INTRODUCTION
The present case report describes a case of atypical varicella zoster infection with secondary haemophagocytic lymphohistiocytosis syndrome. Clinical manifestations, complications and prevention are discussed. This article is to enlighten that complications of varicella zoster infection and HLH secondary to VZV infection in adults can be life-threatening even in immunocompetent individuals. The intention is to remind clinicians that although varicella is most often a relatively benign and self-limiting childhood illness, the disease can be associated with a variety of serious and potentially lethal complications in both immunocompromised and immunocompetent individuals.

CASE PRESENTATION
A 27-year-old previously healthy female with a contact history of chicken pox from her younger brother was brought to our emergency department on November 2016 with alleged history of fever for 2 days, which was high grade and associated with chills and rigors and complaints of rashes all over the body. Varicella zoster infection and HLH secondary to VZV infection in adults can be life-threatening even in immunocompetent individuals. The intention is to remind clinicians that although varicella is most often a relatively benign and self-limiting childhood illness, the disease can be associated with a variety of serious and potentially lethal complications in both immunocompromised and immunocompetent individuals.

On arrival to the emergency, patient was conscious and oriented. Her blood pressure was 130/80 mm Hg, with pulse rate of 130/min, respiratory rate of 20/min. She was afebrile and her room air saturation was 100%. Patient had jaundice and pleomorphic skin rashes (macules, papules, pustules and vesicles) with no scabs present all over the body sparing the palms and soles. Systemic examination revealed bilateral cerebellar signs, no signs of meningitis and mild epigastric tenderness with no organomegaly.

On day 2, patient developed altered sensorium. MRI brain was done and found to be normal. Lumbar puncture was planned but deferred in view of thrombocytopenia. 2D Echo done revealed normal chamber dimensions, no wall motion abnormality, and ejection fraction = 64%. Repeat Trop T was also negative. Hence, myocarditis was ruled out but patient continued to have persistent fever spikes. On 29/11/2016, repeat investigations revealed Hb of 5.4, total count of 800, platelet of 81,000, INR - 1.16, with RFT and serum electrolytes within normal limits. In view of the patient’s condition, a suspicion of probable haemophagocytic lymphohistiocytosis syndrome was made. Serum ferritin and triglycerides were elevated. Haematology opinion was obtained and patient was diagnosed to have HLH and probable myocarditis. Patient was initially treated with Inj. Aciyclvir 500 mg i.v TDS, Inj. Ceftriaxone 2gm i.v BD, IV fluids and other supportive measures.

On day 4, patient was managed symptomatically. This case is atypical in terms of the rapidity of clinical deterioration and multi organ systems involvement along with secondary HLH.

KEYWORDS
Atypical Varicella Infection, Complications, Adult Chickenpox, Haemophagocytic Lymphohistiocytosis
On 30/11/2016, patient developed tachypnoea and tachycardia with complaints of breathlessness. Patient was intubated and was on mechanical ventilation on pressure control mode. CBC was monitored daily and platelets were found to be persistently dropping to a lowest of 21,000. Patient was transfused with multiple units of platelets, fresh frozen plasma and packed cells as and when required based on daily monitoring. On 03/12/2016, repeat investigations revealed pancytopenia and deranged bicarbonate value as shown below in TABLE 1. On the same day, around 08:00 P.M, patient had profuse ET tube bleed with ET block. Hence, patient was extubated and re-intubated. Despite mechanical ventilation, patient had persistent hypoxia. Repeat chest X-ray showed diffuse infiltration in the right hemithorax with left upper lobe opacities (IMAGE 2). Pulmonologist reviewed the patient and planned for bronchoscopy but the procedure was deferred in view of the patient’s poor haemodynamic status. Patient developed sudden cardiac arrest. Patient was revived according to ACLS protocol and continued on ventilatory and inotropic support. 12 units of platelets were transfused along with 2 units of packed cells and 4 units of fresh frozen plasma. On the same day, patient developed oliguria. Nephrology opinion was obtained in view of oliguric AKI and patient was advised Lasix infusion with i.v fluids at 50 ml/hr.

On 04/12/2016, patient had nil urine output. Labs revealed deranged Renal Function Test values and Serum Electrolytes as shown below in TABLE 1. Acyclovir and Amikacin were withheld in view of AKI. Nephrology opinion was obtained and patient was planned for haemodialysis. In view of hypotension, patient was planned for Continuous Renal Relacement Therapy instead of Haemodialysis. On 05/12/2016, at 4:30 a.m, patient went into asystole. Patient was resuscitated according to ACLS protocol. Inspite of all efforts, patient could not be revived and succumbed to the disease at 06:56 a.m on 05/12/2016.

DISCUSSION
Varicella zoster is a DNA virus belonging to the family of Herpes viridae. The attack rate for varicella is approximately 90% in susceptible individuals. [1] Disease in children is usually well tolerated. Manifestations are more severe in adults, pregnant women and the immunocompromised with severe rashes and visceral involvement.[2]

Prior to the introduction of varicella vaccination, the fatality rates for varicella were approximately 1 per 100,000 cases among children 1-14 years of age, 2.7 per 100,000 cases among persons 15-19 years of age, and 25.2 per 100,000 cases among adults 30-49 years of age. Adults accounted for only 5% of reported cases of varicella but approximately 35% of mortality. According to CDC, groups at increased risk of complications include – persons older than 15 year of age, infants younger than 1 year of age, immunocompromised and newborns of women with rash onset within 5 days to 2 days after delivery. [3] Our patient was a healthy 27-year-old healthy immunocompetent female with fulminant varicella infection, multisystem dysfunction and secondary haemophagocytic lymphohistiocytosis syndrome.

The typical clinical presentations of varicella and herpes zoster are distinctive and readily recognized by most experienced clinicians. However, atypical clinical presentations and uncommon complications of these diseases can pose diagnostic and therapeutic challenges. The most common infectious complication of varicella is secondary bacterial superinfection of the skin Most often by staphylococcus or streptococcus species. The most common extra cutaneous site of involvement is CNS - acute cerebellar ataxia, aseptic meningitis and encephalitis. Transverse myelitis, Guillain-Barré syndrome and Reye’s syndrome can also occur. Varicella

### TABLE 1: LABORATORY INVESTIGATIONS OF THE PATIENT

<table>
<thead>
<tr>
<th>Date</th>
<th>Hb (g/dl)</th>
<th>WBC (K)</th>
<th>Platelets (K)</th>
<th>S. Creat (mg/dl)</th>
<th>HbA1C (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30/11/16</td>
<td>15.2</td>
<td>15.7</td>
<td>58,000</td>
<td>0.6</td>
<td>6.29</td>
</tr>
<tr>
<td>01/12/16</td>
<td>9.9</td>
<td>12.3</td>
<td>21,000</td>
<td>0.4</td>
<td>7.33</td>
</tr>
<tr>
<td>02/12/16</td>
<td>8.3</td>
<td>12.5</td>
<td>18,000</td>
<td>0.4</td>
<td>7.85</td>
</tr>
<tr>
<td>03/12/16</td>
<td>8.0</td>
<td>13.0</td>
<td>19,000</td>
<td>0.3</td>
<td>7.79</td>
</tr>
</tbody>
</table>

**IMAGE 3:** MRI Brain of the patient revealing Normal Study.
pneumonia is the most serious complication following varicella infection, developing more commonly in adults (upto 20% of cases) than in children. Other rare complications include myocarditis, corneal involvement, arthralgia, bleeding diathesis, acute glomerulonephritis and hepatitis. [4]

Pneumonitis is rare in healthy children but occurs with increased frequency in immunocompromised persons of all ages and in immunocompromised adolescents and adults. 2.7%–16.3% will have radiographic evidence of VYZ pneumonia, but only about one-third of those with abnormal chest radiographs will have respiratory symptoms. With the advent of antiviral treatment and intensive supportive care, the mortality rate has been reduced from 30% to less than 10%. [5]

Symptomatic cerebellar ataxia occurs in about 1 in 4000 varicella cases. Ataxia may develop from several days before to 2 weeks after the onset of varicella, although the neurologic symptoms most often occur simultaneously with rash. The cerebellar dysfunction associated with varicella is self-limited. The vast majority of patients recover without apparent sequelae within 1–3 weeks. Encephalitis, the most serious CNS complication of varicella, has an incidence of 1–2 episodes per 10,000 varicella cases, with the highest incidence in adults and infants. Neurologic symptoms (headache, fever, vomiting, and altered sensorium) most often occur about 1 week after the onset of the varicella rash and may be accompanied by seizures in 29%–52% of cases. The mortality for varicella encephalitis is 5%–10%.

Long-term sequelae, including seizure disorders, may be present in 10%–20% of survivors.[5] The demyelinating disorders can be effectively managed using methylprednisolone or i.v immunoglobulins.[6]

Three methods are used for the prevention of VZV infection. First, a live attenuated varicella vaccine is recommended for all children > 1 yr of age (up to 12 years of age). Secondly, varicella zoster immunoglobulins (VZIg) can be administered. This should be given within 96-h of the exposure. Lastly, antiviral therapy can be given as prophylaxis to individuals at high risk of developing complications who are ineligible for vaccine or VZIg.

Haemophagocytic lymphohistiocytosis (HLH), is an uncommon, life-threatening hyperinflammatory syndrome caused by severe hypercytokinemia with excessive activation of lymphocytes and macrophages due to a highly stimulated but ineffective immune process. [7] It may be Primary or Secondary (acquired). The overall reported mortality for acquired HLH exceeds 50%. In cases of infection-associated HLH or malignancy-associated HLH, the immediate treatment of the underlying disease is indicated. [8] Patients may be classified into high-risk and low-risk groups, with only the high-risk groups receiving the etoside (i.e. VP-16) regimen. Patients who are at low risk may be treated as effectively with only cyclopovine, corticosorsteroids or IVIG. Recent case reports show promising results with an anti-TNF approach and plasmapheresis. Supportive care is needed to ensure that the patient with HLH remains stable until a bone marrow donor can be found. This includes transfusions of RBCs, platelets, and fresh frozen plasma, as well as nutritional support in addition to the treatment protocol. [9]

CONCLUSION:

- Varicella Zoster infection is most often a relatively benign and self-limiting childhood illness. However, the disease can be associated with a variety of serious and fatal complications in both immunocompromised and immunocompetent adults.
- Multi organ dysfunction syndrome is a potentially lethal complication of varicella infection in adults associated with high morobidy. So, early treatment of varicella in adults along with appropriate supportive measures for suspected complications is required in high risk individuals.
- Haemophagocytic lymphohistiocytosis syndrome can occur very rarely secondary to varicella infection and warning signs must not be overlooked.

- Varicella vaccine should be considered for seronegative immunocompetent individuals and VZIg for post-exposure high risk patients.

REFERENCES: