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Role and Relationship of Immunoglobulin M with Aminotransferase Enzyme in Patients with Hepatitis A

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Running Title: **Immunoglobulin M with Aminotransferase Enzyme in Patients with Hepatitis A**

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Abstract

Background: Hepatitis A virus (HAV) contamination causes liver irritation, resulting in improved aminotransferase enzyme levels. **Objectives**: This study aimed to investigate the correlation among HAV-particular immunoglobulin M (IgM) antibodies and liver enzyme activity, **including** alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total serum bilirubin (TSB), across varying ranges of ailment severity. **Method:** A total of 170 sufferers with HAV contamination have been categorized into mild (n = 60), moderate (n = 25), and severe (n =85) organizations. Serological exams (HAV IgM) and liver characteristic tests were performed. **Result:** Significant increase in ALT, AST, and TSB levels has been determined with sickness severity ($p < 0.0001$ and $p = 0.003$, respectively), even as ALP showed no large variation ($p = 0.967$). Correlation evaluation discovered strong, high-quality relationships between HAV IgM degrees and ALT ($r = 0.648$, $p < 0.0001$) and AST ($r = 0.523$, $p < 0.0001$); however, no association with ALP ($r = 0.1/2$, $p = 0.943$). **Conclusion:** These findings recommend that ALT and AST are reliable biomarkers for assessing liver harm severity in HAV infections, while HAV IgM levels may also function as a trademark of ailment development. The study underscores the significance of habitual monitoring of aminotransferase enzymes and HAV IgM levels in coping with HAV patients. Future research needs to focus on longitudinal research to validate these findings and investigate the underlying mechanisms of HAV-brought liver damage.

Keywords: Liver Function Tests (LFTs), AST, ALT, Immunoglobulin M (IgM).

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Introduction:

Hepatitis A (HA) is an acute infectious disease caused by the hepatitis A virus (HAV). HA usually occurs in the form of a local epidemic, and it is mainly transmitted via the fecal-oral route. It is estimated that the worldwide incidence of the disease exceeds 1.4 million cases each year, with the health cost being between 1.5 to 3.0 billion dollars annually [1]. The transmission of the virus is due to poor sanitation conditions and lack of hygiene in the area, whereby infection is acquired through the fecal-oral route [2]. The lack of availability of food and water, as well as scarcity of safe water for use in developing countries, has been reported as the main cause of high disease incidence, with the WHO reporting about 1.4 million cases per year [3, 4]. The different clinical features that result from the hepatitis A virus infection range from complete to acute hepatitis or acute liver failure, the latter being very rare [5]. Immunity to the virus is manifested by the development of IgM antibodies, especially at the early stages of infection, even before the age of 6 months [6]. Diagnosis of acute infection is confirmed by determination of the concentration of IgM antibodies specific to HAV as the standard; however, the detection of IgG antibodies is used to confirm previous exposure to the infection and to monitor long-term immune protection [7]. Liver function tests (LFTs) are essential to determine the severity of liver injury in cases of hepatitis. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the main enzymes that are released into the bloodstream when the hepatocyte is injured; ALT demonstrates a stronger liver specificity because it is extremely abundant within hepatocytes [8]. AST is also released from hepatocytes but is also present in other tissues, including cardiac and skeletal muscle, thus diminishing specificity [9]. Alkaline phosphatase (ALP) would be elevated in cases of cholestasis or biliary obstruction, but does not necessarily indicate direct hepatocyte injury [10]. Serum total bilirubin (TSB) levels would increase in response to hepatic conjugation and excretion impairments, further indicating the severity of hepatic dysfunction [11].

Historically, there has been insufficient and inconsistent data indicating a relationship between the magnitude of the IgM antibody response and the severity of hepatic injury in HAV; additional research may clarify this relationship and provide clinical significance by allowing risk-stratification of patients based on the degree of liver disease severity and risk of hepatic complications.

This study focused on examining the relationship between HAV IgM titers and liver enzyme activity (ALT, AST, ALP, and TSB) among diverse levels of disease severity. Such associations may be crucial to enabling the optimization of diagnostics to monitor patients with acute hepatitis A.

Aim of the study:

This study aimed to demonstrate the relationship between the levels of IgM antibodies against hepatitis A virus (HAV) and liver functions indicated by ALT, AST, and ALP enzymes, as well as serum total bilirubin at varying levels of disease, and to evaluate the ability of the analyzers to identify the degree of liver damage after acute hepatitis A infection in the patients concerned.

Materials and Methods:

Study Design:

This study was carried out over a six-month duration, from July 2024 to December 2024, and concerned 170 patients recognized with hepatitis A virus (HAV) infection. Participants were randomly sampled from outpatient gastroenterology (GIT) clinics and then assigned to one of three separate companies depending on the severity of their disease: 60 individuals were assigned to the mild group, 25 to the moderate, and 85 to the severe. The severity and seriousness of HAV infection were established from an aggregate of scientific history, laboratory tests, and medical and health practitioner assessments. All persons underwent the following standardized diagnostic methods to confirm HAV infection and maintain consistency in group arrival.

For this study, a 5-mL blood sample was obtained from each subject via sterile venipuncture. Blood samples are allowed to stand clotting for approximately 20 minutes at room temperature after sampling and before being processed.

Inclusion and Exclusion Criteria:

To ensure the reliability of the results and reduce confounding variables, strict inclusion and exclusion standards were applied. Patients eligible for inclusion in the have a look at have been people with a confirmed diagnosis of acute hepatitis A virus infection. Confirmation was based on scientific symptoms and serological detection of HAV-specific immunoglobulin M (IgM) antibodies. Participants included within the study were elderly between 18 and sixty-five years old and had no prior records of continual liver illnesses.

Exclusion criteria have been designed to eliminate capacity-confounding elements. Patients with persistent ailments, including diabetes mellitus, chronic liver disease, or some other conditions.

Laboratory Procedures Liver Function Test (LFTs):

The quantity of liver damage in HAV-inflamed sufferers was evaluated the usage of a complete liver function test (LFT) panel. The serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) were measured using a completely automatic biochemical analyzer (Cobas C311, Roche Diagnostics). These enzymes had been selected because of their elevated function as signs of hepatocellular harm. ALT and AST are mainly sensitive markers of liver inflammation and injury, while ALP is more closely associated with biliary obstruction or cholestasis. Total serum bilirubin (TSB) tiers had been additionally measured to assess the liver’s capacity to metabolize and excrete bilirubin and to evaluate the extent of hepatocellular dysfunction.

HAV IgM Antibody Detection:

The presence and working level of HAV-specific IgM antibodies in the serum were assessed using an enzyme-linked immunosorbent assay (ELISA) kit available from commercial sources. The ELISA system was administered according to the manufacturer's instructions to ensure accuracy and reliability of results. HAV IgM was quantified and reported in milli-international units per milliliter (mIU/mL). The antibody levels were a marker of acute HAV infection and correlated with liver enzyme activity and clinical severity of disease.

Statistical Analysis

SPSS model 26 (IBM Corp.) was used for the statistical analysis of the records with statistical significance at p-values $\leq$ 0.05. Descriptive statistics were calculated, including means and standard deviations, to describe the data for each parameter. The following statistical processes were used to determine and evaluate the effects:

Ethical Considerations:

The study received ethical approval from the institutional review board and followed the ethical study requirements. All participants received written informed consent before participation in the study. Participants were debriefed about the purpose, methods, and potential risks, and confidentiality was maintained throughout the research. All procedures were performed in accordance with ethical standards as outlined in the Declaration of Helsinki.

Results:

HAV IgM Antibody Levels and Disease Severity

Table 1 illustrates that the levels of HAV IgM antibodies were different across all three groups (mild, moderate, and severe infection). The group of patients that were classified as mild exhibited the lowest levels of HAV IgM antibodies (2.42 ± 1.71 mIU/mL), while the group of patients classified as severe displayed the highest levels of HAV IgM antibodies (10.91 ± 2.88 mIU/mL). Furthermore, the moderate group patients had levels of HAV IgM that were classified as intermediate (7.1 ± 0.46 mIU/mL). The variance in levels of HAV IgM in all three groups exhibited was proven statistically highly significant ($p < 0.0001$). The results of the tests on the liver function were significantly different across the three groups (mild, moderate, and severe infection), which is confirmed by Table 2. The accentuated and progressive increase, which was documented in all the stages of the HAV IgM's gradual ascending tiers, is directly proportional and reflects the advancing disorder's HAV IgM dilution depth. This means that with the depth of disorder severity, more markers of infection can be observed. Such results, demonstrating the order of HAV IgM, serve to confirm that this measurement can be utilized, as well as the depth of the reaction, to assess and manage the infection. To assess the relationship between liver function and HAV IgM levels, Pearson correlation analysis was done.

The results revealed significant positive correlations between HAV IgM levels and ALT, AST, and TSB, while no significant correlation was observed with ALP.

In Table 3. A strong positive correlation was found between HAV IgM levels and ALT ($r = 0.648$, $p < 0.0001$), meaning that higher HAV IgM levels are related to higher ALT levels. These results support the hypothesis that HAV IgM levels reflect hepatocellular damage severity, as ALT is released into the bloodstream during liver inflammation/damage. HAV IgM levels were also positively correlated with AST moderately ($r = 0.523$, $p < 0.0001$). Though AST is less tissue-specific for liver injury than ALT, AST elevations observed during HAV infection demonstrate how much damage the hepatocyte sustained. In this regard, both HAV IgM and AST levels are correlated, which represent two markers of hepatocellular injury.

There was a weaker (but still statistically significant) positive correlation with HAV IgM levels and TSB ($r = 0.257$, $p = 0.001$). In other words, although HAV IgM levels are related to bilirubin metabolism, it is a weaker correlation than the aminotransferases relationships. Elevation of TSB levels is also a likely secondary effect of hepatocellular injury (i.e., further impaired liver metabolism of bilirubin due to inflammation/damage to the liver cells). There was no observable correlation between HAV IgM levels and ALP ($r = 0.005$, $p = 0.943$). The absence of an association supports the premise that HAV infection primarily impacts hepatocytes, as opposed to bile ducts, which is consistent with the stable ALP values among severity groups. The absence of a correlation between HAV IgM and ALP accentuated the specificity of HAV-induced liver injury to hepatocytes. There was a weaker but statistically significant correlation among HAV IgM ranges and TSB (r = 0.257, p = 0.001). This demonstrates that HAV IgM levels may associate with bilirubin metabolism; however, that association is not always as robust as it is with aminotransferases. Increased TSB levels are likely a secondary consequence of hepatocellular injury

Table 1. Severity of Viruses HAV AB IgM

Parameter	**Mild** Means ± SD N=60	**Moderate** Means ± SD N=25	**Severe** Means ± SD N=85	P-value
HAV AB IgM(mIU/mL)	2.42±1.71	7.1±0.46	10.91±2.88	<0.0001
P-value according to the F-test				

Table 2. The Severity of Viruses with LFT.

Parameter	**Mild** Means ± SD N=60	**Moderate** Means ± SD N=25	**Severe** Means ± SD N=85	P-value
TSB	5.00±4.59	6.59±2.71	7.11±2.98	0.003
ALT	501.30±3.49.64	971.42±360.31	1484.66±662.79	<0.0001
AST	335.33±334.08	729.48±331.67	1124.788±745.55	<0.0001
ALP	424.82±254.424	422.48 ±186.06	421.64 ± 183.02	0.967
P-value according to the F-test				

Table 3. The Correlation of HAV-IGM Ab with LFT

Parameter		TSB	ALT	AST	ALP
HAV IgM	**r**	0.257**	0.648**	0.523**	0.005
	P	0.001	<0.0001	<0.0001	0.943
***. Correlation is significant at the 0.01 level (2-tailed).*					

Visual Representation of Correlations

The relationships among HAV IgM ranges and liver enzymes were illustrated through scatter plots, imparting a visible representation of the statistical correlations. Figure 1a shows a robust, fantastic correlation between HAV IgM and ALT levels, with a clear upward trend in ALT levels as HAV IgM stages increase. This highlights the sensitivity of ALT as a marker of liver injury in HAV infection. Similarly, Figure 1b depicts a slightly higher-quality correlation between HAV IgM and AST degrees, showing a less steep but nonetheless significant upward trend. In evaluation, Figure 1c illustrates the dearth of correlation between HAV IgM and ALP stages, as the scatter plot indicates no discernible pattern. These visualizations support the findings from the statistical evaluation and offer, in addition, proof of the connection between HAV IgM stages and specific liver feature parameters

The results of this study displayed an association between HAV IgM antibody and liver function parameters, especially ALT and AST, which are markers of hepatocellular damage. ALT showed the strongest correlation with HAV IgM tiers, emphasizing its application as a sensitive biomarker of liver harm in HAV contamination. AST correlated moderately with HAV IgM levels, whilst TSB confirmed a weaker affiliation. ALP ranges, however, remained extraordinarily solid and confirmed no correlation with HAV IgM, indicating that HAV usually affects hepatocytes rather than bile ducts

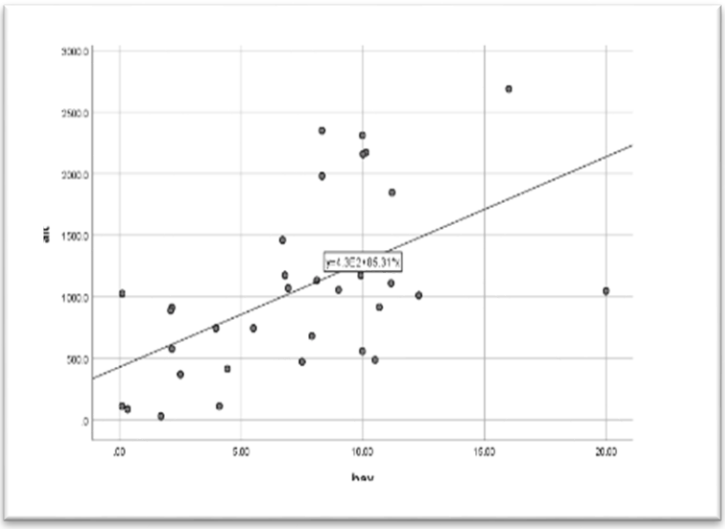

Figure 1a: The Correlation of HAV IGM AB with ALT activity

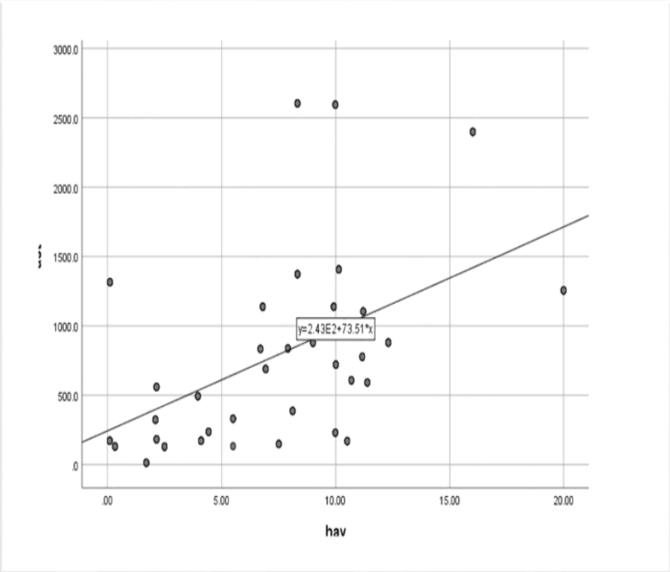

Figure 1b: The Correlation of HAV IGM AB with AST activity

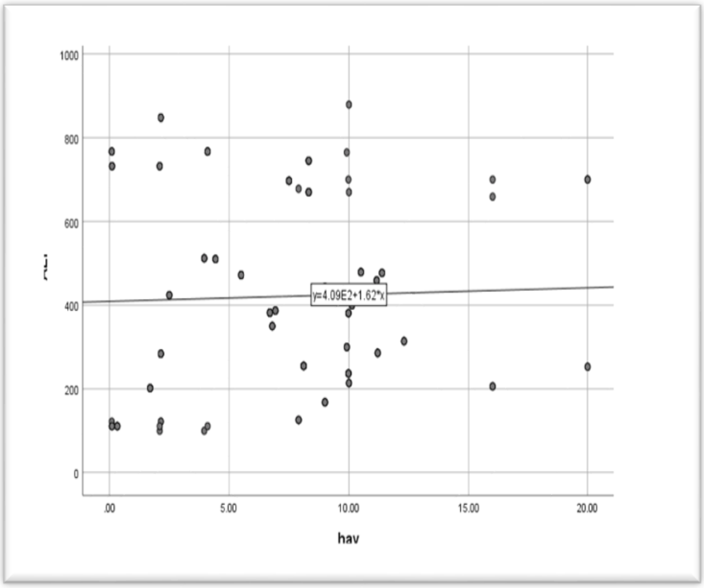

Figure 1c: The Correlation of HAV IGM AB with ALP enzyme

Discussion

This study aimed to assess the relationship between hepatitis A virus (HAV) IgM antibodies and liver function parameters, and also determine which HAV infection affects liver characteristics according to disease severity. Such effects have appeared in differences of the HAV IgM and liver enzymes between various agencies (mild, moderate, and severe contamination). These findings are consistent with previous literature and provide valuable information on the pathophysiology of HAV and its effects on liver function.

Observation found a strong correlation between HAV IgM titer and liver function tests, including alanine aminotransferase (ALT)/aspartate aminotransferase (AST). The findings demonstrated that with the degree of HAV, ALT, and AST levels along with serum HAV IgM concentrations have increased. These results are in keeping with previous studies showing that prolonged aminotransferase elevations are surrogate markers of liver infection and damage among patients with viral hepatitis (5).

The association of ALT with HAV IgM ($r = 0.648$, $p < 0.0001$) supports that it is a sensitive marker of liver injury in HAV infection. ALT is generally synthesized in the hepatocytes and released into the blood during liver injury or infection The current study demonstrated further moderate positive correlation of HAV IgM with AST ($r = 0.523$, $p < 0.0001$), as has also been reported by other researchers that showed that while less liver specific than ALT, AST levels go up in cases of hepatic inflammation (8). These results endorse the assumption that the increase of aminotransferase enzymes does represent liver cell necrosis or injury caused by HAV inflammatory response (14,15). Liver function tests, most pronounced with the transaminases (ALT and AST), were also strikingly abnormal depending on the severity of HAV infection. ALT and AST values were highest in the severe group (1484.66±662.79 and 1124.79±745.55 U/L, respectively), with P-values <0.0001, which aligns with reports describing acute hepatocellular injury as a hallmark of HAV infection [16–18]. In contrast, alkaline phosphatase (ALP) levels showed no significant variation across groups (P=0.967), suggesting that cholestasis plays a less prominent role in HAV pathogenesis compared to hepatocellular injury [19,20]. Total serum bilirubin (TSB) was also significantly higher in patients with severe infection (7.11±2.98 mg/dL), with a P-value of 0.003. Although bilirubin levels are not specific to HAV, they serve as supportive markers of hepatocellular dysfunction [21,22]. The correlation analysis further validated the clinical significance of HAV IgM titers. HAV IgM levels correlated strongly with ALT (r=0.648, P<0.0001) and AST (r=0.523, P<0.0001), and modestly with TSB (r=0.257, P=0.001), while showing no correlation with ALP (r=0.005, P=0.943). These correlations affirm that the elevation of HAV IgM titers parallels hepatocellular enzyme derangement, reflecting active immune-mediated hepatic injury during the acute phase [23–25]. It is noteworthy that some patients with mild clinical symptoms presented with elevated liver enzymes and detectable IgM levels, which underscores the variability in host response and the necessity of biochemical evaluation regardless of clinical presentation [26,27]. In agreement with other observational studies, our findings highlight the utility of HAV IgM levels not only as a diagnostic tool but also as a potential marker for disease severity. This may help in stratifying patients for closer monitoring or hospitalization [28–30]. While this study offers valuable insight, certain limitations must be acknowledged. First, the observational design precludes causality assessment. Second, the sample size in the moderate group was relatively small, which may affect statistical power. Lastly, this study did not assess long-term hepatic outcomes or co-infections, which may influence enzyme levels and clinical interpretation [31–33]. Future research should include longitudinal follow-up and exploration of inflammatory cytokines and immune markers to better understand the host-virus interaction and its role in liver injury during HAV infection [34–37].

Conclusion

In the end, this study demonstrated an extensive correlation among HAV IgM stages and liver enzyme activity, highlighting the application of aminotransferase enzymes as biomarkers of liver injury in HAV infection. The findings underscore the innovative nature of liver disorders with increasing ailment severity and provide precious insights into the pathophysiology of HAV-caused liver injury. These outcomes have critical implications for the clinical control of HAV contamination, emphasizing the need for habitual tracking of liver enzymes and HAV IgM tiers to manual treatment selections and enhancing patient outcomes. Future studies should build on these findings to further elucidate the mechanisms of HAV-precipitated liver injury and expand predictive tools for sickness severity and progression.

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Conflicts of interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Source of Funding

No funding was received for this study

Conflict of interest: NIL

Authors Contribution

All authors contributed equally to the conception, design, data collection, analysis, and writing of this study. Each author has read and approved the final manuscript.

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