	4,819277	4,82
November	28	11,24498	11,24
December	21	8,433735	8,43
Total	249	100	100

Table 19: Regional distribution of patients according to the seasons of each region during the study period (2020-2024).

Chelghoum Laid

Season	Count	%	~
Spring	38	20,43011	20,43
Summer	26	13,97849	13,98
Automn	55	29,56989	29,57
Winter	67	36,02151	36,02
Total	186	100	100

Tadjenanet

Season	Count	%	~
Spring	26	32,91139	32,91
Summer	11	13,92405	13,92
Automn	15	18,98734	18,99
Winter	27	34,17722	34,18
Total	79	100	100

Ferdjioua

Season	Count	%	~
Spring	18	10,71429	10,72
Summer	25	14,88095	14,88
Automn	100	59,52381	59,52
Winter	25	14,88095	14,88
Total	168	100	100

Mila

Season	Count	%	~
Spring	89	35,45817	35,46
Summer	56	22,31076	22,31
Automn	52	20,71713	20,72
Winter	54	21,51394	21,51
Total	251	100	100

Table 20: Regional distribution of patients according to the years of each region during the study period (2020-2024).

Chelghoum Laid

Year	Count	%	~
2020	13	6,989247	6,99
2021	9	4,83871	4,84
2022	16	8,602151	8,6
2023	69	37,09677	37,1
2024	79	42,47312	42,47
Total	186	100	100

Tadjenanet

Year	Count	%	~
2020	0	0	0
2021	12	15,18987	15,19
2022	9	11,39241	11,39
2023	19	24,05063	24,05
2024	39	49,36709	49,37
Total	79	100	100

Ferdjioua

Year	Count	%	~
2020	0	0	0
2021	0	0	0
2022	22	13,09524	13,1
2023	100	59,52381	59,52
2024	46	27,38095	27,38
Total	168	100	100

Mila

Year	Count	%	~
2020	8	3,187251	3,19
2021	75	29,88048	29,88
2022	10	3,984064	3,99
2023	54	21,51394	21,51
2024	104	41,43426	41,43
Total	251	100	100

Table 21: Regional distribution of patients according to the type of hepatitis of each region during the study period (2020-2024).

Chelghoum Laid

Hepatitis Type	Count	%	~
Hepatitis A	164	88,17204	88,17
Hepatitis B	14	7,526882	7,53
Hepatitis C	8	4,301075	4,3
Total	186	100	100

Tadjenanet

Hepatitis Type	Count	%	~
Hepatitis A	74	93,67089	93,67
Hepatitis B	2	2,531646	2,53
Hepatitis C	3	3,797468	3,8
Total	79	100	100

Ferdjioua

Hepatitis Type	Count	%	~
Hepatitis A	145	86,30952	86,31
Hepatitis B	18	10,71429	10,71
Hepatitis C	5	2,97619	2,98
Total	168	100	100

Mila

Hepatitis Type	Count	%	~
Hepatitis A	227	90,43825	90,44
Hepatitis B	14	5,577689	5,58
Hepatitis C	10	3,984064	3,98
Total	251	100	100

Table 22: Distribution of patients according to sex ratio during the period (January – May 2025)

Sex	Count	%	~
Male	11	57,8947	57,89
Female	8	42,1053	42,11
Total	19	100	100

Table 23: Distribution of patients according to age groups during the period (January – May 2025)

Age Group	Count	%	~
[0 - 1]	0	0	0
[2 - 4]	1	5,26316	5,27
[5 - 9]	4	21,0526	21,05
[10 - 14]	2	10,5263	10,53
[15 - 19]	4	21,0526	21,05
[20 - 44]	3	15,7895	15,79
[45 - 64]	1	5,26316	5,26
65+	4	21,0526	21,05
Total	19	100	100

Table 24: Distribution of patients according to the months during the period (January – May 2025)

Month	Count	%	~
January	4	21,0526	21,05
February	6	31,5789	31,58
March	5	26,3158	26,31
April	2	10,5263	10,53
May	2	10,5263	10,53
Total	19	100	100

Table 25: Distribution of patients according to types of hepatitis during the period
(January – May 2025)

Hepatitis Type	Count	%	~
Hepatitis A	14	73,6842	73,68
Hepatitis B	3	15,7895	15,79
Hepatitis C	2	10,5263	10,53
Total	19	100	100

One-Sample Test

Test Value = 0

	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Sex	265,861	6030	,000	1,642	1,63	1,65
Age	345,839	6030	,000	6,158	6,12	6,19
Month	149,121	6030	,000	6,402	6,32	6,49
Seasons	180,970	6030	,000	2,502	2,47	2,53
Years	147,392	6030	,000	6,042	5,96	6,12
Type	58,909	6030	,000	2,875	2,78	2,97
Region	200,228	6030	,000	3,123	3,09	3,15

ANOVA ONE WAY

		Sum of Squares	df	Mean Square	F	Sig.
Sex	Between Groups	2,898	10	,290	1,261	,247
	Within Groups	1383,783	6020	,230		
	Total	1386,680	6030			
Age	Between Groups	52,721	10	5,272	2,766	,002
	Within Groups	11476,320	6020	1,906		
	Total	11529,041	6030			
Month	Between Groups	227,307	10	22,731	2,048	,025
	Within Groups	66806,822	6020	11,097		
	Total	67034,129	6030			
Seasons	Between Groups	24,171	10	2,417	2,100	,021
	Within Groups	6927,553	6020	1,151		
	Total	6951,724	6030			
Type	Between Groups	194,915	10	19,492	1,358	,193
	Within Groups	86422,819	6020	14,356		
	Total	86617,734	6030			
Region	Between Groups	66,649	10	6,665	4,571	,000
	Within Groups	8777,798	6020	1,458		
	Total	8844,448	6030			

MANOVA

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	Sex	3,350 ^a	12	,279	1,215	,266
	Age	57,235 ^b	12	4,770	2,502	,003
	Region	68,852 ^c	12	5,738	3,935	,000
	Type	320,651 ^d	12	26,721	1,863	,034
Intercept	Sex	2316,609	1	2316,609	10078,109	,000
	Age	32431,510	1	32431,510	17013,261	,000
	Region	8260,982	1	8260,982	5665,095	,000
	Type	5703,377	1	5703,377	397,730	,000
Month	Sex	,383	1	,383	1,664	,197
	Age	,084	1	,084	,044	,834
	Region	,003	1	,003	,002	,962
	Type	47,264	1	47,264	3,296	,069
Seasons	Sex	,023	1	,023	,099	,753
	Age	3,501	1	3,501	1,837	,175
	Region	1,518	1	1,518	1,041	,308
	Type	9,649	1	9,649	,673	,412
Years	Sex	2,926	10	,293	1,273	,240
	Age	52,906	10	5,291	2,775	,002
	Region	66,708	10	6,671	4,575	,000
	Type	201,458	10	20,146	1,405	,171
Error	Sex	1383,330	6018	,230		
	Age	11471,806	6018	1,906		
	Region	8775,596	6018	1,458		
	Type	86297,083	6018	14,340		
Total	Sex	17641,000	6031			
	Age	240207,000	6031			
	Region	67648,000	6031			
	Type	136467,000	6031			
Corrected Total	Sex	1386,680	6030			
	Age	11529,041	6030			
	Region	8844,448	6030			
	Type	86617,734	6030			