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A RETROSPECTIVE ANALYSIS OF HEPATITIS A INFECTION IN DADRA & NAGAR HAVELI.

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Abstract

Background: It is crucial to research the long-term trends of the Hepatitis A (HAV) virus given the diversity of socioeconomic and demographic factors in a large country like India. Their seroprevalence and long-term trends in a tertiary care facility in Dadra and Nagar Haveli, which is close to Gujarat and Maharashtra, are described in this study.

Methods: Six years were covered by the current retrospective observational study (January 2019 to December 2024). IgM antibodies against HAV were detected through serological testing utilizing the enzyme-linked immunosorbent assay.

Results: A total of 1147 samples were tested during the study period, of which 149 (12.99%) were reactive for Anti-HAV IgM antibody. Among HAV group, 83 (55.70 %) were less than or equal to 12 years, 58 (38.92 %) were 13 to 60 years, and 8 (5.36 %) were more than 61 years. At the same time fluctuation was reported in the serum total bilirubin along with SGOT (Serum Glutamic Oxaloacetic Transaminase) AND SGPT (Serum Glutamic Pyruvic Transaminase).

Conclusions: The shift in seroprevalence among children, along with an increasing trend of the number of cases reporting to the hospital, warrants active surveillance of HAV. Intervention, such as universal childhood vaccination program, must be properly implemented and time correctly.

Keywords: Hepatitis A, Seroprevalence, Viral Hepatitis

Introduction

Type A viral Hepatitis is an enterically transmitted form of acute hepatitis caused by the hepatitis A virus (HAV), an unusual, plus-strand RNA virus belonging to the genus Hepatovirus and the family Picornaviridae[1]. Hepatitis A, an old disease, is thought to have plagued humanity since the transition from hunter-gatherer to communal living in larger settled communities 8,000 to 10,000 years ago. It is still widespread in underdeveloped places, particularly Sub-Saharan Africa, where 50% of

children are infected before the age of five.[2]. HAV was discovered in 1973 in the faeces of prisoner volunteers who were experimentally infected with the virus in the 1960s. After hepatitis A vaccines were licensed in the 1990s, research on HAV and hepatitis A went into a period of relative dormancy[3]. Hepatitis A is often an acute, self-limiting liver illness spread via the faecal-oral route[4]. The WHO estimates that roughly 1.5 million people become infected with HAV each year. Endemic rates are high in a developing country with low socioeconomic status and inadequate sanitation and hygiene standards. Exposure in these developing countries typically occurs in childhood. Infection rate is low in developed countries such as the United state, Canada, and Western Europe. High-risk groups in low endemicity countries have been identified as injection-drug users, men who have sex with men, people traveling to endemic areas, and isolated communities such as nursing homes and even day-care centers. The incidence of HAV in a given population correlates with socioeconomic properties such as income, the density of housing, sanitation, and water quality. With the implementation of vaccination, the incidence of HAV in the Unites state has significantly decreased[5]. Approximately 85% of people infected with HAV recover totally clinically and biochemically within three months, and virtually everyone recovers completely by six months. It has been shown that severe symptoms are more likely in young adults necessitating hospitalisation, with an overall case fatality rate of .3%. HAV is believed to be endemic in India. According to the National Centre for Disease Control, India, HAV is responsible for around 10-30% of acute hepatitis cases in patients with acute liver failure in India[6]. Human HAV is noncytopathic and highly hepatotropic, invading the liver in a stealthy way[7]. It is secreted by infected hepatocytes in tiny vesicles that lack any virally encoded protein on their surface. The production of quasi-enveloped virions (eHAV) is similar to that of exosomes. They are contagious, and the only type of virus found in blood[8].

Virology

Taxonomy and classification

HAV belongs to the family Picornaviridae and was previously classified as an Enterovirus. However, subsequent investigation revealed that the virus was sufficiently distinct from other picornaviruses to be placed inside its own genus, Hepatovirus.

HAV is one of nine Hepatovirus species, and it is the only one that infects humans. HAV has six genotypes, three of which infect humans and three of which impact primates, but only one serotype. The remaining members of the genus infect a variety of species, including bats, hedgehogs, shrews, and rodents. Phylogenetic study indicates that the genus began in small mammals and that human HAV originated in rodents[8], while a zoonotic reservoir no longer exists.

Virion structure

HAV is a non-encapsulated icosahedral virus. The lack of a lipid envelope in a virus gives it a substantial advantage in terms of spreading in the environment, as evidenced by foodborne and waterborne epidemics that are synonymous with hepatitis A[9].

Epidemiology and Transmission

The World Health Organisation estimates that 1.4 million cases of hepatitis A are reported worldwide each year, resulting in around 7,000 fatalities[10].

HAV spreads mostly by fecal-oral contact, although it can also be transmitted through contaminated food or water. Men who have sex with men are at a higher risk of infection, as are all people who engage in oral-anal sexual contact, regardless of gender or sexual orientation. Parenteral transmission via contaminated blood products has been described, and injecting drug users are at high risk, with greater prevalence positively related to low wages[11]. An infected person sheds the virus in their stool from about 2 weeks before symptoms appear, as well as for a few days after symptoms appear, but this may last for several weeks. Even with strict cleanliness and sanitation standards, the prevalence of infection among cases' close contacts is high, indicating particularly efficient interpersonal transmission. The rate and pattern of HAV transmission varies greatly

between regions of the world, and are mostly influenced by socioeconomic variables. Infection rates are lower in areas with smaller family sizes, improved sanitation, and more access to clean drinking water. Surprisingly, reduced rates of transmission do not imply fewer sickness. In resource-poor, high-endemic countries, such as Africa, portions of Asia, and South America, HAV infection in early childhood is common. In most situations, young children are asymptomatic or endure a very mild illness. HAV infection normally confers permanent immunity. Childhood exposure is less common in high-income, low-endemic locations such as North America, Western Europe, Japan, and Australia. As a result, only a small minority of adults have anti-HAV antibodies. If HAV is introduced, substantial outbreaks may occur, especially among high-risk groups such as males who have sex with men[12], homeless persons, and recreational drug users[13]. These epidemics primarily affect teens and adults, who are more likely to become very ill. Over the last few decades, advances in hygiene and sanitation in some low- and middle-income countries have reduced HAV transmission and raised the average age of infection[14]. This "epidemiological transition" brings the epidemiological pattern closer to that of industrialised countries, resulting in a paradoxical increase in both morbidity and mortality linked with hepatitis A.

Clinical Picture

Acute infection

Hepatitis A clinical symptoms usually appear after 14 to 28 days of incubation, but they can appear up to 50 days after exposure[11]. The clinical picture varies from asymptomatic to fulminant hepatitis. The condition progresses more severely with age; extremely young children frequently exhibit no signs at all. The normal presentation consists of two phases: a prodromal phase lasting 3 to 10 days and characterised by malaise and myalgia, and an icteric phase[15]. The icteric phase is characterised by mixed hepatic and cholestatic jaundice, as well as anorexia, nausea, and exhaustion. This period lasts between one and three weeks. Acute liver failure occurs in approximately 0.3% of cases, although it varies greatly by age; in children and adults under the age of 40, the case fatality rate ranges between 0.1% and 0.3%, while in individuals over the age of 49, it is 1.8%. Co-existing chronic infection with HBV or HCV enhances the risk of acute liver failure caused by HAV[16]. A proportion of patients with hepatitis A may exhibit unusual symptoms. Up to 5% of patients may develop cholestatic hepatitis, which is characterised by prolonged jaundice lasting 12 weeks or more. The typical clinical course in these individuals includes severe jaundice, pruritis, fever, weight loss, diarrhoea, and malaise[17]. Liver function tests (LFTs) reveal a cholestatic picture, with substantial elevations in bilirubin and alkaline phosphatase and a slight to moderate increase in alanine aminotransferase (ALT). In most cases, people with cholestatic hepatitis just require supportive care and recover completely.

Chronic infection

Although HAV does not induce persistent infection.

Extrahepatic manifestations

Extrahepatic symptoms of HAV infection are most commonly described in patients with cholestatic hepatitis or recurrent hepatitis A. A rash and/or arthralgia affect 10 to 15% of patients, but a variety of less common problems have also been reported. They include vasculitis, cryoglobulinemia, and thrombocytopenia[17].

Materials and Methods

The present study was a retrospective observational study conducted from January 2019 to December 2024 at a tertiary care center in the western part of India. All patients presenting to the hospital with features of AVH (Acute Viral Hepatitis) whose samples were received for serological and liver function testing against hepatitis A and liver enzymes in the department of Microbiology and Biochemistry laboratory of the institute during the study period were included in the study.

Repeat samples were excluded from the study so that each patient is represented by a single sample only.

For microbiological confirmation, serological testing was done using enzyme-linked immunosorbent assay (ELISA) 3rd generation based anti-HAV IgM, and a liver function test was done. Three milliliters of blood were collected in two separate blood collection vials without additives under strict aseptic precautions, and the serum was separated by standard methods. If it was not possible to put them up immediately, the sera were stored at -20 °C until testing (usually up to 1–7 days). Sera exhibiting hemolysis, lipemia, and turbidity were rejected. ELISA testing was performed as per manufacturer instructions supplied as package inserts and kit literature along with the ELISA kits. Positive and Negative controls supplied with the kits were run for test validation as per instructions, and internal quality control was also set up by testing known positive samples every time ELISA testing was done on patient samples. The same standard was followed for the liver function test.

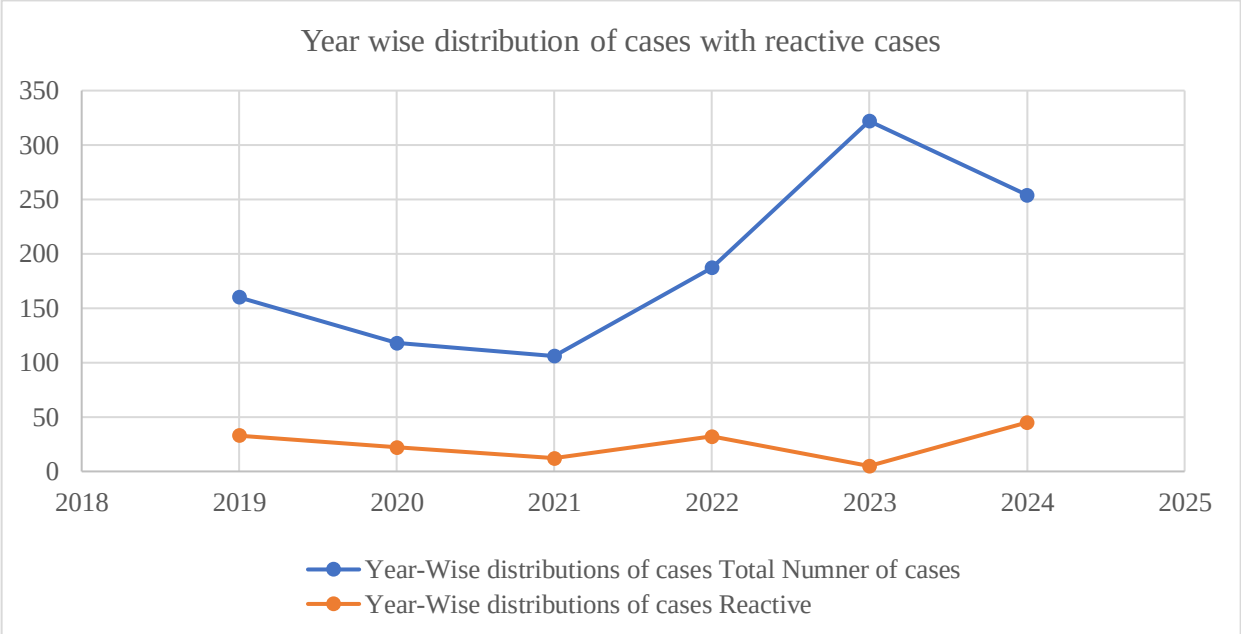
Data were collected from the laboratory and hospital records for the study. Patients were categorized into three groups for analysis: (I) Pediatric (II) Adult patients and (III) Senior citizen. The categorization into pediatric and adult was as per the previous description [14] and was based on the hospital protocol for patient enrolment in the pediatrics (≤12 years) or medicine and other (>12 years) specialties.

Results and Discussion

A total of 1147 patients' samples were included in the study, of which 149 (12.99%) were reactive for anti-HAV IgM antibodies. Gender-wise, more patients were female (599, 52.22%) as compared to male (548, 47.77%). But the reactivity was higher in males (77,51.60%) than females (72,48.32%).

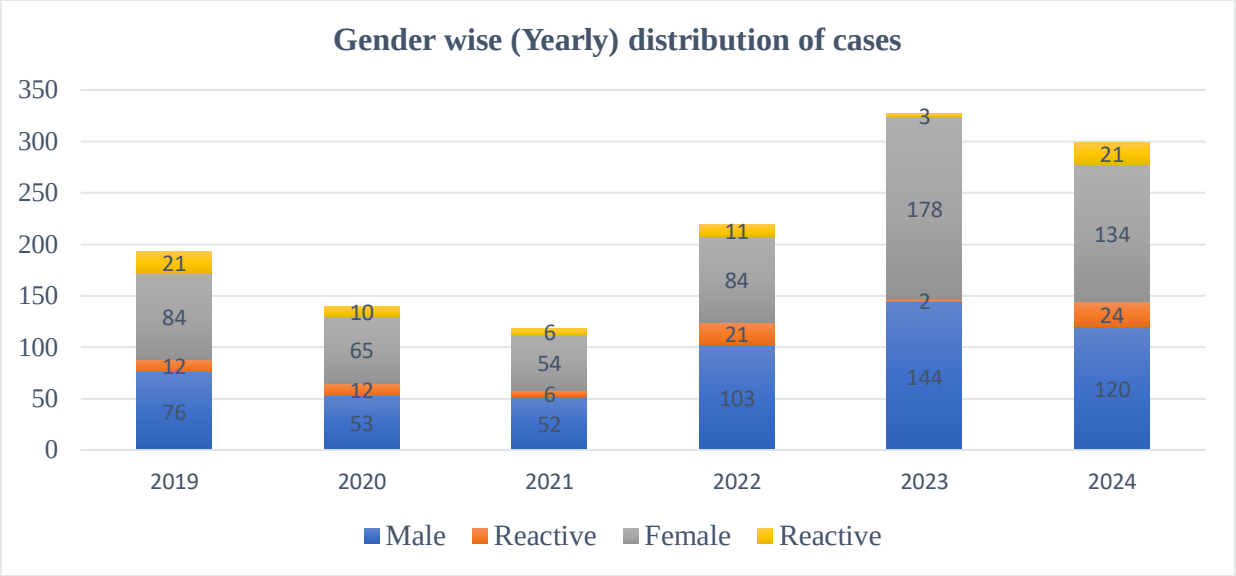
The year-by-year distribution of cases revealed an overall trend of somewhat rising HAV cases during the research period (Figure -I). The highest number of cases occurred shortly after the covid-19 epidemic. But we can see that the positive rate was low. People took care of themselves, as well as the food and drinking water.

Figure – I



The gender-wise (yearly) distribution among the patients was analyzed, and the number of females 599 (52.22%) was somewhat higher than the male 548 (47.77%). Figure II. HAV was more typically related with infection in males (77/14.5%) than females (72/12.02%). HAV reactivity grew year after year until July 2024, when 45 (17.71%) instances were declared reactive. In 2023, the reactivity was 5 (1.55%), which is quite low in comparison to previous years.

Figure – II



The cases are further classified into three age categories: equal to or less than 12 years, 13 to 60 years, and over 61 years. We also split based on gender. Maximum testing was performed on individuals aged 13 to 60 and flowing by equal and less than 12 years who arrived at the hospital as outpatients and inpatients. In comparison to other age groups, there were extremely few patients beyond the age of 61. However, the maximum passivity was shown in females aged 12 or younger 46 (33.57%), while less positivity was seen in females from 13 to 60 years old 23 (5.23%), followed by males 35 (9.56%). Maximum reactive reactivity was discovered in equal and less than.

Figure – III

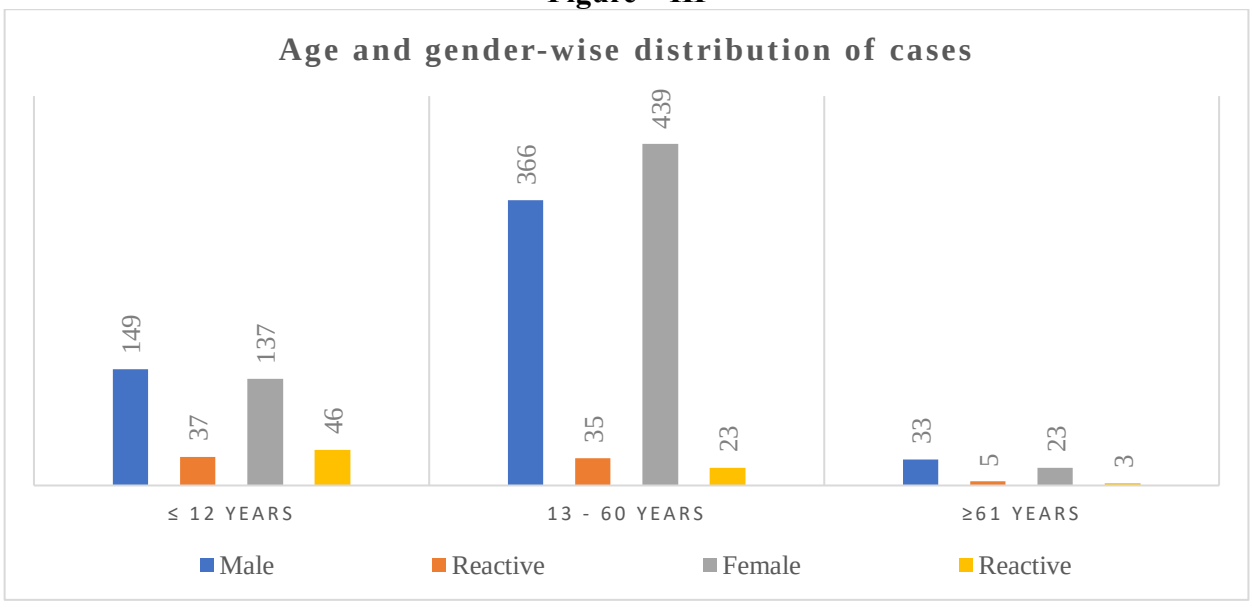
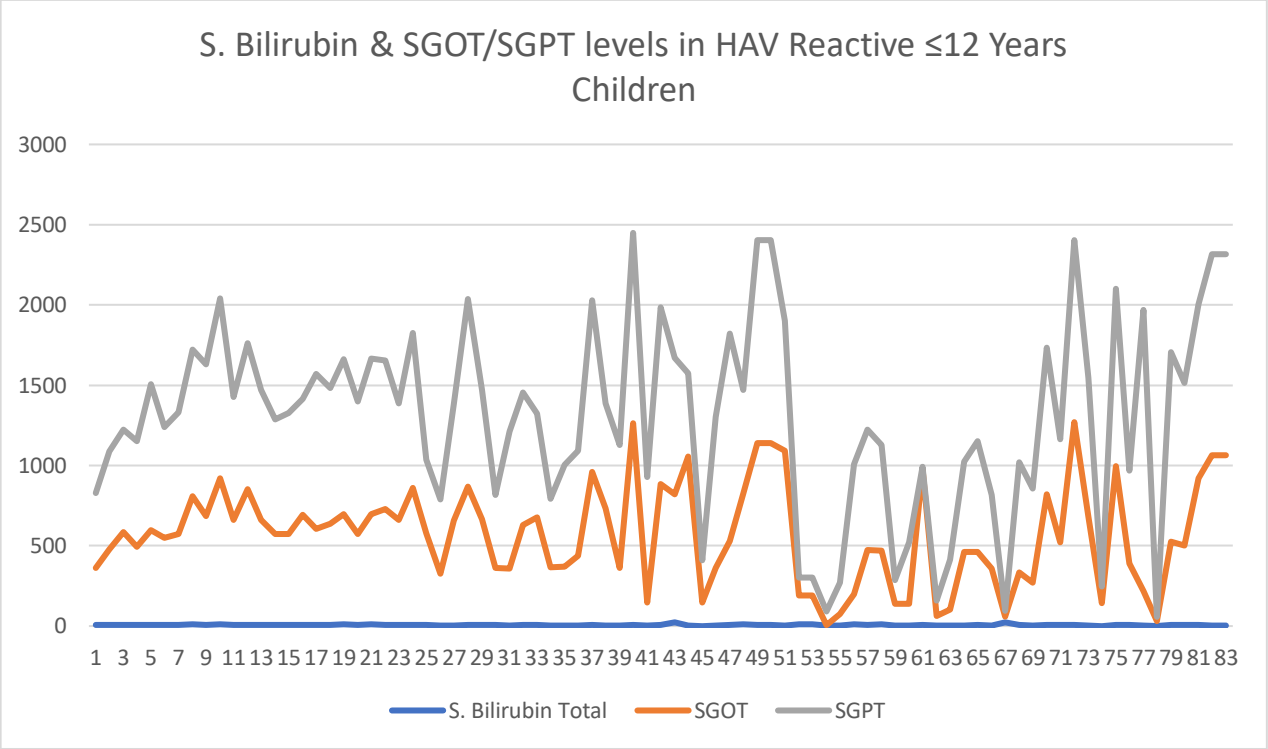
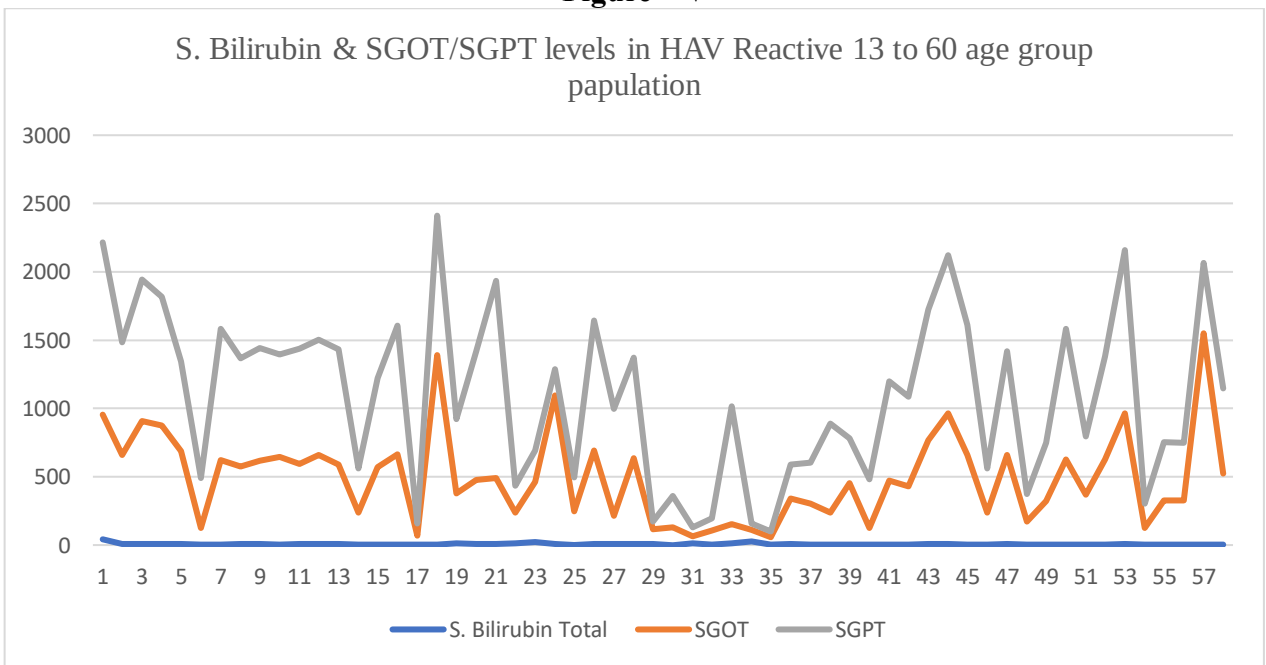


Figure – IV



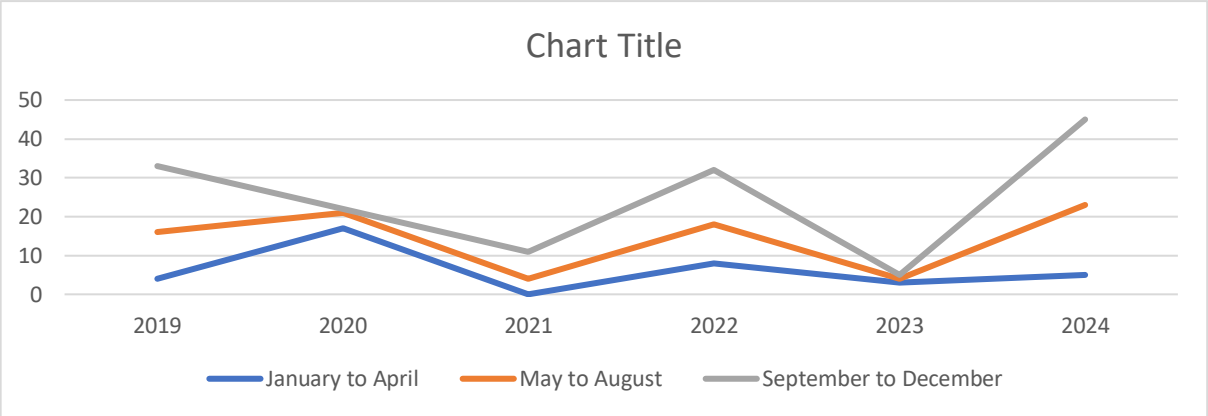
During the study period, 1147 tests were performed, and 83 (7.23%) ≤ 12 years tested positive for HAV. At the same time, we performed liver function tests. The highest fluctuation was reported in serum bilirubin total (0.3 to 23.3), SGOT (10 to 1262), and SGPT (13 to 1749).

Figure – V



During the study period, 1147 tests were performed, and 58 (5.05%) 13 to 60 years tested positive for HAV. At the same time, we performed liver function tests. The highest fluctuation was reported in serum bilirubin total (0.36 TO 42) SGOT (54 TO 1545), and SGPT (42 TO 1441).

Figure – VI



A total of 149 reactive samples were examined throughout the course of six years (2019–2024). The highest reactivity was observed from September to December, followed by May to August and January to April.

Discussion

The present study was conducted over a period of 6 years and highlights the changing trend of infection caused by HAV in a hospital-based setting. There was overall rise in the number of cases of hepatitis A infection. A total 1147 HAV suspected cases were enrolled over a period. The age between one month to 80 years patients were tested. Anti-HAV was 12.99 (149/1147) per cent (Figure – II).

An earlier study from our center in 2019 observed HAV seroprevalence of 20.6 per cent. The HAV positive has declined over the time, and this may be due to the covid-19 and continuous effort by the government in improving sanitation and hygiene; however, the need for continuous surveillance can be emphasized looking at the changing pattern. High HAV seropositivity in the early age group depicted HAV endemicity in DNH, India (Figure – III).

HAV positivity among seropositivity cases was found to be 12.99 per cent in our study. A similar finding of HAV seropositivity (16.9%) was reported from Chandigarh in a hospital-based study on 5319 HAV patients[18].

Regarding HAV, it's also important to note that 55.70% of the cases in our study involved children younger than 12 years old. According to the model outlined by Aggarwal et al., this puts a significant percentage of individuals at risk of getting jaundice[18]. The neighbourhood may also be impacted by the study's increasing percentage of adult hepatitis A patients. Given India's 2014 Clean India Mission and 2018 NVHCP, this merits more research. The literature from India has reported a seroprevalence of above 80% in children under the age of ten[19]. Over the past 20 years, there has been a discernible change in the seroprevalence and a slow decline in seropositivity in children under the age of ten[20]. In their evaluation of the literature, Agrawal et al. observed that seroprevalence shifted significantly towards teenagers and adults in both urban regions and those with higher or moderate socioeconomic position relative to those in rural areas and those with lower socioeconomic status, respectively[21]. However, Arankalle et al. found that this change was only noticeable among urban areas' higher socioeconomic groups, while children from cities' lower socioeconomic groups and those from rural households belonging to all socioeconomic groups showed comparable, high seroprevalence[20].

Overall seropositivity was high in males (77/548) as compared to females (72/599). We tested 286 samples out of 83 (29.02%) serologically reactive for HAV seropositivity in the age group under 12 years. We performed a liver enzyme test at the same time and noticed the variation (Figure IV). But less than 12 years, the seropositivity is higher in females (46/137) compared to males (37/149). It’s a significant observation in our study.

HAV infections were shown to occur all year round, however there was a noticeable seasonal change in the occurrence, with the highest number of cases recorded during the monsoon and post-monsoon seasons, which run from September to December.

This result is in line with earlier research conducted in India[22] (Figure – V).
The present study has a few limitations. First, this was a hospital-based study, and since asymptomatic individuals (usually children) are less likely to know their illness and seek medical assistance, the seroprevalence in the community may comprise a fraction of children/pediatric population that did not report to the hospital. Second, we could not do molecular or genotype study owning to financial constraints and the fact that the study was a retrospective study. Lastly, serological diagnosis of HAV is challenging as the assays demonstrate a wild variation in performance characteristics such as sensitivity as well as specificity owing to factors such as high titers of IgG interfering with IgM detection assay or lower antibody levels in immunocompromised as compared to immunocompetent individuals.

Conclusions

The aetiological agent of the present investigation is Hepatitis A virus which emerged from an outbreak in our region. The changing epidemiological patterns that HAV displays in response to socioeconomic progress in developing countries require careful attention. Interventions, such as universal childhood vaccination program, must be properly implemented and timed correctly. If a vaccination program introduced to a low-endemic region achieved inadequate coverage, it would likely exacerbate the epidemiological transition it was intended to ameliorate.

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