Original Article

Chickenpox: presentation and complications in adults

Ali Hassan Abro,[1] Abdulla Muhammed Ustadi,[2] Kirpal Das,[3] Ahmed Muhammed Saleh Abdou,[4]
Hina Syeda Hussaini,[5] Fatma Saifuddin Chandra[6]

Infectious Diseases Unit, Rashid Hospital Dubai, United Arab Emirates,[1,2,4-6]
Medical Department, Jinnah Postgraduate Medical Center, Karachi, Pakistan.[3]

Abstract

Objective: To describe the clinical manifestations laboratory findings and frequency of complications in adult chickenpox patients admitted in the hospital.

Methods: This was a hospital based descriptive study, conducted at the Infectious Diseases Unit, Rashid Hospital Dubai, UAE, from March 2005 to February 2008.The study was designed to include demographics (age, sex, nationality); clinical information, radiological and biochemical changes observed in each patient and data was entered into the proforma separately. Full blood count, urea, electrolytes and blood sugar were done for all the patients, whereas, other tests were carried out when and where it was indicated. Patients were treated according to the standard protocol for the management of Chickenpox and its complications.

Results: A total of 102 adult patients were entered into the study. The main presenting symptoms were itchy skin rash, fever, cough, sputum, breathlessness, throat pain, vomiting, abdominal pain, confusion and headache. Whereas, the most common complications observed were raised Alanine aminotransferases (ALT) levels (51.9%) and the levels were greater than 10-folds of normal value in 4.9%, thrombocytopenia (42.1%), varicella pneumonia (28.4%), skin infection (25.4%), septicaemia (10.7%), Encephalitis/Meningitis (8.8%), Acute Respiratory Distress Syndrome (ARDS) (6.8%), acute renal failure (2.9%) and acute hepatic failure (1.9%). The frequency of varicella pneumonia was noted to be higher in males, older age group ($p < .005$), smokers ($p < .002$) and patients with respiratory symptoms ($p < .0001$). Total five (4.9%) patients expired, whereas, mortality rate was 17.2% in varicella pneumonia patients and 45.5% in mechanically ventilated patients.

Conclusion: Chickenpox in adults causes severe systemic manifestations leading to high frequency of complications with increased mortality rate, particularly in the older age group and in smokers who develops varicella pneumonia and require mechanical ventilation (JPMA 59:828; 2009).

Introduction

Chickenpox (Varicella) is a common benign childhood illness caused by varicella-zoster virus, typically associated with fever and characteristic exanthematous vesicular skin rash.[1] However, reports have shown that the incidence of Chickenpox in adults has doubled in recent years and this has been paralleled with an increase in hospital admissions[2] and mortality.[3] The reason for this age shift is not known, though it may be the result of decreased exposure to Varicella-Zoster virus (VZV), increased virus virulence, the immigration of non immune adults from the tropics, increasing vaccine coverage and a decrease in transmission may result in accumulation of susceptible adults followed by a shift of incidence into the older age group.[4] Furthermore, as compared to children the clinical presentation in adults is severe and more commonly associated with complications.[5] This study

was conducted to describe the clinical presentation, laboratory findings and frequency of complications in adult chickenpox patients admitted in the hospital.

Patients and Methods

This was a hospital based descriptive study conducted from March 2005 to February 2008 at the Infectious Diseases Unit, Rashid Hospital Dubai, UAE. Rashid hospital is one of the biggest tertiary hospitals in Dubai, accredited by the Joint Commission International (JCI). A separate proforma was filled for each case entered into the study. The study was designed to include demographics (age, sex, nationality); clinical information, radiological and biochemical changes observed in each patient. Data was entered into a proforma separately.

The patients who presented with typical pleomorphic skin rash of chickenpox or recently had chickenpox but rash had subsided at the time of presentation and these patients were admitted with one of the complications of chickenpox, were included in the study. The patients with skin rash only were considered to have simple chickenpox, whereas, those with evidence of involvement of systemic organs particularly with significant hepatic dysfunction were considered to have disseminated disease. On admission, full blood count (FBC), blood sugar, urea and electrolytes were done for all the patients, whereas, liver function test (LFT), viral hepatitis serology, serum amylase, coagulation profile, Mycoplasma antibodies, Legionella antibodies, sputum culture, blood culture, x-ray chest, ultrasound abdomen, CT brain, lumbar puncture, CT chest, MRI brain, EEG and nerve conduction study were done when and where it was necessary. The patients were considered to have varicella pneumonia if the chest radiograph on admission showed changes consistent with acute infection (diffuse nodular/reticular changes).[6]

Management was done as per standard guidelines for the management of chickenpox and its complications. The patients who presented within 72 hours of development of skin rash, varicella pneumonia, encephalitis, pregnant females, patients on immune suppressive therapy and with immune deficiency state received intravenous Acyclovir 10mg/kg body weight in three divided doses for 7-10 days. The majority of the patients with varicella pneumonia, secondary bacterial skin infection and those with evidence of systemic bacterial infection also received antibiotics. Intravenous steroids, Immunoglobulin, ventilator support and haemofiltration were used as an adjunctive or supportive therapy in a few patients; particularly in patients with severe varicella pneumonia associated with multi-organ failure and Guillain Barre Syndrome (GBS). Data was analyzed by SAS Enterprise Guide 4.1. A p value of <.05 was taken as significant for difference in all statistical analysis.

Results

A total of 102 patients were included in the study. Overall, the mean age of the patients included in the study was 33.02 ± 10.20 years (14-65 years), males outnumbered the females, 86 (84.3%) vs 16 (15.6%) and there was no significant age difference between the two groups. Most of the patients were expatriates who visited or lived in the UAE. Out of 102 patients, 75 (73.5%) were Indian and 27 (26.4%) were from Pakistan, Sri Lanka, Philippines and other nationalities. Majority of the male patients were labourers, working in construction companies, agriculture fields and industries. Most of the patients were living in labour camps or sharing accommodation and had positive history of contact with chickenpox patient. Pleomorphic itchy skin rash and fever were the most common presenting symptoms; however three patients presented with history of recent skin rash which subsided at the time of presentation and these patients presented with neurological complication of the disease (Table-1).

Table-1: Clinical data of 102 patients with chickenpox.

Clin. Parameter	No (%)	Clin. Parameter	No (%)
Males	86(84.3)	Sputum	32(31.3)
Females	16(15.6)	Breathlessness	22(21.5)
Smoker	37(36.2)	Throat pain	19(18.6)
Diabetes	13(12.7)	Vomiting	15(14.7)
Pregnant	3(2.9)	Abdomen pain	13(12.7)
Immunosuppressive	3(2.9)	Confusion	10(9.8)
Skin rash	99(97)	Headache	9(8.8)
Fever	87(85.3)	Loose motions	6(5.8)
Itching	68(66.6)	Chest pain	3(2.9)
Cough	39(38.2)	Fits	3(2.9)

Out of 102 study patients, 53 (51.9%) had alanine transaminase (ALT) levels above the reference range, with mean ALT levels 244.26 ± 139.09 U/L (range = 12-8153 U/L) and levels exceeded 10-fold the upper value in 5 (4.9%) patients. Two patients developed acute hepatic failure. Thrombocytopenia was observed in 43 (42.1%) patients, with mean platelet count 176.15 ± 107.42x10^3/ul (24-937x10^3/ul).

Table-2: Complications of Chickenpox in 102 adult patients.

Complication	No (%)	Complication	No (%)
V.Pneumonia	29(28.4)	Encephalitis/ Meningitis	9(8.8)
ARDS*	7(6.8)	Guillain Barre Syndrome	1(0.9)
Skin infection	26(25.4)	Cerebellar Ataxia	2(1.9)
Septicaemia	11(10.7)	Stroke	1(0.9)
Raised ALT	53(51.9)	Thrombocytopenia	43(42.1)
Acute hepatitis	5(4.9)	Leucopenia	2(1.9)
Hepatic failure	2(1.9)	Leucocytosis	27(26.4)
Pancreatitis	2(0.9)	Raised urea	14(13.7)
Appendicitis	1(0.9)	Acute renal failure	3(2.9)
Cholecystitis	1(0.9)	Myocarditis	1(0.9)
Mega colon (Fig-1)	1(0.9)	Multi-organ failure	5(4.9)

Twenty nine (28.4%) patients developed varicella pneumonia and all of them were males except two (Table-2). The frequency of varicella pneumonia was noted to be greater than three times in patients aged 35 years and above, Odds Ratio (OR) 3.4 (1.4-82), P <.005, whereas smokers had more than two times the risk to develop varicella pneumonia, OR- 2.77 (1.15-6.68), P <.02. The males and the patients with chest symptoms (breathlessness, OR- 17.5 (5.48-55.93) P <.0001, cough OR- 11.5 (4.17-31.64) P <.0001, and sputum OR- 17.0 (5.97-48.31.6) P <.0001) also had increased frequency of varicella pneumonia.

Twenty six (25.4%) patients had skin infection. Streptococcus and Staphylococcus aureus were the most common organisms isolated on culture. Eleven (10.7%) patients had evidence of septicaemia and majority of them also had varicella pneumonia and Staphylococcus aureus was the common (in 8 patients) organism isolated on blood culture. Seven (6.8%) patients developed acute respiratory distress syndrome (ARDS). Nine (8.8%) patients were diagnosed to have encephalitis/meningitis after lumbar puncture and MRI. Blood urea was raised above the reference range in 14 (13.7%) patients and 3 (2.9%) patients developed acute renal failure. Creatinine phosphokinase (CPK) was raised in 6 (5.8%) patients above the reference range (82-2163 U/L).

Overall, 78 (76.4%) patients received intravenous Acyclovir and 58 (56.8%) patients were also given Antibiotics. Eleven (10.7%) patients received steroids as an adjunctive therapy due to severe thrombocytopenia, GBS and severe varicella pneumonia. Immunoglobulin was used in two patients who had thrombocytopenia and GBS. Two patients with ARF required haemodialysis, whereas plasmapheresis was advised in one patient who had GBS. Among 11 (10.7%) patients who required mechanical ventilation due to severe respiratory distress, 10 (9.8%) patients had varicella pneumonia. The mean hospital stay was 7.45 ± 4.55 days (3-25 days) and it was longer in patients with varicella pneumonia than those without it, with mean hospital stay 10.1 ± 5.96 vs 6.39 ± 3.36 days, p <.003. Total five (4.9%) patients expired and all of them had severe varicella pneumonia (17.2% of varicella pneumonia patients) required mechanical ventilation and accounted for 45.4% of mechanical ventilated patients. The patients with GBS, cerebellar ataxia and stroke were discharged with minimal disability and they recovered completely within six weeks.

Figure: Gross distension and wall thickening of the colon, particularly the ascending colon.

Discussion

Chickenpox (Varicella) is a common infection of childhood typically affecting children aged 2-8 years and usually follows a benign outcome.[7] However, adults have severe clinical manifestations with high complication and mortality rate.[8] There is limited data on pathogenesis of varicella, infection usually occurs by an air borne route but it is uncertain whether route of entry is conjunctiva, pharynx or lungs.[7] Primary viremia starts at 96 hours, probably following replication in the regional lymph nodes. The second stage of viral replication takes place in the lymph nodes, lungs, bone marrow, liver, pancreas and adrenal glands, and involves mainly macrophages.[9] Due to the systemic nature of the disease, varicella can involve any organ of the body; as it was observed in this case series. Males, smokers, pregnancy and immunodeficient individuals are associated with higher complication rates.[10,11] Varicella pneumonia is the most common complication in adults and its incidence has been reported variably. Gregorakos et al[1] reported the incidence of varicella pneumonia as high as 50%, whereas Hockberger et al[12] reported the incidence in 15-25% adults with chickenpox. In this study, 28.4% of the patients with chickenpox developed varicella pneumonia which is almost consistent with the above reports. Varicella-Zoster virus is frequently associated with mild hepatitis but rarely with acute liver failure.[13] The sub clinical hepatitis and elevated liver enzymes are more common in adults and frequently associated with varicella pneumonia.[14] In this case series, 51.9% patients had ALT above the reference range and five (4.9%) of them had ALT in the range of acute hepatitis, a significantly high percentage, as of our knowledge not reported earlier. Furthermore, the patients with varicella pneumonia were also found to have significant derangement of liver function tests including two who developed acute hepatic failure.

The haematological changes in chickenpox are not uncommon, particularly thrombocytopenia. In our study, we observed thrombocytopenia in 42.1% patients, a figure higher than reported by Ali et al (30%)[15] and Anne G (1%).[16] Secondary bacterial infection of skin lesions is a common complication and Streptococci and Staphylococci are the most commonly implicated bacterial pathogens. Farhan et al[17] have reported the incidence of superimposed bacterial skin infection in adult chickenpox patients as 25%, we also had the same observation (25.4%). Gastrointestinal manifestations of varicella are well recognized. Acute hepatic failure, acute cholecystitis and acute pancreatitis have been reported.[18,19] In this study, we also had the same observation. However, one patient developed toxic megacolon, a complication, which is probably not reported in the literature. Neurological complications caused by chickenpox are reported variably. Cerebellar ataxia and encephalitis are seen frequently, while transverse myelitis, aseptic meningitis, Guillain Barre syndrome, meningoencephalitis, ventriculitis, optic neuritis, post-herpetic neuralgia, herpes zoster ophthalmiscus, delayed hemiparesis, peripheral motor neuropathy and facial nerve paralysis are rarely observed.[20,21] Girija et al[22] have also reported cerebellar ataxia the most common neurological complication caused by chickenpox. However, in this study encephalitis was the most common neurological complication followed by aseptic meningitis, cerebellar ataxia, Gullain Barre syndrome and stroke.

Chickenpox is considered to be a benign infectious disease, however sometimes it can be fatal, particularly when it occurs in adults or persons with impaired immunity.[23] In this study, five patients died due to severe varicella pneumonia and two of them also had acute hepatic failure. Mortality rate due to severe varicella pneumonia has been reported 10-30% in the general population;[1] in this case series 17.2% patients with varicella pneumonia expired which accounted 45.5% of ventilated patients, a figure which is near to the observation of Feldman S et al[24] who have reported a mortality rate up to 50% in severe varicella pneumonia patients requiring mechanical ventilation.[24] Prompt administration of Acyclovir and corticosteroids, in combination with mechanical ventilation, may be of benefit; particularly in severe varicella pneumonia complicated by ARDS and multiple organ failure.[25] In our study, an overall, eleven patients received steroids as adjunctive therapy; five of them had severe varicella pneumonia and two of them died. However, the use of corticosteroids as adjunctive therapy for the treatment of life threatening varicella pneumonia is controversial and has been not well studied.

Conclusion

Chickenpox is considered to be a benign disease of childhood; however it can be serious in adults with systemic manifestations leading to high frequency of complications with increased mortality rate, particularly in the older age group, immunocompromised and smokers. Furthermore, despite mechanical ventilator support, anti viral therapy and ICU care, mortality is still high in Varicella pneumonia.

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