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ORIGINAL ARTICLE

Impact of Hepatitis a Virus Infection on the Liver in Children Infected in Upper Egypt, Case Control Study

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ABSTRACT

Background: *Infection with hepatitis A virus (HAV) occurs worldwide and is the most common cause of acute hepatitis. Egypt is considered an area of high prevelance for HAV infection, with the highest prevalence of infection in early childhood.* ***Objective:*** *the aim of the work is to study the viral effect and pathophysiological changes in the liver as a result of HAV infection in children in Upper Egypt.* ***Methodology:*** *It is a case-control study of 250 children with suspected HAV infection confirmed by HAV-IgM using enzyme-linked immunosorbent assay (ELISA). In order to investigate liver pathophysiology before starting the treatment protocol, fifty affected children were randomly selected to undergo biochemical tests, including Alanine aminotransferase, Aspartate transaminase, alkaline phosphatase, Gamma glutamyl transpeptidase, total bilirubin, direct bilirubin, Lactate dehydrogenase, and total Leukocyte count. These tests were performed after 1 and 2 weeks of treatment, and the results were compared with 25 children who were confirmed to have no antibodies to HAV as proof.* ***Result:*** *Our results showed that 70 (28%) children were infected with hepatitis A virus. Our findings demonstrated that the levels of HAV-IgM, total Leukocyte count, Alanine aminotransferase, Aspartate transaminase, alkaline phosphatase, Gamma glutamyl transpeptidase, total bilirubin and direct bilirubin all had strong statistical significance between normal and HAV-infected children. While our results showed that there are no statistical differences between children after third week of treatment and normal children in in the level of HAV-IgM, total Leukocyte count, Alanine aminotransferase, Aspartate transaminase, alkaline phosphatase, Gamma glutamyl transpeptidase, total bilirubin and direct bilirubin. Accordingly, the vital functions of the liver improved to normal after the third week of treatment for HAV.* ***Conclusion:*** *After the third week of treatment (liver support, multivitamins), the liver functions of HAV infected children well be full recovered.*

INTRODUCTION

Infection with Hepatitis A Virus is common worldwide, with varying epidemiology based on age of exposure and HAV vaccination. Globally, there are about 1.4 million hepatitis A cases annually[1]. The level of environmental cleanliness and the current socioeconomic and hygienic conditions are strongly correlated with the prevalence of HAV infection[2]. The fecal–oral pathway is the most frequent way that hepatitis A is spread[3]**.** Because poor sanitation practices encourage the virus's spread, developing nations have the highest prevalence of this infection[2].

The majority of infections in high endemicity areas occur in early childhood. The infection is typically mild, nonspecific, or asymptomatic in this age group, and it produces anti-HAV antibodies that provide lifetime protection against reinfection[4].

Egypt was once thought to be a region with high endemicity for HAV infection, with early childhood infection having the highest prevalence[5]**.**

The host immunological reaction to HAV results in hepatic damage. Hepatocyte cytoplasm is where the virus replicates, and human leukocyte antigen-restricted, HAV-specific CD8+ T-lymphocytes and natural killer cells induce hepatocellular damage and the death of infected hepatocytes[6]. It seems that interferon-gamma plays a key part in encouraging the removal of infected hepatocytes[7]. Severe hepatitis is linked to an overwhelming host response, which is indicated by a

significant decrease in the circulation of HAV ribonucleic acid (RNA) after acute infection[8]. This study aims to investigate the biochemical effect on the liver as a result of infection with HAV.

METHODOLOGY

Sample collection

A survey was conducted on 250 children aged between 4 and 11 years, attending Pediatrics Department at Sohag University Hospital from July 2024 to October 2025, during which a rapid study was conducted to find HAV by detecting HAV-IgM antibodies by using Enzyme Linked Immunosorbent Assay (ELISA) .

All serum samples were taken for the children, taking into account all infection control precautions while taking blood samples, 70% isopropyl alcohol in water and 1% iodine were used for a minute, then the site was carefully cleaned until dry, and about 5 ml of blood was extracted into a sterile tube to avoid contamination of the sample, the blood samples were centrifuged for 10 minutes at 4000 RPM, and the serum was collected and preserved at -70C. Also, 2 ml of whole blood was taken in tubes containing ethylene diamine tetraacetic acid (EDTA), in order to study the number of Total leucocyte count.

Our results for 250 children revealed that 70 infected children had antibodies to HAV (28% Positive HAV-IgM) and 180 sick children were completely free of antibodies.

Fifty affected children were randomly selected to undergo biochemical tests, e.g. ALT, AST, ALP, GGT, T.Bil, D.Bil, LDH and TLC test for each patient to report the liver function tests before starting the treatment protocol. Follow-up of these tests was conducted a week after receiving treatment, as well as two weeks after onset of symptoms, and these effects were compared with 25 children not infected with HAV which was confirmed by the absence of antibodies to HAV.

Hepatitis A virus treatment

There was no specific treatment required for HAV infection. Only symptomatic and supportive can be given for symptomatic patients. Patient with fulminant liver cell failure may require ICU admission. At our study the patients received liver support and multivitamins and followed after one week, two week and three weeks from starting treatment.

Serum markers for HAV infection

All groups under study had venous blood samples (5 ml) aseptically extracted in plain vacutainer tubes. The samples were centrifuged for 15 minutes at about 1000 x g after being allowed to clot for 4 hours at room temperature. The clear sera kept frozen at -80°C. Repeated freeze-thaw cycles were avoided.

Detection of anti-HAV IgM:

Anti-HAV IgM ELISA Assay Kit (ZEUS Diagnostic, Inc. ELISA kit) is an enzyme immunoassay used to detect anti-HAV IgM. Serum samples are diluted and added to a microtiter plate coated with antibodies against human IgM antibodies. Specific antibodies bind to the antibodies, and HAV is added. Substrate was added after thorough washing, and when horseradish peroxidase enzyme-catalyzed, the substrate turned blue. The reaction was stopped by adding a sulfuric acid solution, and the color shift was recorded using spectrophotometry at 450 nm. The O.D. of the samples was then compared to the standard curve to ascertain the concentration of HAV-IgM in the samples.**(Stat fax 4700 ELISA Reader)**.

Liver function test:

The liver function tests were determined using the Spectrophotometer system (Photometer 5010 by Robert Riele GMbH & Co KG,German made) which is based on the principle of Colorimetric in total bilirubin, direct bilirubin tests, as well as enzymatic methods for ALT, AST, ALP, GGT and LDH tests. Every test was conducted using solutions produced by the German company Human Diagnostic Worldwide.

Statistical analysis

SPSS version 21 was the statistical software used to code and enter the data. For quantitative variables, the mean, standard deviation, and median were used to describe the data; for categorical variables, the frequencies (number of cases) and relative frequencies (percentages) were used. When comparing more than two groups, the nonparametric Kruskal-Wallis test was used to compare quantitative variables; when comparing two groups, the nonparametric Mann-Whitney U test was used. When appropriate, the chi square or Fisher's exact test was employed to compare the groups. We computed odds ratios and their 95% confidence intervals. P values ≤ 0.05 were regarded as statistically significant.

RESULTS

A survey was conducted on 250 children to detect hepatitis A virus who carry symptoms such as fever, jaundice, colic, and diarrhea. Our results showed that there are 70 (28%) children infected with hepatitis A virus. These results were confirmed by HAV-IgM using Enzyme linked immunosorbent assay (ELISA). **(Table 1)**

Table 1: HAV-IgM detection rate in blood samples

No. children / Total	Percent (%)	HAV-IgM
180 / 250	74 %	Negative
70 /250	28 %	Positive

Our study showed that males were more HAV-IgM positively compared to females and there is no significant difference (P. value = 0.035) between males and females in positive and negative cases of HAV-IgM. **(Table 2)**

Table 2: HAV-IgM Estimating Gender-Related Patients

Gender specific positive and negative HAV-IgM					
Variables			**Sex**		***P*-value**
			Male	**Female**	
HAV-IgM	Positive	Count	46	24	0.035
		% within Sex	65.7%	34.3%	
	Negative	Count	124	56	
		% within Sex	68.9%	31.1%	
Total		Count	170	80	
		% within Sex	100.0%	100.0%	

Our statistics on self-reported symptoms when children with HAV-IGM were admitted to the hospital showed that the most common symptoms were fever and jaundice at a rate of 77.1% and 97.1% respectively, while less frequent symptoms included such as choluria, diarrhea, and expistaxis, occurring at a rate of 30% and 25.7%. % and 14.2%, respectively **(Table 3)**

Table 3: The most common symptoms of children infected with HAV-IgM

Common Symptoms	No. of Cases	Percent (%)
Fever	54	(77.1%)
Jaundice	68	(97.1%)
Choluria	21	(30.0 %)
Diarrhea	18	(25.7%)
Epistaxis	10	(14.2%)

Table 4 shows the statistical significances of the biochemical tests for children infected with HAV and normal children. Our results showed that there are high statistical significances (P. value < 0.05) in the level of HAV-IgM, TLC, ALT, AST, ALP, GGT, T. Bili. and D. Bili.

Table 4: Comparison of biochemical tests between children infected with hepatitis A virus and normal children

Variables		Children infected with HAV	Normal children	*T*. test [a]	*P*-value	Sig.
HAV-IgM	Mean±SD	23.83±8.86	0.31±0.15	15.46	0.000	H.S
TLC (X10 ^{3}/mm^3)	Mean±SD	21.68±2.40	9.01±2.89	19.08	0.000	H.S
ALT (U/L)	Mean±SD	2288.60±679.83	23.08±9.23	17.56	0.000	H.S
AST (U/L)	Mean±SD	1797.66±422.69	24.10±7.02	22.72	0.000	H.S
ALP (U/L)	Mean±SD	401.38±128.30	215.01±54.16	6.84	0.000	H.S
GGT (U/L)	Mean±SD	174.76±126.09	22.04±7.00	5.59	0.000	H.S
LDH (U/L)	Mean±SD	883.47±77.83	302.80±46.71	25.40	0.000	H.S
T. Bil (mg/dl)	Mean±SD	5.65±0.91	0.95±0.29	20.31	0.000	H.S
D. Bil (mg/dl)	Mean±SD	4.66±0.95	0.16±0.005	21.87	0.000	H.S
N.S: Non Significant **S :** Significant **H.S :** Highly Significant						

The biochemical test results for children with hepatitis A virus before and after therapy during the first week are displayed statistically in Table 4. Our findings demonstrated that the levels of HAV-IgM, TLC, ALT, AST, GGT, T. Bili, and D. Bili all had strong statistical significance (P. value < 0.05). Additionally, the statistical significance revealed that the levels of ALP did not change in a way that was statistically significant (P. value > 0.05) **(table 5)**.

Table 5: Different changes in biochemical tests between children infected with hepatitis A virus before and after the first week of treatment

Variables		Children infected with HAV	Children after treatment in the first week	*T.* test[a]	*P*-value	Sig.
HAV-IgM	Mean±SD	23.83±8.86	10.45±3.25	17.57	0.000	H.S
TLC (X10 ^{3}/mm^3)	Mean±SD	21.68±2.40	19.12±1.49	8.27	0.000	H.S
ALT (U/L)	Mean±SD	2288.60±679.83	978.60±355.70	15.098	0.000	H.S
AST (U/L)	Mean±SD	1797.66±422.69	673.06±285.19	22.03	0.000	H.S
ALP (U/L)	Mean±SD	401.38±128.30	395.90±120.86	0.224	0.824	N.S
GGT (U/L)	Mean±SD	174.76±126.09	79.26±23.19	5.38	0.000	H.S
LDH (U/L)	Mean±SD	883.47±77.83	669.20±117.32	6.91	0.000	H.S
T. Bil (mg/dl)	Mean±SD	5.65±0.91	3.32±0.93	16.58	0.000	H.S
D. Bil (mg/dl)	Mean±SD	4.66±0.95	2.26±0.53	18.70	0.000	H.S
N.S: Non Significant **S :** Significant **H.S :** Highly Significant						

Table 6 shows the statistical significances of the biochemical tests for children infected with hepatitis A virus before treatment and after receiving treatment in the second week. Our results showed that there are high statistical significances (P. value < 0.05) in the level of HAV-IgM, TLC, ALT, AST,GGT, T. Bili. and D. Bili. The statistical significance also showed that there were no statistically significant differences (P. value > 0.05) in the levels of ALP.

Table 6: Different changes in biochemical test between children infected with hepatitis A virus before and after the second week of treatment

Variables		Children infected with HAV	Children after treatment in the second week	*T.* test [a]	*P*-value	Sig.
HAV-IgM	Mean±SD	23.83±8.86	2.27±1.29	22.11	0.000	H.S
TLC (X10 ^{3}/mm^3)	Mean±SD	21.68±2.40	15.48±3.19	10.41	0.000	H.S
ALT (U/L)	Mean±SD	2288.60±679.83	160.04±88.81	23.07	0.000	H.S
AST (U/L)	Mean±SD	1797.66±422.69	133.34±129.14	27.30	0.000	H.S
ALP (U/L)	Mean±SD	401.38±128.30	403.10±125.46	-0.70	0.944	N.S
GGT (U/L)	Mean±SD	174.76±126.09	36.34±8.48	7.79	0.000	H.S
LDH (U/L)	Mean±SD	883.47±77.83	543.27±88.24	26.47	0.000	H.S
T. Bil (mg/dl)	Mean±SD	5.65±0.91	1.71±0.57	19.69	0.000	H.S
D. Bil (mg/dl)	Mean±SD	4.66±0.95	1.79±0.47	12.80	0.000	H.S
N.S: Non Significant **S :** Significant **H.S :** Highly Significant						

The statistical significance of the biochemical tests for children infected with hepatitis A virus before treatment and after receiving treatment in the third week is displayed in Table 6.According to our findings, the levels of HAV-IgM, TLC, ALT, AST, ALP, GGT, T. Bili, and D. Bili all had significant statistical significance (P. value < 0.05) (table 7).

Table 7: Different changes in biochemical test between children infected with hepatitis A virus before and after receiving treatment in the third week

Variables		Children infected with HAV	Children after treatment in the third week	*T*. test [a]	*P*-value	Sig.
HAV-IgM	Mean±SD	23.83±8.86	0.27±0.086	22.77	0.000	H.S
TLC (X10 ^{3}/mm^3)	Mean±SD	21.68±2.40	9.08±2.96	24.43	0.000	H.S
ALT (U/L)	Mean±SD	2288.60±679.83	22.96±8.87	23.49	0.000	H.S
AST (U/L)	Mean±SD	1797.66±422.69	26.12±7.79	29.54	0.000	H.S
ALP (U/L)	Mean±SD	401.38±128.30	213.2±54.21	9.58	0.000	H.S
GGT (U/L)	Mean±SD	174.76±126.09	22.84±7.47	8.59	0.000	H.S
LDH (U/L)	Mean±SD	883.47±77.83	299.07±77.84	25.40	0.000	H.S
T. Bil (mg/dl)	Mean±SD	5.65±0.91	0.93±0.29	34.84	0.000	H.S
D. Bil (mg/dl)	Mean±SD	4.66±0.95	0.19±0.042	33.28	0.000	H.S
N.S: Non Significant **S :** Significant **H.S :** Highly Significant						

Table 8 shows the statistical significances in biochemical test between children after treatment in the third week and normal children. The statistical significance also showed that there were no statistically significant differences (P. value > 0.05) in the level of HAV-IgM, TLC, ALT, AST, ALP ,GGT, T. Bili. and D. Bili. (table 8, figure1).

Table 8: Show averages for the relations in biochemical test between children after treatment in the third week and normal children

Variables		Children after treatment in the third week	Normal children	*T*. test [a]	*P*-value	Sig.
HAV-IgM	Mean±SD	0.27±0.086	0.31±0.15	-0.122	0.904	N.S
TLC (X10 ^{3}/mm^3)	Mean±SD	9.08±2.96	9.01±2.89	0.088	0.931	N.S
ALT (U/L)	Mean±SD	22.96±8.87	23.08±9.23	0.299	0.768	N.S
AST (U/L)	Mean±SD	26.12±7.79	24.10±7.02	0.126	0.965	N.S
ALP (U/L)	Mean±SD	213.2±54.21	215.01±54.16	1.468	0.155	N.S
GGT (U/L)	Mean±SD	22.84±7.47	22.04±7.00	-1.32	0.201	N.S
LDH (U/L)	Mean±SD	299.07±77.84	302.80±46.71	-1.72	0.107	N.S
T. Bili. (mg/dl)	Mean±SD	0.93±0.29	0.95±0.29	0.980	0.337	N.S
D. Bili. (mg/dl)	Mean±SD	0.19±0.042	0.16±0.005	-0.53	0.958	N.S
N.S: Non Significant **S :** Significant **H.S :** Highly Significant						

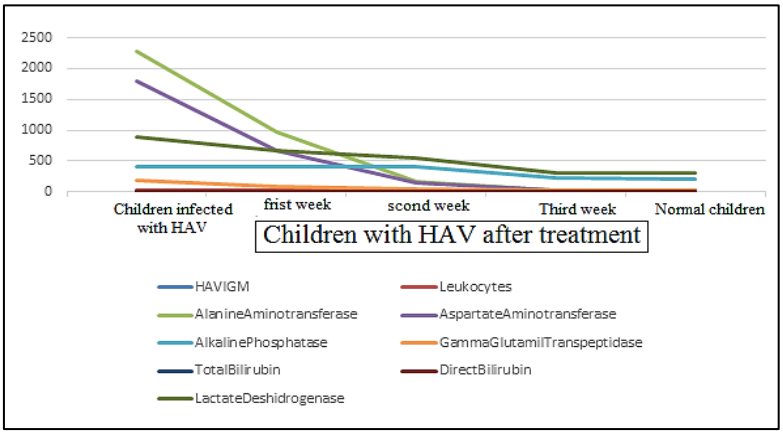

Fig. 1: Shows the effect of the hepatitis A virus on the vital functions of the liver during the infection stage and the treatment

DISCUSSION

An estimated 1.4 million new cases of hepatitis A virus (HAV) infection occur annually throughout the world[3]. In 2004, a different Egyptian study found that children aged 3 to 18 years had a higher prevalence of HAV Ab (86.2%)[9]. The prevalence was also higher than ours in other, earlier Egyptian investigations[10]. Our results showed that there are 28% children infected with hepatitis A virus.

HAV spreads throughout the world and is spread by the fecal-oral pathway. When fecal HAV shedding is still happening and serum aminotransferase activity is high during acute sickness, antibodies to HAV (anti-HAV) can be found. Rarely lasting six to twelve months, this early antibody response is primarily of the IgM class. However, IgG-class anti-HAV antibodies take over as the most common antibody after convalescence. Hepatitis A does not develop into chronic liver disease and stays self-limited[11]. Males had higher levels of HAV-IgM than females, according to our study, and there was no significant difference between males and females in HAV-IgM positive and negative cases. In contrast, 46/70 (65.7%) males and 24/70 (34.3%) females have positive HAV-IgM, whereas 124/180 (68.9%) males and 56/180 (31.1%) females have negative HAV-IgM.

A previous study reported that the majority of patients were from the lower middle class, with higher lower class coming in second. A useful screening tool and a reliable method for identifying hepatic impairment are liver function tests (LFT)[12]. Several studies have identified consequences such prolonged hepatitis, recurrence, hepatic failure, hematological abnormalities etc. in hepatitis A case. Our findings demonstrated that the levels of HAV-IgM, TLC, ALT, AST, ALP, GGT, T. Bili, and D. Bili all had strong statistical significance between normal and HAV-infected children.

Numerous aminotransferase enzymes are found in the liver; when inflammation damages the liver, these enzymes are discharged into the bloodstream in significant amounts. A high blood ALT serum level is indicative of necro-inflammation. A prolonged immune response will raise the risk of liver cirrhosis. Liver damage manifests during the immune clearance process. The analysis of ALT enzymes provides crucial details regarding the condition of liver function.The primary test for hepatitis patients is the liver function test (LFT), which can be used to identify the condition as well as evaluate its severity and prognosis[14]. The main test for hepatitis patients is LFT. The increase in ALT may outweigh the increase in AST in cases of acute hepatitis[13]. Patients with viral hepatitis had noticeably increased levels of alanine aminotransferase (ALT), where Patients with viral hepatitis had considerably higher levels of aspartate amino-transferase (AST) [15].Sequentially, Our results showed that there are high statistical significances in the level of HAV-IgM, TLC, ALT, AST, GGT, T. Bili. and D. Bili. between children with hepatitis A virus before and after therapy during the first week In contrast, there were no statistically significant differences in the levels of ALP between children with hepatitis A virus before and after therapy during the second week. While our results showed that there are no statistical differences between children after treatment in the third week and normal children in in the level of HAV-IgM, TLC, ALT, AST, ALP, GGT, T. Bili. and D. Bili.

Ethics approval and consent to participate

The ethical approval was obtained from the Ethics Board of the Faculty of Medicine, Sohag University for the study. All patients signed an informed consent before participating in the study.

Approval number of ethics committee: Soh-Med-25-1—6PD

Conflict of interest: All authors declared that there were no conflicts of interest.

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