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Outbreak-Associated Cases Of Human Hepatitis Viruses (HAV, HBV & HCV) With Herpes Simplex Virus And HIV Infections Detected in Blood-Based Biomarkers

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ABSTRACT: *Hepatitis A vaccines are based on classic first-generation inactivated virus vaccines and have been developed by different biopharmaceuticals. HAV is found in the stool, blood of people who are infected and foodborne hepatitis. HBV is a short-term disease and is one of the major causative agents of chronic liver illness. For others, it can become a long-term, chronic infection like liver disease or liver cancer. The analysis of genomic variability of HBV isolates is fundamental for molecular and epidemiological studies. HCV has a higher rate of mutation existing inside an individual as quasispecies. In this sense, this study addresses an analysis of viral hepatitis A/B/C, Herpervirus Simplex (HSV) type 1/2 and the human immunodeficiency virus (HIV) as topics related to comprehensive care for people with sexually transmitted infections (STIs). A total of 2.750 samples were collected from 2.713 patients, of which 38,43% were for HCV; 31,20% for HIV research; 30,25% for HAV and 0,10% for HSV. In all, eight biomarkers of the hepatitis B virus (HBV) were investigated, of which the HBsAg marker was non-reactive in 44,01% (2022 y) and 47.66% (2023 y). About 31,41% (2022 y) and 31.99% (2023y) were reactive for anti-HBs. The highest percentage of investigated samples (98.38%) was recorded in March 2022 with a average proportion of 55.25 ± 12.96 (CV = 0.234) for the non reactive IgM biomarker. The authors suggest follow-up with new serological research associated with molecular assays aimed specifically at reactive and inconclusive results.*

KEY WORDS: Outbreak-associated, blood serum, biomarkers, hepatitis viruses.

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INTRODUCTION

The laboratory medical corporate organization aims to establish, implement, and maintain the continuous improvement of the management system to ensure better delivery of its products with efficiency and compliance in the provision of proposed services. Strategically meet the needs and expectations of the market to satisfy the target customer and standardize the lab's department through standard operating procedures for greater competitiveness and process optimization. Several study models select and characterize aptamers considered analogues of monoclonal antibodies, as promising candidates for various therapeutic applications in viral infections [1].

Hepatitis A virus (HAV)

Hepatitis A virus (HAV) belongs to the *Pircornaviridae* family, genus Hepatovirus. The occurrence of outbreaks of hepatitis A in recreational water and drinking water have been reported since it´s an enteric virus transmitted by the fecal-oral route in which the ingestion of contaminated water and food or even direct contact with people the person are forms of viral infection. Among the classic symptoms, there is jaundice, choluria and fecal acholia [2, 3, 4].

Hepatitis A vaccines are based on classic first-generation inactivated virus vaccines and have been developed by different biopharmaceuticals such as Havrix® (Glaxo Smith Kline Biologicals), Twinrix® also by the same biopharma, but in this case it is a multiple compound vaccine by several immunogens, and the vaccine VAQTA® from the manufacturer Merck & Co. With regard to the same biopharmaceutical, the vaccine against Herpes-zoster (Merck & Co) developed the so-called Zostavax® with attenuated live virus available on the market. Herpes simplex viruses type 1 and 2 belong to risk class 2 of the laboratory biosafety level [3].

Hepatitis A is a vaccine-preventable liver infection caused by the hepatitis A virus (HAV). HAV is found in the stool and blood of people who are infected and most people with hepatitis A do not have long-lasting illness. Hepatitis A can be transmitted through close personal contact with an infected person or through eating contaminated food or drink [5]. About 10 outbreak-associated cases of hepatitis A reported that frozen organic strawberries are the likely source of this outbreak. The hepatitis A virus strain causing illnesses in this outbreak is genetically identical to the strain that caused a foodborne hepatitis A outbreak in 2022, which was linked to fresh organic strawberries imported. Symptoms of hepatitis A usually appear 2 to 7 weeks after exposure and can include Yellow skin or eyes; not wanting to eat; upset stomach; stomach pain; throwing up; fever; dark urine or light-colored stools; joint pain; diarrhea and feeling tired [5].

Hepatitis B virus (HBV)

Hepatitis B virus (HBV) is classified in the *Hepadnaviridae* family divided into two genera: *Orthohepadnavirus* and *Avihepadnavirus* [2]. The genome is composed of a

3,200base pairs (bp) of a circular double stranded DNA presenting four open reading frames (ORFs) designated as: Pre–S/S, Pre C/C, P and X. The Pre–S/S ORF corresponds to the Hepatitis virus surface gene (HBsAg). The Pre–S1, Pre–S2 and S regions have three initiation codons in the same reading phase that, after being translated, originate the proteins: L "Large" (400aa), Middle "M" (281aa) and "Small" (226aa). These three proteins that comprise the HBsAg are found in the serum of infected individuals in two ways: Small glycosylated (GP27) and Small non–glycosylated (P24), Middle glycosylated (GP33) and Middle di-glycosylated (GP36), and Large glycosylated (GP42) and Large non–glycosylated L (P39). HBV B is a short-term disease and is one of the major causative agents of chronic liver illness. For others, it can become a long-term, chronic infection like liver disease or liver cancer [3, 5].

It is estimated that about 350million people worldwide are carriers of the HBV and approximately 2 million are infected individuals in Brazil. The first reports of variability of the Hepatitis B virus (HBV) were described by Le Bouvier (1971), who identified two mutually exclusive antigenic determinants, d and y, located in HBsAg. Two additional determinants, w and r, were subsequently enunciated by Bancroft et al. (1972). Thus, nine subtypes have been described: ayw1, ayw2, ayw3, ayw4, adw2, adw4, ayr, adrq+ and adrq–, which share a common conformational epitope present in HBsAg. There are eight HBV genotypes (identified as A–H) that exhibit more than 8% divergence between complete genomic sequences. The analysis of genomic variability of HBV isolates is fundamental for molecular and epidemiological studies [3].

HBV infection produces two types of viral particles: full, spherical, HBV genome–containing infectious particles (42nm), as well as non–infectious spherical or filamentous (22nm) subviral particles composed exclusively of HBsAg. An expression system (as used in the Papilloma vaccines, the first recombinant vaccine licensed and produced from yeast expression) was used for Hepatitis B surface– antigen isolation from human plasma of chronic HBV patients (Heptavax–B, Merck & Co), and was released in 1981.16 Worldwide over the last 30years, HBsAg has been used as a commercial vaccine against hepatitis B. It is best way to prevent HBV among aged 18-59 may get the vaccine [5]. The Advisory Committee on Immunization Practices (ACIP) recommends hepatitis B vaccination among all adults aged 19–59 years and adults >60 years with risk factors for hepatitis B [5].

Actually, there are two types of successful vaccines based on virus–like particles (VLP) involving Hepatitis B virus surface antigen (HBsAg) and core antigen (HBcAg) expressed in *Escherichia coli*. Conditions on the immunogenicity can be tested in mice with alternative routes of administration of HBV vaccine and novel formulations assays. The development of recombinant vaccines composed exclusively of HBsAg (Engerix–B, SmithKline and Recombivax, Merck & Co) was possible with the advance of genetic engineering. Clinicians should screen all adults aged 18 years and older for HBV infection at least once during their lifetime using the triple panel test which includes hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and total

antibody to hepatitis B core antigen total (anti-HBc). In the United States, there are three single-antigen hepatites B vaccines (Engerix-B; Recombivax HB; Heplisav-B); one three-antigen vaccine (PreHevbrio), and three combination vaccines currently licensed (i) Pediarix: Combined hepatitis B, diphtheria, tetanus, acellular pertussis (DTaP), and inactivated poliovirus (IPV) vaccine; (ii) Twinrix: Combined hepatitis A and hepatitis B vaccine; (iii) Vaxelis: Combined DTaP, IPV, Haemophilus influenzae type b, and hepatitis B vaccine) [5].

Hepatitis C virus (HCV)

Hepatitis C virus (HCV) affects more than 70% of an estimated population of 170 million, inducing chronic lesions of hepatitis, severe fibrosis, cirrhosis and hepatocellular carcinoma. The viral envelope glycoproteins E1 and E2 are the target of neutralizing antibody responses, but they are also the two most variable proteins. In the research by Simões and collaborators on the chimeric development of a vaccine against HCV, however, there are no vaccines available on the market. Detection of the HCV viral genome is done by molecular RT-PCR. The therapy adopted is the use of conventional or pegylated interferon alpha (IFN-α) in association with ribavirin. However, the treatment will depend on the virus genotype and the viral load obtained by q-RT-PCR (Real-time PCR) [6, 7].

Hepatitis C virus (HCV) belongs to the *Nidovirales* order, *Flaviridae* family, *Hepacivirus* genus. HCV is an enveloped virus presenting a single strand of positive polarized RNA genome with approximately 9,400 nucleotides. HCV illness is a chronic infection that affects more than 2% of the global population and causes end– stage liver diseases as chronic hepatitis. It is a worldwide public health problem that affects more than 70% of the estimated 170 million people inducing chronic lesions hepatitis. This virus leads to severe fibrosis and cirrhosis, hepatic failure, or hepatocellular carcinoma. HCV has a higher rate of mutation existing inside an individual as quasispecies. HCV is divided into six genotypes and multiple subtypes. The envelope glycoproteins E1 and E2 are the natural targets to neutralizing antibodies response, but are also the two of the most variable HCV proteins. Production of specific antibodies in rabbits against conserved and potentially immunogenic peptides of the HCV envelope glycoprotein E2 has been described. HCV displays a high variability and is classified into seven genetically distinct genotypes which differ by approximately 30% at the nucleotide level. Envelope (E1/E2) proteins of HCV may generate neutralizing antibodies. At the end N–terminus of the E2 protein there is a region of 27 amino acids called hypervariable region 1 (HVR1), very important in neutralizing HCV. Despite the high degree of variability of E2 protein, some amino acid positions are conserved and this protein is the target of several neutralizing monoclonal antibodies. More biotechnological studies are need to investigate the clinical and epidemiological aspects and to associate the presence of antibodies with the progression of liver diseases. However, the high variability of this antigenic fragment plays a key role in the viral escape mechanism of the host immune response and represents the major obstacle in the development of an HCV vaccine. New biotechnologies in molecular biology as quimeric vaccine production using conserved peptides are possible

candidates of peptide vaccine against HCV infection. Some studies involved the detection of antibodies in rabbits with immunogenic potentially activity by synthetic peptides of the HCV envelope glycoprotein E2 in chronic HCV infections. Until the date HCV vaccine has not been available [3]

Herpesvirus (HSV)

Another oncogenic virus is the Herpesvirus (HSV) that infect and establish latent state (episomal) inside the nucleus. Herpes simplex virus type 1 (HSV–1) or Human herpesvirus 1 (HHV–1) induce an acute infection associated with vesicles in the oral region. Herpes simplex virus (HSV–2) or Human herpesvirus 2 (HHV–2) had been described causing strong lesions in the genital area. These herpesviruses are members of the Alphaherpesviruses subfamily and it´s common the co-infections. There are others types as Human herpesvirus 3 (HHV–3) or varicella–zoster virus is highly contagious and Human Herpesvirus 4 (HHV–4) or Epstain–Barr virus (EBV). In addition, there are several types of tumors associated with Epstein–Barr virus (EBV) such as Burkitt's lymphoma and Human Herpesvirus–5 (HHV–5) or Human Cytomegalovirus (HCMV) mainly detected in transplanted patients. Human herpesvirus 6 (HHV–6) and human herpesvirus 7 (HHV–7), Human herpesvirus 8 (HHV–8), also known as Kaposi's sarcoma–associated herpesvirus (KSHV) had been documented associated with others infections diseases [3].

Human immunodeficiency virus (HIV)

HIV is classified in the *Retroviridae* Family, *Lentivirus* and develops the Acquired immunodeficiency syndrome (AIDS) that attacks immune system. Regarding HIV, which mainly infects CD4+ helper T lymphocytes and antigen-presenting cells such as macrophages and dendritic cells, there is an association of several antiviral drugs that are reverse transcriptase enzyme inhibitors, CCR5 and CZCR4 cell receptor antagonists, and protease inhibitors. as combinations of antiretroviral agents. Due to the great genetic variability of HIV and given the importance of CD8+ T cells in the antiviral response, anti-HIV vaccines have been developed advocating the inactivation of the virus and, more recently, the third-generation vaccine technology using mRNA, since vaccine immunogens are based on the specific recognition of antigens generating an immune response [3].

MATERIAL AND METHODS

This is a descriptive epidemiological study, which evaluated cases of viral hepatitis A vírus (HAV), hepatitis B vírus (HBV) and C (HCV), Herpesvirus and HIV in the city of Rio de Janeiro. All samples collected during the period from January 1, 2022 to March 31, 2023 at the All Lab were selected. For HIV-1/2 screening, the 4th generation immunoassay test was performed using the Chemiluminescence (CMIA) and Electrochemiluminescence (ECLIA) methods. This examination includes step 1, according to flowcharts 3 and 6 of the Technical Manual for the Diagnosis of HIV Infection, defined by Ordinance No. 29 of 12/17/2013 of the MS/SVS/DEPTºDST, AIDS

and H.V. According to flowcharts 3 and 6 of the Technical Manual, molecular assays (RT-PCR and Western Blotting) must be performed to confirm positive results. Herpes Simplex types 1 and 2 antibodies and hepatitis A virus research were carried out using the Chemiluminescence method – CLIA. The presence (reactive) or absence of anti-HCV antibodies (non-reactive) was also investigated by the Electrochemiluminescence method - ECLIA.

RESULTS

A total of 2,750 samples were collected from 2,713 patients, of which 38.43% were for HCV; 31.20% for HIV research; 30.25% for HAV research and 0.10% for herpes simplex. According to the reference values, the absence of p24 antigen and HIV antibodies determines a non-reactive sample for HIV, while the presence of antigen and/or HIV antibodies in the sample is characterized by a reactive sample for HIV. On the other hand, in cases of samples suspected of HIV infection and non-reactive or even indeterminate results, a new sample was collected 30 days after the date of the first collection. To confirm the reagent results in the laboratory diagnosis, a new sample was collected and analyzed for the simultaneous investigation of the p24 antigen and HIV-1/2 antibodies with a cutoff of 0.9 by the Chemiluminescence (Abbott) and Electrochemiluminescence (Roche) tests.

In the year 2022, 645 patients were seen in the hematology sector of the All Lab for HIV research, of which 59.68% were male and 40.31% were female. Of a total of 647 samples collected in this period, 4.94% were reagent samples, with the month of August reaching a percentage of 13.04%, obtaining the highest prevalence rate. On the other hand, 95.05% resulted from non-reactive samples, with the month with the highest prevalence being March (98.46%).

On 2022, there was no reactive sample for the biomarker HBc IgM and IgG between the January and December. It had been analyzed about 2,222 samples from 1660 patients, which females were more prevalent (60.60%) and males (39.39%). In all, eight biomarkers of the hepatitis B vírus (HBV) were investigated, of which the HBsAg marker was non-reactive in 44.01% of the total samples analyzed and 31, 41% reactive for anti-HBs.

For another hand, in the year 2023, there was no reactive sample for the biomarker HBc IgM and HBsAg between the January and March. In theses months, 472 samples had been collected of 411 patients. So there was a higher prevalence of females (54.98%) and males (45.01%). In all, 8 biomarkers for the hepatitis B virus (HBV) were investigated, of which the research for non-reagent HBs Ag with 47.66% and Anti-HBs with 31.99% stand out at 2023.The highest percentage of investigated samples (98.38%) was recorded in March 2022 with a average proportion of 55.25 ± 12.96 (CV = 0.234) for the non reactive IgM biomarker (Table 1 and 2). All serological biomarkers of the hepatitis A virus (HAV) are better represented in graphic 1 and 2.

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Table 1: Percentage of HAV biomarkers by months in the 2022 and 2023 year

Biomarkers	**IgM**			**IgG**		
Months/ 2022	Reactive	Non Reactive	Inconclusive	Non Reactive	Reactive	Inconclusive
January	-	96,55 %	-	-	3,44 %	-
February	1,69%	89,83 %	-	1,69%	6,77 %	-
March	-	98,38 %	-	1,61%	-	-
April	2,32%	90,69 %	1,16%	1,16%	4,65 %	-
May	0,74%	52,23 %	0,74%	9,70%	36,56%	-
June	-	84,72 %	1,38%	6,94%	6,94 %	-
July	-	95,08 %	-	1,63%	3,27 %	-
August	-	95,34 %	2,32%	-	-	2,32%
September	-	88,46 %	-	-	11,53%	-
October	-	82,35 %	-	11,76 %	5,88 %	-
November	-	98,18 %	-	-	1,81 %	-
December	-	98,27 %	-	-	1,72 %	-
Months/ 2023	**IgM**			**IgG**		
January	-	100%	-	0	-	-
February	-	100%	-	0	-	-
March	-	92%	-	2%	-	-

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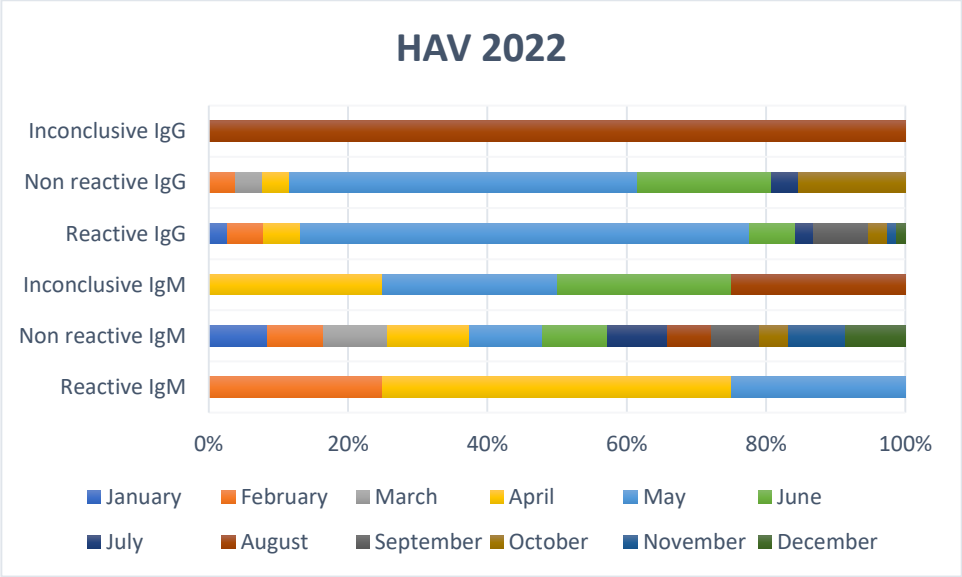
Table 2: Analysis of means, standard deviation and coefficient of variation of HAV biomarkers in
the 2022 and 2023 years

Biomarkers	**IgM**			**IgG**		
Year	Reactive	Non Reactive	Inconclusive	Non Reactive	Reactive	Inconclusive
2022	0,33± 0,65 (CV = 1,96)	55,25± 12,96 (CV=0,234)	0,33 ± 0,49 (CV=1,484)	2,16 ± 3,78 (CV = 1,747)	6,33± 13,57 (CV = 2,143)	0,08 ± 0,288 (CV = 3,469)
2023	-	52,66 ± 6,11 (CV = 0,116)	-	0,33 ± 0,577 (CV = 1,72)	-	-

Graphic 1: Serum biomarkers of the hepatitis A virus (HAV) investigated in the 2022 year.



Graphic 2: Serum biomarkers of the hepatitis A virus (HAV) investigated in the 2023 year.

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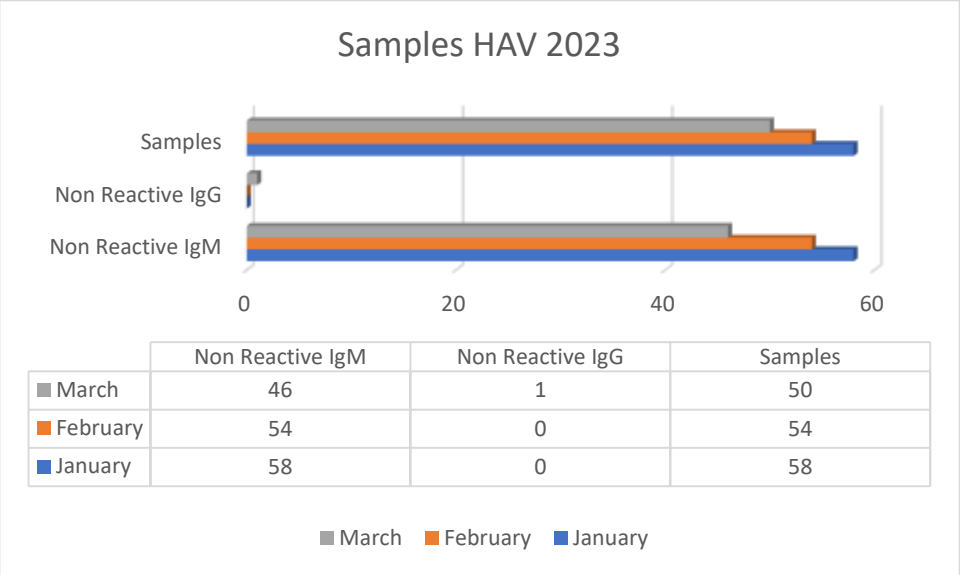

	Non Reactive IgM	Non Reactive IgG	Samples
March	46	1	50
February	54	0	54
January	58	0	58

About 774 blood samples were analyzed for the hepatitis A virus (HAV) from 740 patients with a average proportion of 61.66 ± 22.08 (CV = 0.358). Thus, 417 were male with a mean ratio of 34.75 ± 8.34 (CV = 0.24) and 323 were female with 26.91 ± 14.46 (CV = 0.537) (Table 3).

Table 3: Percentage of samples HAV collected by gender among months/years.

Gender	**Female**	**Male**
Months/2022		
January	43,85%	56,14%
February	38,59%	61,40%
March	52,45%	47,54%
April	47,56%	52,43%
May	55,37%	44,62%
June	39,39%	60,60%
July	37,93%	62,06%
August	33,33%	66,66%
September	40,00%	60,00%
October	38,23%	61,76%
November	36,36%	63,63%
December	40,35%	59,64%
Total	43,64%	56,35%

In 2023, 162 samples were analyzed, of which 159 patients were analyzed, mostly 62.26% of male samples with a average proportional of 33 ± 8.54 (CV = 0.258) and 37.73% of females with a mean proportion of 20 ± 3.46 (0.173) (Table 4 and Graphic 3).

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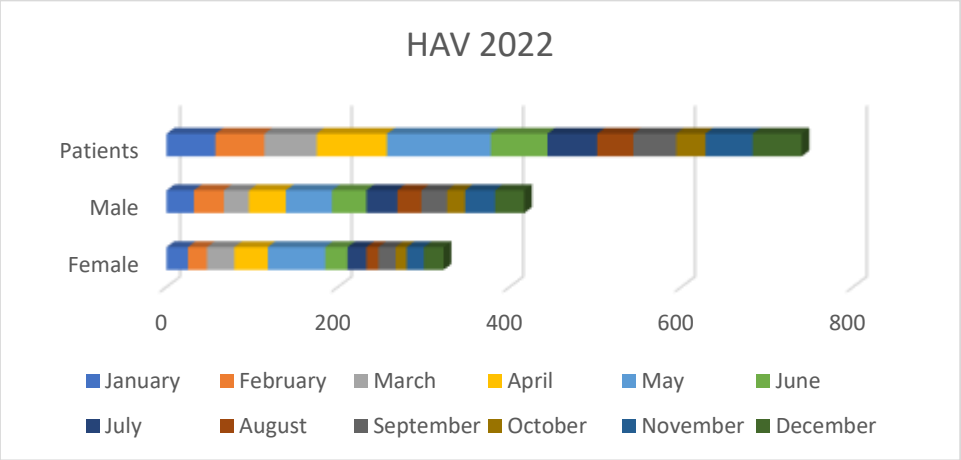
Table 4: Analysis of means, standard deviation and coefficient of variation of all patients HAV including female and male collected in the 2022 and 2023 years

Gender Year	Female	Male	Patients
2022	26,91 ± 14,46 (CV = 0,537)	34,75 ± 8,34 (CV = 0,24)	62,66 ± 22,08 (CV = 0,358)
2023	20 ± 3,46 (CV = 0,173)	33 ± 8,54 (CV = 0,258)	53 ± 5,56 (CV = 0,105)

In 2022/23 years, all samples colected among female and male investigated in the serological biomarkers of the hepatitis A virus (HAV) are better represented in graphic 3 and 4, respectivaly.

Graphic 3: Samples colected among female and male investigated serum biomarkers of the hepatitis A virus (HAV) investigated in the 2022 year.



Graphic 4: Samples colected among female and male investigated serum biomarkers of the hepatitis A virus (HAV) investigated in the 2023 year.

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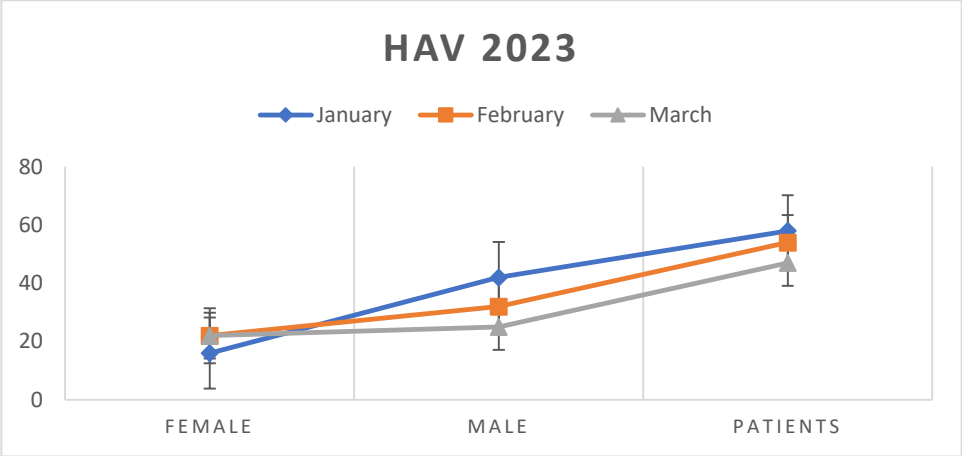

The serological findings HBV were calculated among the 2.222 samples collected from 1660 patients and 477 samples from 411 patients from the year 2022 and 2023, respectively. In all, eight biomarkers of the hepatitis B virus (HBV) were investigated, of which the HBsAg marker was non-reactive in 44.01% of the total samples analyzed and 31,41% reactive for anti-HBs (table 5 and graphic 5).

Table 5: Percentage of HBV biomarkers by months in the 2022 year

Biomarkers	**HBc IgM**	**HBc IgG**	**Anti-HBs**		**HBsAg**		**Anti-Hbe**	**Hbe Ag**	**Anti-HBc**	**HBc Ag**
Months/2022	Non Reactive	Non Reactive	Reactive	Non Reac.	Reactive	Non Reac.	Non Reactive	Non Reac.	Non Reac.	Non Reac.
January	5,70%	5,70%	35,30%	11,40%	-	0,92%	5,48%	5,48%	-	-
February	6,63%	6,16%	29,38%	6,63%	-	38,86%	-	-	6,16%	6,16%
March	0,44%	5,38%	26,00%	12,55%	-	47,98%	-	3,58%	4,03%	3,58%
April	1,08%	3,80%	26,08%	11,41%	-	56,52%	-	0,54%	0,54%	1,08%
May	2,03%	2,03%	33,50%	13,19%	-	47,20%	1,01%	-	-	-
June	3,82%	3,82%	38,25%	13,66%	-	38,25%	1,09%	-	-	1,09%
July	2,11%	2,11%	32,39%	10,56%	-	52,81%	-	-	-	-
August	4,26%	4,87%	28,65%	9,14%	-	40,85%	9,75%	2,43%	-	-
September	3,80%	5,71%	22,85%	11,42%	-	56,19%	-	-	-	-
October	4,16%	4,16%	22,91%	11,45%	-	50%	6,25%	1,04%	-	-
November	0,80%	0,80%	37,09%	10,48%	0,80%	50%	0,80%	0,80%	-	-
December	-	0,72%	35,03%	11,67%	1,45%	51,09%	-	-	-	-

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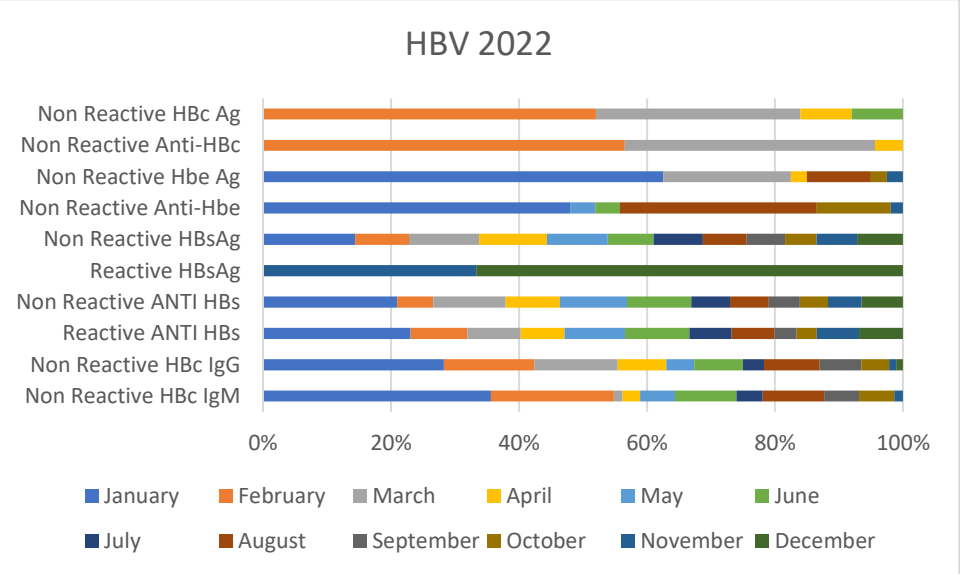
Total	3,28%	4,14%	31,41%	11,16%	0,13%	44,01%	2,34%	1,80%	1,03%	1,12%

Graphic 5: Percentage of HBV biomarkers by months in the 2022 year



It was analyzed the of means, standard deviation and coefficient of variation of HBV bood serum biomarkers collected in the 2022 and 2023 years as showed in table 6/7 and Graphic 6.

Table 6: Analysis of means, standard deviation and coefficient of variation of HBV biomarkers in
the 2022 and 2023 years

Biomarkers	**HBc IgM**	**HBc IgG**		**Anti-HBs**		**HBsAg**		**Anti-Hbe**	**Hbe Ag**	**Anti-HBc**	**HBc Ag**
Year	Non Reactive	Reactive	Non Reactive	Reactive	Non Reac.	Reactive	Non Reac.	Non Reactive	Non Reac.	Non Reac.	Non Reac.
2022	6,08 ± 7,31 (0,003)	-	7,66±6,90 (0,900)	58,16±35,53 (0,610)	20,66± 11,44 (0,553)	0,25±0,62 (2,484)	81,5±25,85 (0,317)	4,33±7,98 (1,841)	3,33±7,22 (2,168)	1,91±4,33 (2,263)	2,083±4,144 (1,989)
2023	2,00±00 (0,00)	0,66±1,15 (1,732)	1,33±1,15 (0,865)	75,5±17,61 (0,23)	25,00±6,55 (0,262)	-	75,00±13,07 (0,174)	0,33±0,577 (1,732)	0,33±0,577 (1,732)	1,00±1,00 (1,00)	1,00±1,00 (1,00)

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Graphic 6: Percentage of HBV biomarkers by months in the 2023 year

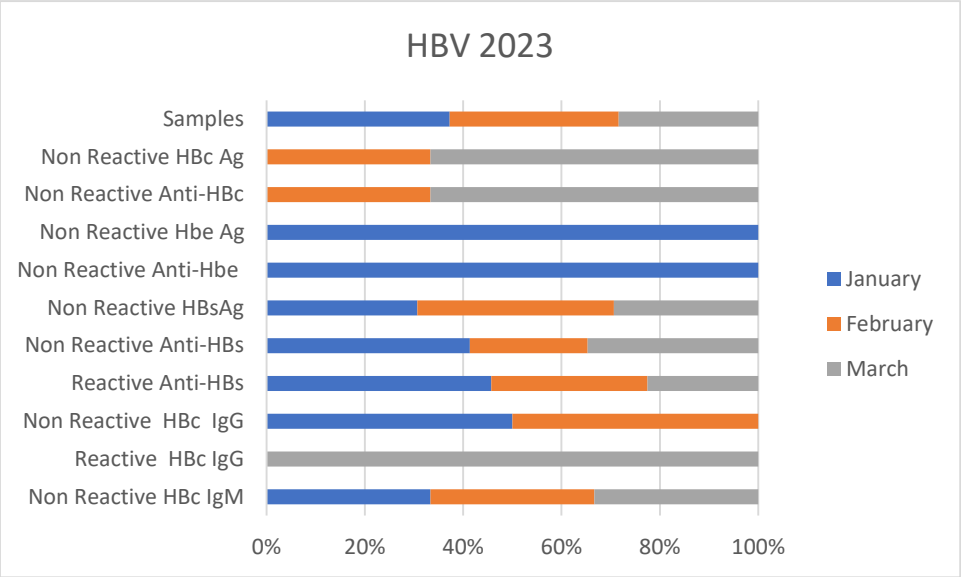

Table 7: Percentage of HBV biomarkers by months in the 2023 year

Biomarkers	**HBc IgM**	**HBc IgG**		**Anti-HBs**		**HBsAg**	**Anti-Hbe**	**Hbe Ag**	**Anti-HBc**	**HBc Ag**
Months/2023	Non Reac.	Reactive	Non Rea	Reactive	Non Reac.	Non Reac.	Non Reactive	Non Reac.	Non Reac.	Non Reac.
January	1,13%	-	1,13%	39,20%	17,61%	39,20%	0,56%	0,56%	-	-
February	1,23%	-	1,23%	29,62%	11,11%	55,55%	-	-	0,61%	0,61%
March	1,49%	1,49%	-	25,37%	19,40%	49,25%	-	-	1,49%	1,49%
Total	1,27%	0,42%	0,84%	31,99%	15,88%	47,66%	0,21%	0,21%	0,63%	0,63%

On 2022, there was no reactive sample for the biomarker HBc IgM and IgG between the January and December. It had been analyzed about 2,222 samples from 1660 patients, which females were more prevalent (60,60%) and males (39,39%) as table 8 and graphic 7/8 below.

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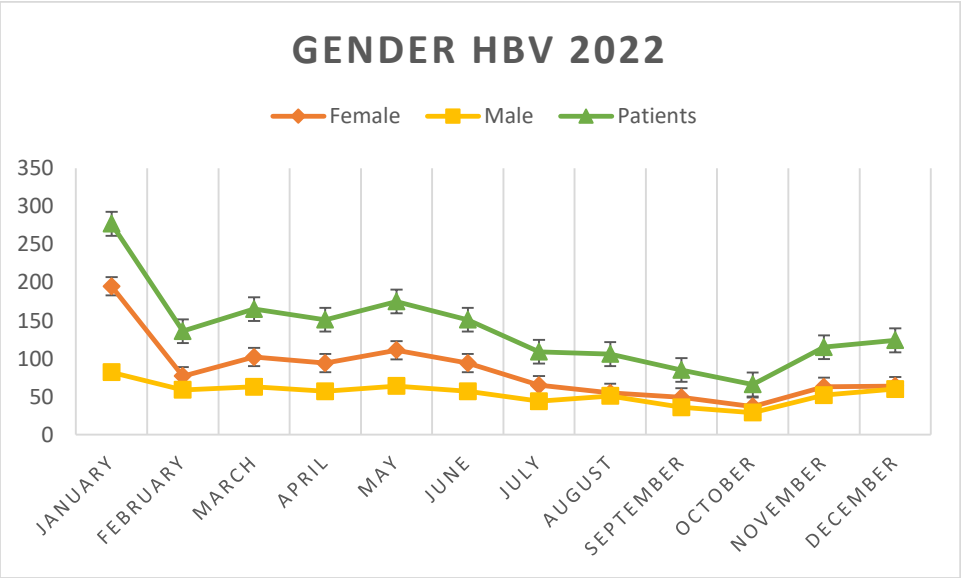
Table 8: Percentage of samples HBV collected by gender among months/years.

Gender	**Female**	**Male**
Months/Year 2022		
January	70,39%	29,60%
February	56,61%	43,38%
March	61,81%	38,18%
April	62,25%	37,74%
May	63,42%	36,57%
June	62,25%	37,74%
July	59,63%	40,36%
August	51,88%	48,11%
September	57,64%	42,35%
October	56,06%	43,93%
November	54,78%	45,21%
December	51,61%	48,38%
Total	60,60%	39,39%
Months/Year 2023		
January	50,29%	49,70%
February	52,27%	47,72%
March	65,17%	34,82%
Total	54,98%	45,01%

Graphic 7: Percentage of samples collected by gender among months in the 2022 years.



Graphic 8: Percentage of samples collected by gender among months in the 2023 years.

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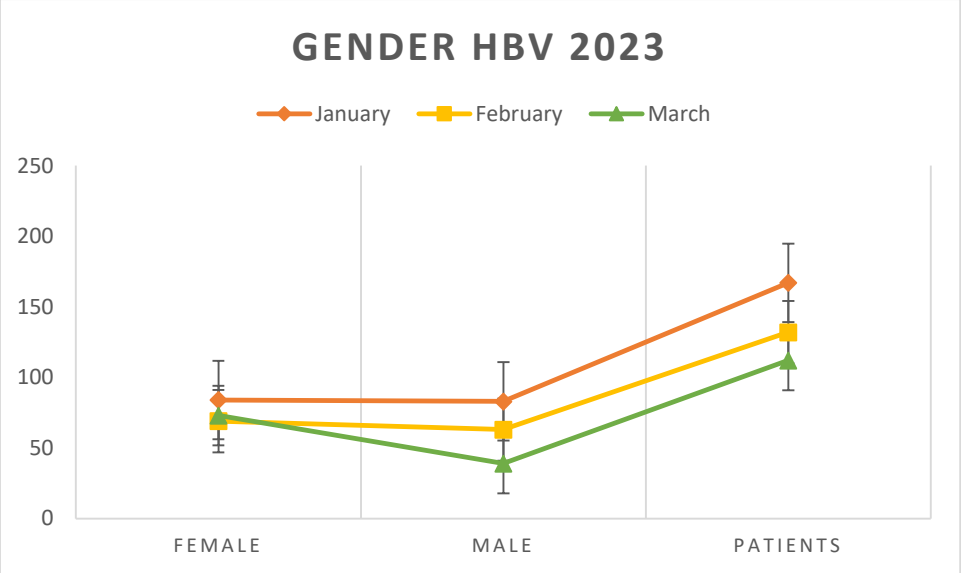

It was analyzed the of means, standard deviation and coefficient of variation of all patients collected in the 2022 and 2023 years as showed in table 9 bellow.

Table 9: Analysis of means, standard deviation and coefficient of variation of all patients HBV including female and male collected in the 2022 and 2023 years

Gender Year	Female	Male	Patients
2022	83,83±41,66 (0,497)	54,5±13,82 (0,253)	138,33±54,22 (0,391)
2023	75,33±7,76 (0,103)	61,66±22,03 (0,357)	137,00±27,83 (0,203)

About 854 blood samples were collected for HCV virus testing with average proportion of 71,16 ±15,18 (CV = 0,213) of which most samples were taken from 440 (51,52%) men with 36,66 ± 6,87 (CV = 0,187) and 414 (48,47%) women with 34,5 ±10,12 (CV = 0,293), represented by table 10. The anti-HCV biomarker was non-reactive mainly in April 2022 (graphic 9).

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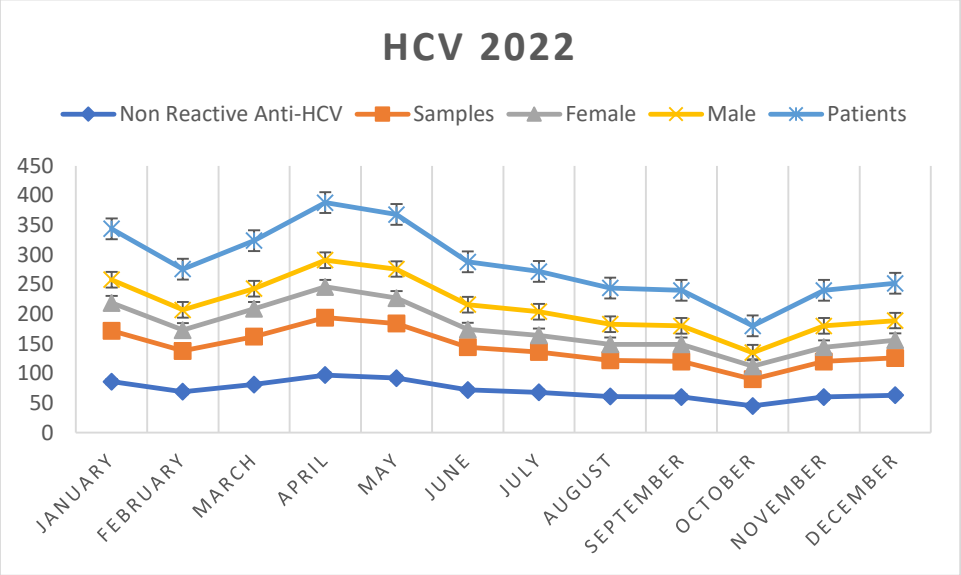
Table 10: Percentage of samples HCV collected by gender among months/years.

Gender	Female	Male
Months/Year 2022		
January	47 (54,65%)	39 (45,34%)
February	35 (50,72%)	34 (49,27%)
March	47 (58,02%)	34 (41,97%)
April	52 (53,60%)	45 (46,39%)
May	43 (46,73%)	49 (53,26%)
June	30 (41,66%)	42 (58,33%)
July	28 (41,17%)	40 (58,82%)
August	27 (44,26%)	34 (55,73%)
September	29 (48,33%)	31 (51,66%)
October	22 (48,88%)	23 (51,11%)
November	24 (40,00%)	36 (60,00%)
December	30 (47,61%)	33 (52,38%)
Total	414 (48,47%)	440 (51,52%)
Months/Year 2023		
January	22 (33,33%)	44 (66,66%)
February	31 (46,26%)	36 (53,73%)
March	39 (55,71%)	31 (44,28%)
Total	92 (45,32%)	111 (54,67%)

Graphic 9: Serum biomarkers of the hepatitis C virus (HCV) investigated in the 2022 year



In the year 2023, about 203 samples were collected with a prevalence of 54,67% for men with a average proportional of 37± 37,38 (CV = 1,01) and 45,32% for women with a average proportional of 30,66 ± 31,44 (CV = 1,025), represented in the table 11 and graphic 10.

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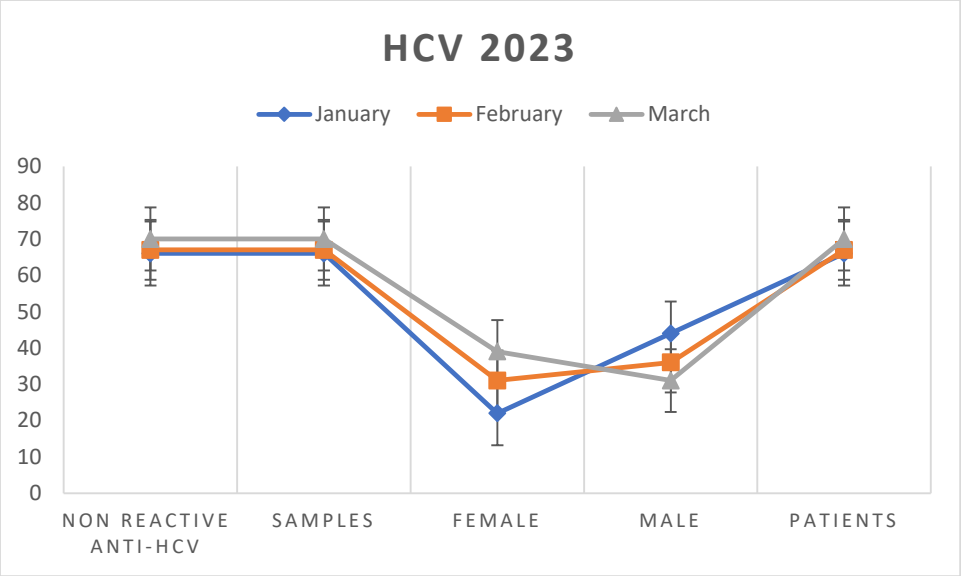
Table 11: Analysis of means, standard deviation and coefficient of variation of all patients HCV including female and male collected in the 2022 and 2023 years

Gender Year	Female	Male	Patients
2022	34,5 ± 10,12 (CV = 0,293)	36,66 ± 6,87 (CV = 0,187)	71,1 6± 15,18 (CV = 0,213)
2023	30,66 ± 31,44 (CV = 1,025)	37 ± 37,38% (CV = 1,01)	67,66 ± 67,68 (CV = 1)

Graphic 10: Serum biomarkers of the hepatitis C virus (HCV) investigated in the 2023 year.



In the year 2022, 647 samples were analyzed for the HIV virus, obtaining as results 615 (95.05%) non-reactive samples with an average proportion of 51,25 ± 10,60 (CV = 0,206) and only 32 (4,94%) samples positive with 2,66 ± 1,72 (CV = 0,646) of which 385 (59,50%) samples were collected from males with 32,08 ± 4,83 (CV = 0,15) and 260 (40,18%) female samples with a average proportion of 21,66 ± 6,80 (CV = 0,313) (Table 12 and Graphic 11).

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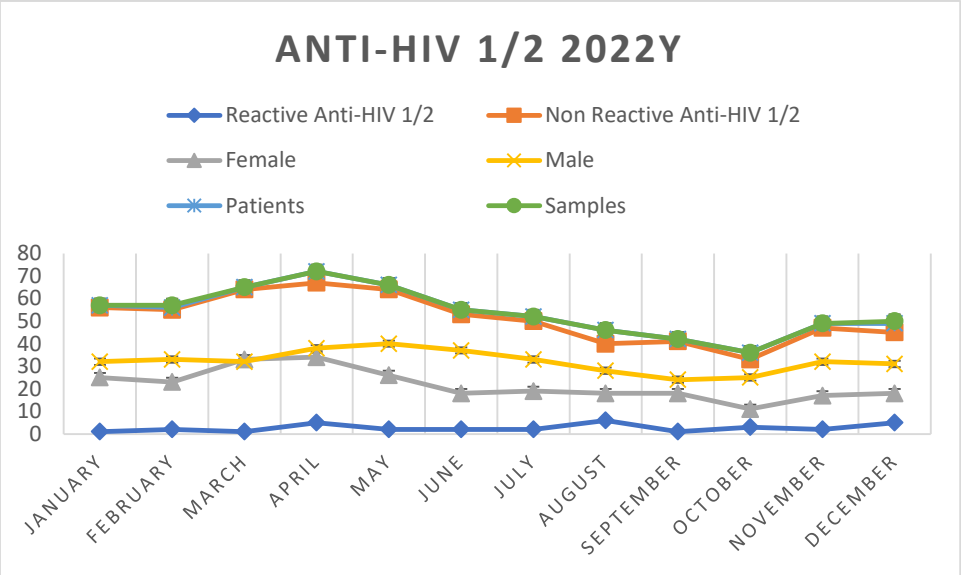
Table 12: Percentage, analysis of means, standard deviation and coefficient of variation of HIV biomarkers of all patients including female and male collected in the 2022 and 2023 years

Biomarkers	**Anti-HIV 1/2**		**Gender**	
Months/2022	Reactive	Non Reactive	Female	Male
January	1,75%	98,24%	43,85%	56,14%
February	3,50%	96,49%	41,071%	58,92%
March	1,53%	98,46%	50,76%	49,23%
April	6,94%	93,05%	47,22%	52,77%
May	3,03%	96,96%	39,39%	60,60%
June	3,63%	96,36%	32,72%	67,27%
July	3,84%	96,15%	36,53%	63,46%
August	13,04%	86,95%	39,13%	60,86%
September	2,38%	97,61%	42,85%	57,14%
October	8,33%	91,66%	30,55%	69,44%
November	4,08%	95,91%	34,69%	65,30%
December	10%	90%	36,73%	63,26%
Total	2,66 ± 1,72 (CV = 0,646)	51,25 ± 10,60 (CV = 0,206)	21,66 ± 6,80 (CV = 0,313)	32,08 ± 4,832 (CV = 0,15)

Biomarkers	**Anti-HIV 1/2**		**Gender**	
Months/2023	Reactive	Non Reactive	Female	Male
January	10,34%	89,65%	25,86%	74,13%
February	3,84%	96,15%	38,46%	61,53%
March	0	100%	51,02%	48,97%
Total	2,66± 1,72 (CV = 0,646)	51,25 ± 10,60 (CV = 0,206)	26,66 ± 12,58 (CV = 0,472)	43,66 ± 20,008 (CV = 0,458)

Graphic 11: Reactive and Non-reactive Anti-HIV 1/2 samples investigated in the 2022 y.



In the 2022, about 201 samples anti-HIV 1/2 non-reactive were detected with na average proportional of 67 ± 28,61 (CV = 0.427) and 10 samples anti-HIV 1/2 positive with na average proportional of 3,33 ± 3,05 (CV = 0,917).

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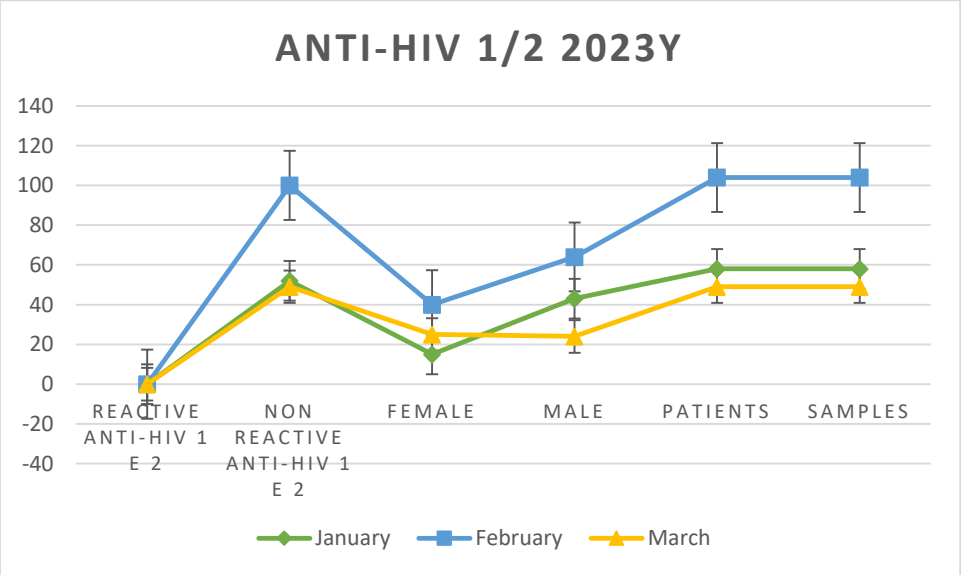
About 211 samples of 131 men with na average proportional of 43,66 ± 20,008 (CV = 0,458) and 80 women with na average proportional of 26,66 ± 12,58 (CV = 0,472) were analyzed in the 2023y (Graphic 12).

Graphic 12: Serum biomarkers Anti-HIV 1/2 samples collected in the 2023 y.



The herpesvirus was detected in only three samples collected in the March and October 2022 and March 2023. Comparing the percentagem, two male samples with average proportion of 0,66 ± 0,57 (CV = 0,874) and one female sample with 0,33 ± 0,57 (CV = 1.748) were serologically detected with reactive findings for IgG / IgM and non-reactive for IgM Herpes vírus (HSV) (Table 13 and Graphic 13).

Table 13: Analysis of means, standard deviation and coefficient of variation of HSV biomarkers of all patients including female and male collected in the 2022 and 2023 years

Biomarkers	**HSV**		**Gender**	
	Reactive IgM	Non Reactive IgM	Female	Male
Total	0,33 ± 0,57 (CV=1,748)	0,33 ± 0,57 (CV=1,748)	0,33 ± 0,57 (CV=1,748)	0,66 ± 0,57 (CV = 0,874)

Graphic 13: Graphic representation of HSV biomarkers of all patients.

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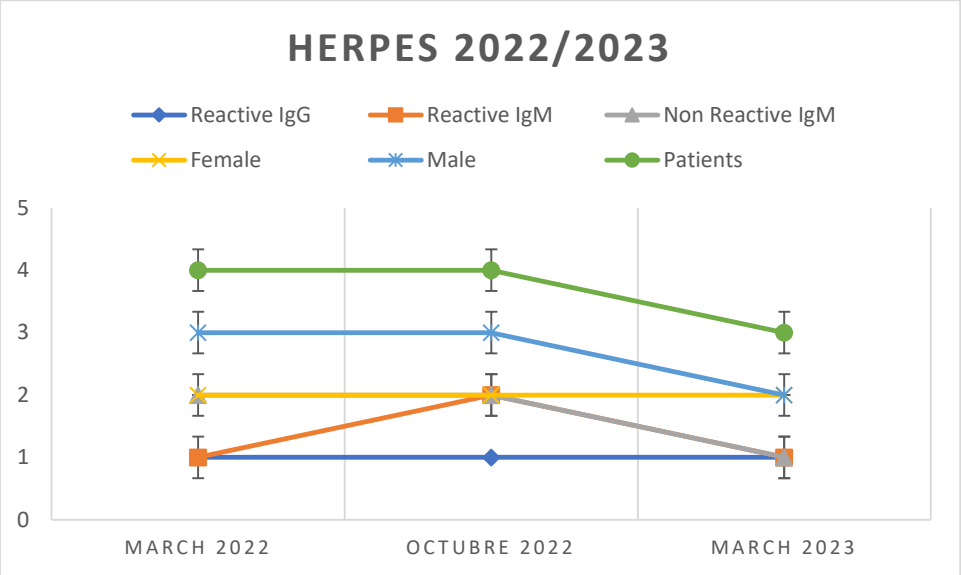

DISCUSSION

The authors suggest follow-up with new serological research associated with molecular assays aimed specifically at reactive and inconclusive results. In addition, the expression of simultaneous positive results indicating the presence of IgM antibodies for different etiological agents does not rule out the possibility of cross-reaction between them. As a result of this work added to the effectiveness of the quality management system, and the internal audits were able to mitigate the critical stages of the organizational process with a focus on risk management. Viral, host and environmental targets of novel biomarkers in the therapeutics development should be incorporated into personalized medicine. In short, our proposal for implementing aptamers as small DNA or RNA molecules chemically synthesized in vitro using the Systematic Evolution of Ligands by Exponential Enrichment (SELEX) technique. These molecules have high specificity and affinity against targets of interest and can act as nanoparticles in oncological studies related to oncovirus infections.

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Conflict of interest
The authors declare that they have no conflict of interest

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