Original Article

Hepatic dysfunction is frequent in varicella Infection

Ali Hassan Abro, Ahmed MS Abdou, Abdulla M Ustadi, Hina Syeda Hussaini, Nadeem Younis Javeed, Ahmed Alhaj Saleh, Dujana A Hamed,

From Infectious Diseases Unit, Rashid Hospital Dubai, United Arab Emirates. Correspondence: Dr. Ali Hassan Abro. Ward-17. Rashid Hospital Dubai, UAE. 4545 Mob: 00971504741939.Tel: 0097143346651. Email: momal65@hotmail.com

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ABSTRACT

Objective: To determine frequency and severity of hepatic dysfunction in adult chickenpox patients admitted in our hospital.

Material and Methods: This was a hospital based descriptive study conducted from January 2005 to December 2007 at the Infectious Diseases Unit, Rashid hospital Dubai, UAE. The demographics, clinical information, radiological and biochemical changes observed in each patient were entered in a proforma. Full blood count, liver function tests, blood sugar, urea and electrolytes were done for all the patients, whereas, patients with clinical and/or biochemical evidence of hepatic dysfunction were subjected to viral hepatitis serology, coagulation profile, blood culture and ultrasound abdomen. Management was done as per standard guidelines for the management of chickenpox and its complications.

Results: A total of 105 patients were entered into the study. Serum alanine transaminases (ALT) levels were above the reference range in 50.9%. Among the 52 patients with raised serum ALT levels, 16 (30.7%) had levels >3 times, 4 (7.6%) had >5 times and 5 (9.6%) had >10 times of normal levels. Serum bilirubin was increased above the normal
value in 20% and was greater than 3-folds in 4.9%. High frequency of thrombocytopenia (p<0.009), pneumonia (p0.004), impaired renal function (p<0.01) and disturbed coagulation profile (p<0.01) were observed in patients with hepatic dysfunction. Overall, five (4.9%) patients expired and two (1.9%) of them had acute fulminant hepatic failure.

**Conclusion:** We observed that liver is frequently involved in adult chickenpox patients and the severity of hepatic dysfunction ranges from mild elevation of transaminases levels to acute fulminant hepatic failure. (Rawal Med J 2008;33:201-204).

**Key words:** Hepatic dysfunction, varicella, adults, ALF.

**INTRODUCTION**

Chickenpox (Varicella) is a common, usually benign exanthematous disease caused by Varicella-Zoster virus, which primarily affects children.

1. Although chickenpox is common in children, in tropical climate 15-20% cases are reported in adults.

Furthermore, as compared to children the clinical presentation in adults is more severe and more commonly associated with complications.

3. Common complication of varicella includes secondary bacterial infection of skin, pneumonia, encephalitis, cerebellar ataxia, hepatitis, arthritis and glomerulonephritis.

1. Hepatitis has been described in adults with varicella infection but is often asymptomatic and limited to mild elevations in the transaminases.

4. This study was undertaken to determine frequency and severity of hepatic dysfunction in adult chickenpox patients admitted in our hospital.

**PATIENTS AND METHODS**

This was a hospital based descriptive study conducted from January 2005 to December 2007 at Infectious Diseases Unit, Rashid Hospital, Dubai, United Arab Emirates.
Demographics (age, gender, nationality), clinical information, radiological and biochemical changes observed in each patient were entered in a proforma. The patients were specifically questioned regarding past medical history of jaundice, medications and alcohol ingestion. Those with history of chronic liver disease, immunocompromized (HIV/Drugs), positive viral hepatitis profile, recent intake of hepatotoxic drugs and active alcohol consumers were excluded from the study.

On admission, full blood count (FBC), liver function test (LFT), blood sugar and urea electrolytes were performed in all patients, whereas, viral hepatitis serology, coagulation profile, blood culture and ultrasound abdomen were done in patients with clinical and/or biochemical evidence of hepatic dysfunction. Management was done as per standard guidelines for the management of chickenpox and its complications. This consisted of intravenous acyclovir, antibiotics, intravenous steroids, fresh frozen plasma, immunoglobulin, ventilator support and hemofiltration depending on patient’s condition.

Statistical analyses included descriptive statistics, bivariate analysis i.e., t-test, chi-square and Analysis of Variance (ANOVA). A $p$ value of $<0.05$ was taken as statistically significant. Data was analyzed by SAS Enterprise Guide 4.1.

RESULTS

A total of 105 patients entered in the study. The mean age was $33.14 \pm 9.91$ years (range 15-65 years) and males outnumbered the females 88 (83.8%) vs 17 (16.2%). Most of the patients were expatriates who lived or visited the UAE. Out of the 105 patients, 78 (74.2%) were from India and 27 (25.7%) from Pakistan, Srilanka, Philippines and other countries. The majority of the male patients were laborers who were working in construction companies, agriculture fields and industries. Most of the patients were living
in labor camps or sharing accommodation and had positive history of contact with chickenpox patients. Pleomorphic itchy skin rash and fever were the most common presenting symptoms, whereas, in majority of the patients with significant hepatic dysfunction, in addition to the above symptoms, also had abdomen pain and vomiting. Five (4.7%) patients were jaundiced at the time of presentation.

Table 1. Biochemical and Hematological data of Chickenpox patients (n=105)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pts. with high ALT</th>
<th>Pts. with normal ALT</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>386.98±1249.03</td>
<td>26.83±7.1 U/L</td>
<td>0.03</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.86±0.56</td>
<td>3.86±0.78 mg/dl</td>
<td>0.9</td>
</tr>
<tr>
<td>Alk Phos.</td>
<td>121.53±82.23</td>
<td>89.22±42.2 U/L</td>
<td>0.03</td>
</tr>
<tr>
<td>T.Bilirubin</td>
<td>1.15±0.91</td>
<td>0.71±0.33 mg/dl</td>
<td>0.001</td>
</tr>
<tr>
<td>Proth.Time</td>
<td>15.15±2.77</td>
<td>13.46±0.92 sec</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>15.51±1.54</td>
<td>14.25±1.95 gm/dl</td>
<td>0.0005</td>
</tr>
<tr>
<td>Platelets</td>
<td>149.75±61.99</td>
<td>206.32±135.58x10^3/ul.</td>
<td>0.009</td>
</tr>
<tr>
<td>WBC</td>
<td>9.32±3.84</td>
<td>8.59±4.49x10^3/ul.</td>
<td>0.3</td>
</tr>
<tr>
<td>Urea</td>
<td>35.19±24.64</td>
<td>25.61±12.63 mg/dl.</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Out of the 105 patients, 52(50.9%) had raised serum ALT levels above the reference range with mean ALT levels 218.91±926.1 U/L. Among the 52 patients with raised serum ALT levels, 16 (30.7%) had levels >3 times, 4 (7.6%) had >5 times and 5 (9.6%) had >10 times of normal levels. Two patients developed acute hepatic failure and were managed in ICU. The patients aged 35 years and above had higher incidence of disturbed liver function tests than those aged less than 35 years (p<0.01). The frequency of hepatic dysfunction was higher in patients who also developed varicella pneumonia than those without pneumonia, (p<0.004)
Serum bilirubin, alkaline phosphate, prothrombin time (PT), platelet and urea were significantly elevated in patients with high ALT (Table 1).

**Fig 1. Complications observed in 105 adult chickenpox patients.**

Besides elevated ALT, thrombocytopenia and pneumonia were commonest complication encountered (Fig. 1). Overall, five (4.7%) patients expired; two of them having acute hepatic failure complicated by multiple organ failure. The patients who survived, the serum ALT levels returned to normal limits with in 3-4 weeks in almost all patients.

**DISCUSSION**

Varicella complications are high in newborns, adults and the immunocompromised and in males, smokers and pregnant women. Varicella infection usually occurs by an air borne route but it is uncertain whether route of entry is conjunctiva, pharynx or lungs.
Viral replication occurs in the regional lymph nodes, lungs, bone marrow, liver, pancreas and adrenal glands, and this mainly take place in the macrophages. In this case series, 50.9% of the patients had liver damage and 4.9% had transaminase levels in the range of acute hepatitis, a finding which has been rarely reported. Varicella has been associated with mild hepatitis but rarely with acute liver failure, whereas, in this study 1.9% patients developed acute liver failure. Hepatitis in adults with varicella infection has been reported but is often asymptomatic and limited to mild elevations in the transaminases. In varicella associated hepatic failure, intracellular virions characteristic of herpesviridae have been demonstrated.

The populations at greater risk of developing acute hepatic failure from varicella-zoster virus are those with either iatrogenic or acquired immunosuppression. However, hepatic failure secondary to varicella-zoster virus in immunocompetent adult patient from a tropical country has been reported. In this case series, all the study patients were adult immunocompetent and were from tropical countries. In this study, we observed that patients with elevated liver enzymes had high frequency of associated varicella pneumonia, as reported by others.

Varicella-zoster induced hepatic failure and pneumonia carry high mortality. The standard treatment for varicella-zoster infection is Acyclovir, 10mg/kg TDS and this should be started immediately upon suspicion of the diagnosis. The few patients with hepatic failure who survived received Acyclovir and/or underwent liver transplantation. Varicella-Zoster immunoglobulin (VZIG) may modify the natural history of infection but only when administered within 72 hours after exposure. The role of corticosteroids as adjunctive therapy for the treatment of acute hepatic failure has been
not well studied.\textsuperscript{20} In conclusion, we found that liver was frequently involved in adult chickenpox patients and its severity ranges from mild elevation of serum transaminases levels to acute fulminant hepatic failure. Furthermore, the patients with hepatic dysfunction also had high frequency of involvement of the other organs leading to increased morbidity and mortality rate.

REFERENCES


