Study subclinical hepatitis A infection in ambulatory patients, with nonspecific abdominal complaints in Mofid hospital of Tehran Iran

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Abstract

Background and Objectives: Epidemiology of Hepatitis A has changed in recent years, and with increasing age, its subclinical nature in childhood turns to more sever hepatitis. Fever and nonspecific gastrointestinal symptoms are found in common viral infections in children; this study tends to detect Hepatitis A infection in these children in an ambulatory referral children centre in Mofid Children Hospital. Tehran, Iran

Methods: Three hundreds and ten children aged 1-15 years old with nonspecific gastrointestinal symptoms came to emergency room of Mofid Hospital were selected. Each patient who had 4 from 10 defined clinical criteria and laboratory finding was eligible to entre our study Patients with any hepatic involvement by a confirmed or nonconfirmed infectious and noninfectious cause and hepatic drug reactions were excluded. All data results entered and analyzed in SPSS 18 software (SPSS Inc Chicaggo)

Results: Three hundred-and-ten patients (184 boys and 126 girls) with mean age of 7.45±4.13 years were investigated. forty (12.9%) were IgM positive and 103 (33.2%) were IgG positive. 90% of hepatiis A IgM positive patients were IgG positive also .54 patients(17.5%) had SGPT more than 90 IU/ml (more than twice normal), 26 of them (48.1%) were HAV IgM Positive. Logistic Regression Model showed IgM Positive patients had higher Bill (CI=0.22-0.69) P=0.001, SGPT (CI=38.3-69.9)P=0.000 and % lymph in CBC (CI=2.7-11.9) P=0.002, and IgG positive patients had higher SGPT (CI=9.7-31.5) P=0.000 and total WBC (CI=578-2185) P=0.001.There was no significant difference between IgM and IgG Positive and Negative groups in number of their positive clinical criteria.

Conclusion: Children with nonspecific gastrointestinal signs with more than twice normal SGPT are in high probability of Hepatitis A. Epidemiologic investigation of Hepatitis A in our community is in first priority and shows the necessity of Hepatitis A mass vaccination.

Key words: Hepatitis A, Epidemiology of Hepatitis A, Subclinical.

Introduction

Over the last two decades, the epidemiology of Hepatitis A virus (HAV) has changed in many Asian and Middle Eastern countries [1-3] Hepatic damage caused by hepatitis A virus is neither cythopathic [4-5] nor antibody-mediated [6] but occurs by killer T-lymphocytes activities[7] .These characteristics explains mild symptoms in younger age and possibility of prevention after exposure either by administration of antibody [8-11]or vaccination[12-13].Lower antibody level at higher age may result in higher proportion of susceptible individuals and ends to more sever mortality and morbidity of Hepatits A in community. In areas with poor water and sanitary conditions. HAV transmission occurs at earlier age. Improvements in socioeconomic and health status leads to delay acquisition of infection from childhood to adulthood.[14] Increase in SGPT more than twice normal level can be a laboratory sign for subclinical Hepatitis A with higher prevalence in developing

countries [15-17]. In this study we investigated Hepatitis A seropositivity in children with nonspecific gastrointestinal symptoms in a referral Children Hospital Mofid 2009-2010 Tehran, Iran.

Materials and methods

Three hundred and ten children with nonspecific gastrointestinal complaints from Ocher 2009-June2010) came to emergency department of Mofid Hospital were subject of our study. The sample size was calculated with Epi Info program assuming of 25% prevalence of HAV Seropositivity and 5% error[18] which was 300 cases. Selection criteria were clinical symptoms more commonly found in patients with subclinical Hepatitis A infections. We used ten sign and symptoms which were 1- abdominal pain 2-fever 3-fatigue 4- anorexia 5- nausea 6-vomiting 7- pain and tenderness on Right Upper Quadrant 8- history of hepatitis in one of family members or day care or school 9- dark colored urine and light colored stool 10- hepatomegaly and having 4 criteria was enough to entre the study. CBC, DIFF and PLATELET, Bill Total and Direct, SGPT, Anti HAV IgG and IgM(Panel 1) were performed for all study cases. In children with a history of HIV and/or HCV in mother and other family members. Anti HIV and Anti HCV was performed (Panel 2) for all patients. And in patients with Gianoti Crosti syndrome or serum sickness like syndrome or arthritis and arthralgia or glumerolonephritis in one to two months ago, cases with susceptible history of hepatitis B vaccination and/or blood and blood products transfusion or a history of Needle Stick (Panel 3), HBsAg was performed. In cases with hepathosplenomegaly with FTT and patients with cirrhosis without obvious cause ANA, Anti SMA, Anti KLM(Panel 4) was performed, all patients with panel 4 were also included in panel 1 to 3. Cases with known hepatic disease on any known infectious disease with hepatic involvement and patients with hepatic drug reactions were excluded from study.CBC tes was performed with Calibrated Kα21N system, SGPT was performed with Parsazmon Kit, and RA – 1000 SYSTEM, Anti HAV IgG and IgM, HBSAg and AntiHIV and AntiHCV were performed by DIALAB Kit (Enzyme Linked Immunosorbent Assay, Microwell Method, Technischen Produkten und Laborinstrumenten, Geselisschaft M.b.h. office@dialab.at. All data results entered and analyzed in SPSS 18 software (SPSS Inc Chicaggo) Descriptive analysis was done by bivariate analysis using chi-square with 5% significance level and Multivariate regression analysis used for independent predictors of seropositivity and 95% CI was calculated.

Results

Three hundred-and-ten patients (184 boys and 126 girls) with mean age of 7.45±4.13 years were investigated. Out of 310 patients .40 (12.9%) patients were IgM positive and 103(33.2%) were IgG positive.90% of HAV IgM positive patients were IgG Positive. 54 patients (17.5%) had SGPT>90 IU/L and 26 patients out of them(48.1%) were IgM positive.130 cases (41.5%) were under 5 years old. (figure 1). There was no significant difference between gender or age and IgM or IgG Positive and Negative results. Logistic Regression Model showed IgM Positive patients had higher Bill (CI=0.22-0.69) P=0.001, SGPT (CI=38.3-69.9) P=0.000 and %lymph in CBC (CI=2.7-11.9) P=0.002, and IgG positive patients had higher SGPT (CI=9.7-31.5) P=0.000 and total WBC (CI=578-2185) P=0.001. There was no significant difference between IgM and IgG positive and negative groups in number of their positive clinical criteria based on ten signs and symptoms which were selected to be checked in patients with nonspecific Gastrointestinal complaints.

Four cases were IgM+ and IgG-, represents 1% of children with nonspecific gastrointestinal signs and symptoms with acute HAV infection. The results of panel 2 were negative for all 11 cases selected. Seven of 23 cases checked for panel3 (30.4%) were HBSAg positive. No patient with indication for panel 4 was found. Two age groups with acute(a) and nonacute (b) infection (IgM+IgG+=a) (IgM-IgG+=b) had no significant difference (CI=-1.6-1.7) (data not shown). Table 1 shows, IgM positive children had higher Bill and SGPT and %lymph in CBC, and IgG positive children, had higher SGPT and total WBC and Logistic regression Multivariate analysis confirmed these results.

Table 1. IgM and IgG seropositivity in different clinical and laboratory variables in children with non-specific gastrointestinal symptoms in Mofid Children Hospital(Tehran, Iran)

Variables		Positive	Negative	95%Ci	P value
gender	IgM S.R*	Male 21	163	-	NS
		Female 19	107	-	NS
	IgG S.R	Male 38	68	-	NS
		Female 68	139	-	NS
Clinical criteria**	IgM S.R	4.4±0.9	4.3±0.6	-0.2-3	NS
	IgG S.R	4.3±0.7	4.3±0.6	-0. -2-1	NS
bilirubin	IgM S.R	1.5±0.7	1.1±0.5	0.22-0.69	0.000
	IgG S.R	1.27±0.6	1.15±0.5	0.15-0.2	0.08
SGPT	IgM S.R	91.7±47	37±41	38.3-69.9	0.000
	IgG S.R	58.3±47.1	37.7±43	9.7-31.5	0.000
Total WBC	IgM S.R	8939±4138	7686±2896	-112.2-2618.2	0.07
	IgG S.R	8768±3669	7286±2673	578-2185	0.001
Lymph%	IgM S.R	57±13	49±16	2.7-11.9	0.002
	IgG S.R	52±14	49±16	-0.3-6.8	0.07
Hct	IgM S.R	40±6	38±5	-0.3-3.7	0.09
	IgG S.R	38±5	38±5	01.9-0.6	0.3

**=Serologic Result*

*** Clinical criteria= FEVER+anorexia+vomiting+nausea+RUQtenderness+darkUrine+paleStool+hepatomegally+fatigue+AbdominaPain+arthritis*

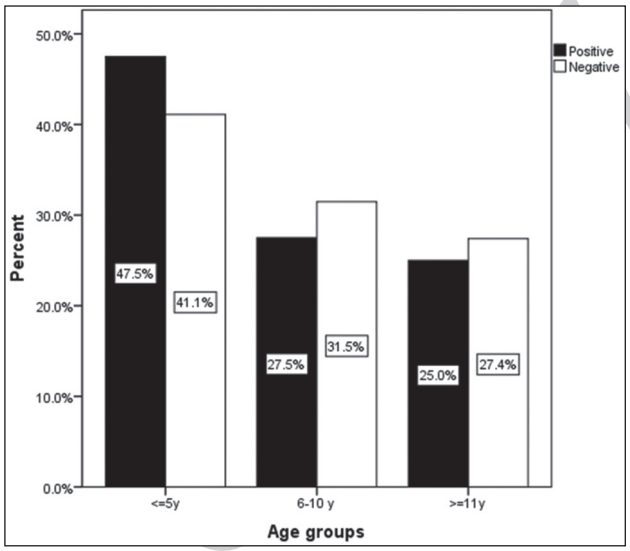

Figure 1. IgM Positive and Negative patints with different age groups in children with nonspecific Gastrointestinal signs and symptoms (Mofid Children Hospital 2009-2010))

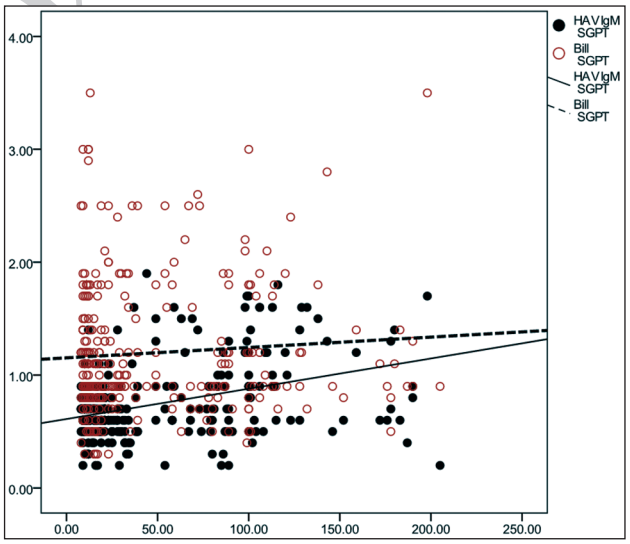

Figure 2. Relation between SGPT value and Bilirubin or HAV IgM in children with nonspecific gastrointestinal signs and symptoms (Mofid Children Hospital 2009-2010)

Discussion

Increase SGPT titer in a child under 5 year with nonspecific GI symptoms can be a laboratory predictor of subclinical hepatitis with the most important etiology of hepatitis A (90% of cases in Pakistan[16] and 50% in USA [19].

In this study 47% of cases with high SGPT had subclinical hepatitis A, means that other viral etiologies are becoming more responsible and hepatitis is shifting towards higher age. Hepatitis A is endemic in developing countries in Asia, Africa and South America. lower socioeconomic status is accompanied by lower age of sickness, in regions with intermediate endemicity, seronegative individuals increase gradually and ends to epidemics with more clinical cases[19]. Approximately 1% of our cases were IgM positive and IgG negative. We assume this phenomena occurs during a three weeks time period, we can calculate the chance of accusing hepatitis A in susceptible children under 15 years old to be approximately 17%, this leaves a high susceptible proportion of children entering adolescence and increases the risk of an epidermis in higher age. As it is seen in figure1, 25% of IgM Positive cases are between 11 and 15 years old. Although we could not found significant statistical difference between age group, but, one fourth of cases with positive results for Hepatitis A in children over 10 years old, is an indication of more susceptible patients at higher age to this infectious disease.

Changing the epidemiologic status of hepatitis A occurs in many countries with higher endemicity history[17-20], In a study in Saudi Arabia, children 1-6 years anti HAV IgG seropositivity was 33.8% overall, increasing age and rural residence and non availability of safe water were the most important independent predictors [21]. Tandon B.N. 1984 Showed 28% IgM positive cases from 90 healthy children, and 3 out of 16 IgM positive children had transaminase level more than two times above normal value . He reported, almost 30% of children below the age of 10 had subclinical acute hepatitis A in north India [22]

Any combination of four or more clinical finding such as fever, anorexia, nausea, vomiting, RUQ tenderness, dark urine, pale stool, hepatomegaly, fatigue, abdominal pain couldn't help us to distinguish hepatitis A in our cases, but IgM seropositivity was accompanied with higher Billirubin and SGPT Titer and lymphocyte predominance in CBC, Higher number of total WBC is accompanied with IgG seropositivity (Table 1), figure 2 shows the positive relationship between SGPT titer and HAV IgM .higher angle for SGPT, HAV IgM line confirms the positive relationship between these laboratory findings in children with hepatitis A infection.

In this study we selected children with a number of clinical findings, accordingly, seroprevalance can be lower in healthy children, the last study in Iran reported the prevalence of total anti-HAV to be 61.6%. HAV prevalence rates according to age groups were 61.5% between 6 months and 1.9 years, 51.7% between 2 and 5.9 years, 52.9% between 6 and 10.9 years, 65.2% between 11 and 15.9 years and 85% between 16 and 20 years.[23]. Our data shows that after approximately five years 50% of children between 6- 15 years with nonspecific gastrointestinal complaint are seronegative for hepatitis A infection, thus more precise investigation of hepatitis A is mandatory to show the changing epidemiology of this disease.

The WHO position paper on hepatitis A vaccines [24] declares that in countries of intermediate endemicity, considering childhood vaccination can be considered as a supplement to health education and improved sanitation.

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