# A rare association of hepatitis A virus infection with type-1 diabetes

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## Abstract

Patients with type-1 diabetes are predisposed to develop a spectrum of liver diseases, which includes fatty liver, steatohepatitis and cirrhosis. The association of hepatitis A infection with type-1 diabetes is extremely rare. To the best of our knowledge, our case is the first case report in children. We described a nine year-old girl who had type-1 diabetes and developed hepatitis A virus infection without complications. A review of the literature is also provided.

## Introduction

Hepatitis A virus (HAV) occurs throughout the world, and humans are thought to be its principal host.[1] Type-1 diabetes is a disorder of glucose metabolism that results from insulin deficiency secondary to autoimmune destruction of insulin-secreting β-cells. Although the pathogenesis of type-1 diabetes is unknown, human leukocyte antigen typing, viral infections and T-cell autoimmunity may be involved.[2] The prevalence of liver disease among diabetics is estimated to be between 17 and 100%.[3] The present paper describes a 9- year-old girl who has type-1 diabetes and presented HAV infection. Both diseases are rare association. A review of the literature is also provided

## Case Report

A 9-year-old girl presented with vomiting and abdominal pain for three days. She describes vomiting is non-bilious, non-bloody and it is food content. It is associated with generalized mild abdominal pain with no relieving or precipitating factors. There was history of jaundice, diarrhea and poor appetite. No history of fever, skin rash, joint pain or recent travel. She had a known history of type-1 diabetes diagnosed at age 5. The family revealed no history of liver disease. The patient had normal developmental milestones. She was taking insulin medications. Physical examination revealed yellowish discoloration of eyes and skin but no evidence of growth retardation. Abdominal examination revealed tender hepatomegaly but no splenomegaly or ascites. Other systemic examination was otherwise unremarkable. The laboratory findings revealed normal hemoglobin, white blood cell, and platelet counts. Other investigations are summarized in Table 1. Abdominal ultrasound showed multiple hyper echoic foci with mild ascites, gallbladder wall was thickened with pericholecystic fluids.

A diagnosis of acute HAV infection was made and the child was managed with diabetes protocol. At 3 months follow up from the onset of disease, she was completely asymptomatic, hepatitis A immunoglobulin M became negative and other laboratory investigations normalized.

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Key words: Hepatitis A virus; type-1 diabetes.

Contributions: all authors have done substantial work. The case was managed by Dr. Mohammed Hasosah.

Conflict of interest: the authors declare no potential conflict of interest.

Received for publication: 18 March 2016.
Accepted for publication: 20 April 2016.


*Clinics and Practice 2016; 6:844*
*doi:10.4081/cp.2016.844*

**Table 1. Laboratory results.**

| | Result | Normal range |
|---|---|---|
| Total bilirubin | 152.2 μmol/L | 2.1-15.5 μmol/L |
| Direct bilirubin | 101 μmol/L | 0.0-9.0 μmol/L |
| AST | 1333 U/L | 10-23 U/L |
| ALT | 1573 U/L | 6-28 U/L |
| Albumin | 33 g/L | 38-54 g/L |
| ALK | 969 IU/L | 1-500 IU/L |
| GTT | 497 IU/L | 7-30 IU/L |
| INR | 0.9 | 0.8-1.2 |
| Serum glucose | 9.1 mmol/L | 3.3-5.6 mmol/L |
| Urine ketones | +++ | –ve |
| HgbA1C | 10.4% | 3.9-6.1% |
| Amylase | 18 U/L | 25-125 U/L |
| Hepatitis A IgM | +ve (reactive) | –ve |
| Hepatitis A IgG | +ve | –ve |
| CMV PCR | –ve | –ve |
| HSV PCR | –ve | –ve |
| EBV IgM | –ve | –ve |
| HBsAg | –ve | –ve |
| HC Ab | –ve | –ve |
| Anti liver kidney microsomal Ab | –ve | –ve |
| Anti mitochondrial Ab | –ve | –ve |
| Anti-smooth Ab | –ve | –ve |

ALT, alanine transaminase; AST, aspartate aminotransferase; ALK, alkaline phosphatase; GGT, gammaglutamyltransferase; INR, international normalized ratio; HBsAg, hepatitis B surface antigen; HC Ab, hepatitis C antibody; CMV PCR, cytomegalovirus polymerase chain reaction; HSV PCR, herpes simplex virus polymerase chain reaction; EBV IgM, Epstein-Barr virus immunoglobulin M; –ve, negative; +ve, positive.

## Discussion

Patients with type-1 diabetes are predisposed to develop a spectrum of liver diseases which includes fatty liver, steatohepatitis, cirrhosis, hepatic failure and hepatocellular carcinoma.[4] The association of HAV Infection with type-1 diabetes have been described in adult.[5-8] To the best of our knowledge, our case is the first case report in a children. Although the pathogenesis of type-1 diabetes is unknown, viral infections may or may not be involved. Kondrashova and colleagues,[9] demonstrated a possible protective effect of microbes in animal models, where HAV has associated with low risk of type-1 diabetes. Another study showed that hepatitis virus infection (HAV, HBV, HCV and HEV) were not associated with type-1 diabetes.[6]

In contrast, patients with diabetes are at risk to contact viral hepatitis infection. Singh and colleagues documented that patients with diabetes mellitus are at high risk to develop severe hepatitis as well as liver failure subsequent to acute viral infection mainly hepatitis B virus but HAV was not involved.[10] Makken and colleagues[8] showed that three patients with diabetic ketoacidosis have been reported within 2-3 weeks of acute hepatitis A, although the C-peptide levels were not measured.

Hwang and colleagues[5] reported an adult man who presented with fulminant type-1 diabetes and acute HAV. Our child did not develop complications of diabetes, and HAV recovered spontaneously. We believe that the immune system in the child may play a role in good prognosis of diabetes and HAV. Ertem and colleagues[11] reported HAV is associated with immune-associated diseases, including autoimmune hepatitis, immune thrombocytopenic purpura, cryoglobulinaemia and vasculitis. The data of Ertem and colleagues[11] taken together with the observation in our patient suggest that HAV is associated with immune-associated diseases such as type-1 diabetes.

## Conclusions

We described a girl who had type-1 diabetes and developed HAV infection without complications. We found that HAV could be associated with immune-associated diseases such as type-1 diabetes. However, the mechanism of hepatitis A virus-induced B-cell destruction is unknown. This case report emphasizes the need for more research to help in understanding the association of type-1 diabetes with HAV infection.

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