

VARICELLA INDUCED THROMBOCYTOPENIA IN ADULTS

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ABSTRACT

Objectives: To describe the frequency and severity of thrombocytopenia associated with adult chickenpox patients admitted in the hospital.

Methodology: This was a hospital based descriptive study conducted from January 2005 to March 2008 at the Infectious Diseases Unit, Rashid Hospital Dubai, United Arab Emirates. The study was designed to record demographics, clinical information, hematological and biochemical changes observed in each patient. The data was entered into a structured proforma separately. Patients with history of chronic liver disease, immunocompromized status (HIV/Drugs), history of blood disorder, recent intake of drugs/conditions which can cause thrombocytopenia and active alcohol consumers were excluded from the study. Full blood count including platelet count was performed by an automated Beckman Coulter machine. To verify the hematological finding, the cases with low platelet count (thrombocytopenia) were subjected to peripheral smear examination.

Results: A total of 110 patients were recruited into the study. The mean age \pm SD of the patients under the study was 32.9 ± 9.7 years and males outnumbered the females, 83.6% vs 16.3%. Forty six (41.8%) patients developed thrombocytopenia and their mean platelet count was $111.8 \pm 30.59 \times 10^3/\text{ul}$ ($24-149 \times 10^3/\text{ul}$). High frequency of thrombocytopenia was observed in patients who also had associated varicella pneumonia, hepatic dysfunction and renal impairment. None of the patients with thrombocytopenia developed bleeding manifestations during the course of the disease. Platelet count returned to the reference range within 1-2 weeks of the treatment of varicella without platelet transfusion.

Conclusion: Thrombocytopenia is frequently associated with chickenpox. The incidence of thrombocytopenia was observed higher in patients with the evidence of disseminated disease. Furthermore, low platelet count usually does not cause bleeding tendency and count improves with the treatment of varicella.

KEY WORDS: Varicella, Thrombocytopenia, Adults.

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INTRODUCTION

Varicella (Chickenpox) is a common, usually benign exanthematous disease, caused by varicella-zoster virus (VZV) and primarily affects children <10 years of age, who account for >90% cases.¹ However, in tropical climate more cases are reported in adults (15-20% of affected cases).² This higher adult susceptibility may result from a lack of exposure to varicella-zoster

virus during childhood due to rural living conditions in the tropics where VZV circulates poorly or due to high ambient temperature of the tropics, that inactivates VZV in cutaneous lesions, thereby lessening its transmission potential.^{3,4} Varicella is highly contagious with secondary household attack rates of >90% in susceptible individuals.⁵ Transmission occurs in susceptible host via contact with aerosolized droplets from nasopharyngeal secretions of an infected individual or by direct cutaneous contact with vesicle fluid from skin lesions. The average incubation period for varicella infection is 14-16 days although this interval can range from 10-21 days.⁶

Varicella is generally considered as a benign, self limiting disease; however, it may be associated with serious complications especially in adults and immunocompromised.⁷ The complication rate has been reported variably; varicella pneumonia, skin infection, encephalitis, cerebellar ataxia and subclinical hepatitis are reported frequently, whereas, acute myocarditis, acute pancreatitis, acute liver failure, glomerulonephritis, disseminated intravascular coagulation (DIC) and rhabdomyolysis are among the rare complications.⁸ Thrombocytopenia is considered a common hematological complication of chickenpox and it is four times more common in adults than children.⁹ This study was undertaken to evaluate the frequency and severity of thrombocytopenia associated with adult chickenpox patients admitted in the Rashid Hospital Dubai.

METHODOLOGY

This was a hospital based descriptive study conducted from January 2005 to March 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). The study was designed to include demographics (age, sex, nationality), clinical information, hematological and biochemical changes observed in each patient and data was entered into a structured proforma separately. The patients were specifically questioned regard-

ing past medical history of blood disorder, liver diseases, medications, recent viral infection and active alcohol ingestion. Patients with history of chronic liver disease, immunocompromised status (HIV/Drugs), blood disorders, recent intake of drugs/ conditions which might cause thrombocytopenia and active alcohol consumers were excluded from the study.

On admission, a blood sample was collected for full blood count (FBC), blood sugar, urea and electrolytes for all the patients, whereas, liver function test (LFT), coagulation profile, blood culture and other tests were done when and where it was indicated. Full blood count including platelet count was performed by an automated Beckman Coulter machine. To verify the hematological finding the cases with low platelet count (Thrombocytopenia) were subjected to peripheral smear examination. According to the platelet count, thrombocytopenia was defined if count was less than $150 \times 10^3 / \text{ul}$ (Ref.range: $150-400 \times 10^3 / \text{ul}$).¹⁰ Management was done as per standard guidelines for the treatment of chickenpox and its complications. The patients who presented within 48 hours of development of the skin rash, varicella pneumonia, encephalitis and pregnant females received intravenous Acyclovir 10mg/kg body weight in three divided doses or oral Valacyclovir 1gm TDS for 7-10 days in addition to supportive and adjunctive therapy. Platelet count was repeated on alternate days and patients were discharged from the hospital once the platelet count returned to the reference range and patients became asymptomatic. Data was analyzed by SAS Enterprise Guide 4.1. 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 significant for difference in all statistical analysis.

RESULTS

A total of 110 patients were entered into the study. The mean age \pm SD of the patients under the study was 32.9 ± 9.7 years (15-65 years) and males outnumbered the females 92(83.6%)

vs. 18(16.3%). There was no significant age difference among the two groups. Most of the patients were expatriates who lived or visited the United Arab Emirates (UAE). Out of the 110 patients, 80(72.7%) were Indian and 30(27.3%) from Pakistan, Srilanka, Philippines and other countries. The majority of the male patients (78%) were laborers who were working in construction companies, agriculture fields and industries. Most of the patients (87%) were living in labor camps or sharing accommodation and had positive history of contact with chickenpox patients (82%). Pleomorphic itchy skin rash and fever were the most common presenting symptoms followed by cough, sputum, breathlessness and headache; however none of the patients had history of bleeding or purpuric rash.

Forty six (41.8%) patients developed thrombocytopenia. The mean platelet count in all study patients was $175.8 \pm 106.6 \times 10^3 / \text{ul}$ ($24-937 \times 10^3 / \text{ul}$), whereas mean platelet count in patients with thrombocytopenia was $111.8 \pm 30.59 \times 10^3 / \text{ul}$ ($24-149 \times 10^3 / \text{ul}$). High frequency of thrombocytopenia was observed in patients who also had associated varicella pneumonia, hepatic dysfunction and renal impairment (Fig-1). Low hemoglobin level was noted in 12 (10.9%) patients, leucopenia in 3 (2.7%) and leucocytosis in 27(24.5%) patients (Table-I). None of the patients with thrombocytopenia developed purpuric spot, echymosis or bleeding manifestation during the course of disease. Other complications observed in this case series included skin infection, encephalitis/meningitis, septicemia, cerebellar ataxia, rhabdomyolysis, acute respira-

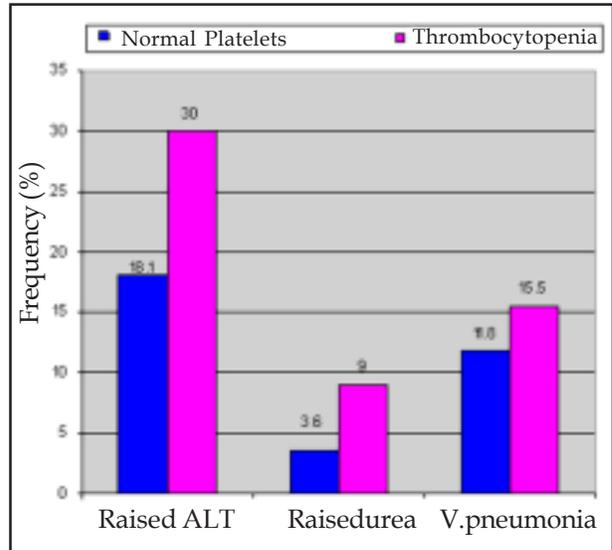


Fig-1: Bar graph shows frequency of thrombocytopenia in patients with hepatic dysfunction, impaired renal function and varicella pneumonia.

tory distress syndrome (ARDS), hepatic failure and acute cholecystitis. Sick patients were treated by intravenous Acyclovir, whereas stable patients received oral Valacyclovir. No patient with thrombocytopenia received platelet transfusion except two who developed septicemia leading to DIC and severe thrombocytopenia. Five (4.5%) patients expired due to associated severe varicella pneumonia and acute fulminant hepatic failure.

DISCUSSION

Varicella generally follows a benign course in healthy children. However, the complication rate is observed to be higher in adults, males, smokers and pregnant women. Furthermore, when the disease occurs in adults and

Table-I: Hematological and Biochemical data of 110 chickenpox patients

Parameter	Pts. with Thrombocytopenia	vs.	Pts. with normal Platelets	P Value
Platelets	111.8+30.5 x103/ul		221.82+114.5x103/ul.	0.006
Hemoglobin	15.4+1.7 gm/dl		14.4+1.7 gm/dl	0.9
WBC	8.7+4.2103/ul		8.9+3.9x103/ul	0.8
ALT	408.1+1376.2 U/L		70.5+128.3 U/L	0.001
T.Bilirubin	1.0+0.7 mg/dl		0.8+0.7 mg/dl	0.3
Proth.Time	14.7+2.4 sec		13.7+0.5 sec	0.06
Urea	36.5+26.5 mg/dl		26.2+12.6 mg/dl	0.01

immunocompromised persons, the likelihood of having visceral involvement increases.^{1,11,12} Thrombocytopenia is considered a common hematological complication of chickenpox infection; however, hemorrhagic manifestations are rare.¹³ In this case series, we also had the same observation. Varicella associated thrombocytopenia is well described in the literature but mechanisms involved in platelet reduction are not well understood.¹⁴ Two likely pathogenetic mechanisms are suggested: one infectious with thrombocytopenia during the period of viremia; the other post infectious with thrombocytopenia continuing for weeks and months.¹⁵ Cr¹⁵-labelled platelet studies suggest marked platelet destruction. IgG and IgM anti-platelet antibody on platelets has been demonstrated, suggesting involvement of immune mediated mechanisms.¹⁶ Thrombocytopenia may be detectable before the characteristic rash appears, suggesting direct destruction of platelets. Immune thrombocytopenia (ITP) is a rare complication of chickenpox which appears as a delayed complication.¹⁷

Thrombocytopenia in varicella usually develops early in the disease process and the incidence has been reported variably. The frequency of thrombocytopenia in chickenpox patients has been reported as 1%, 22.5%, 30% and 45% in various studies.^{2,18,13,19} In this case series 41.8% patients developed thrombocytopenia. The other investigators also have reported thrombocytopenia as a common hematological finding in patients with chickenpox.^{20,21} The temporal pattern of varicella associated thrombocytopenia has been well studied and are described to be either infectious during viremia and the post infectious appearing weeks and months afterward. However, there are no predictive markers that can identify the patients who are more likely to develop complications in the acute infectious phase or ITP later on.²²

In chickenpox, white blood cell (WBC) count may be normal, low or mildly elevated. Marked leukocytosis suggests a secondary infection,²⁰ as it was observed in this case series also, 24.7% patients had leukocytosis with evidence of

secondary bacterial infection of skin lesions or systemic infection. Anemia is generally not associated with chickenpox infection; however, cases of varicella induced hemolytic anemia have been reported.²³ In this study, 10.9% patients had hemoglobin below the reference range which could be explained by the lower socioeconomic status of the majority of patients under the study.

Varicella, once regarded as a benign, self-limiting infectious disease is no longer true. Serious life threatening bleeding has been reported in chickenpox.²⁴ In this case series, five patients died due to associated varicella pneumonia and acute fulminant hepatic failure; however, we did not observe bleeding tendency in our patients with thrombocytopenia, no patient required platelet transfusion and platelet count returned to the reference range within two weeks of the treatment. There are no unequivocal ways to distinguish immune thrombocytopenia (ITP) from other thrombocytopenia, even with state of the art investigations including anti platelet antibodies, thrombopoietin, glyocalicin and platelet reticulocyte counts; diagnosis is established by ruling out the other systemic processes.²⁵

CONCLUSION

Thrombocytopenia is frequently associated with chickenpox. Furthermore, the frequency of thrombocytopenia was observed higher in patients with evidence of disseminated disease such as patients with hepatic dysfunction, renal impairment and varicella pneumonia. Thrombocytopenia is usually not associated with bleeding manifestations and it does not require platelet transfusion and count increases to reference range spontaneously with the treatment of varicella.

REFERENCES

1. Aline CP, Michelle B, James HL. Fatal Varicella-Zoster Hepatitis presenting with sever abdominal pain: A case report and review of the literature. *Digestive Diseases and Sciences* 2006;51(7):1221-5.
2. Anne G. Varicella and Herpes zoster: Clinical disease and complications. *Herpes* 2006;13:2-7A.

3. Mandal BK, Mukharjee P, Murphy C, Mukharjee R, Naik T. Adult susceptibility is a rural phenomenon due to lack of previous exposure. *J Inf Dis* 1998;178:S52-4.
4. Garnett GP, Cox MJ, Bundy DA, Didier JM, St Catherine J. The age of infection with varicella-zoster virus in St Lucia, West Indies. *Epidemiol Infect* 1993;110:361-72.
5. Harper DR, Gilbert RL, Jeffries DJ. Molecular biology of varicella-zoster virus. A review prepared for the UK advisory Group on Chickenpox. *J Infect* 1998;36(Suppl)1: 1.
6. Heininger U, Seward JF. Varicella. *Lancet* 2006;368:1365.
7. Kumar S, Jain AP, Pandit AK. Acute pancreatitis: Rare complication of Chickenpox in an immunocompetent host. *Saudi J Gastroentrol* 2007;13:138-40.
8. Alborzi P. Chickenpox in adults. *SEM J* 2001;2(3):167-170.
9. Bovil B, Bannister B. Review of 26 years hospital admission of chickenpox in North London. *J Inf* 1998;30(suppl)1:17-23.
10. Craig JIO, McClelland DBL, Ludlam CA. In: Davidson's Principles and Practice of Medicine. Blood disorders. 20th Ed: Churchill Livingstone 2006;1011.
11. Popara M, Pendle S, Sackes I, Smego RA. Varicella Pneumonia in patients with HIV/AIDS. *Int J Infect Dis* 2002;6:6-8.
12. Ali ME. Varicella zoster during pregnancy: A strategy for prevention. *J Obst Gynaecol* 2001;21:17-20.
13. Nadir A, Masood A, Irfan Majeed, Waheed uz Zaman T. Chickenpox associated thrombocytopenia in adults. *J Coll Physician Surg Pak* 2006;16(4):270-2.
14. Ho-Yen D, Hardie R, Sommerville RG. Varicella induced thrombocytopenia. *J Infect* 1984;8:274-6.
15. Yeager AM, Zinkham WH. Varicella associated thrombocytopenia: Clues to the etiology of childhood idiopathic thrombocytopenic purpura. *Johns Hopkins Med J* 1980;146:270-4.
16. Feusner LH, Stichter SJ, Harker LA. Mechanism of thrombocytopenia in varicella. *Am J Hematol* 1997;7:255-64.
17. Kaneda K, Koijima K, Shinagawa K, Ishimura F, Ikeda K, Niiya K, et al. An adult patient with varicella preceded by acute thrombocytopenia. *Rinsho Katsueki* 2001;42:1142-4.
18. Rivest P, Bedard L, Valiquette L, Mills E, Lebel MH, Lavoie G, et al. Severe complications associated with varicella: Province of Quebec, April 1994-March 1996. *Can J Infect Dis Med Microbiol* 2001;12:21-6.
19. Tucci PL, Tucci F, Peruzzi PF. The behavior of platelets in some viral diseases in childhood. *Ann Sclavo* 1980;22:431-7.
20. Arfan ul B, Simeen ber R. Hematological abnormalities in adult patients of chickenpox. *J Pak Assoc Dermatol* 2004;14:193-7.
21. Farhan K, Abdulsalam K. Complications of chickenpox in immunocompetent adults. *Jordan Med J* 2003;37(2):167-71.
22. Hamada M, Yasumoto S, Furue M. A case of varicella-associated idiopathic thrombocytopenic purpura in adulthood. *J Dermatol* 2004;31:477-9.
23. Hilmi A, Serap K, Yasar D, Suheya O, Tiraje C, Tufan K, et al. Varicella-induced hemolytic anemia with hepatitis. *Ann Hematol* 2006;85:64-5.
24. Siraneci R, Hatipoglu N, Hatipoglu H, Dundar K, Baygin L, Yildiz C, et al. Acute arterial thrombotic purpura complicating varicella and the role of hyperbaric oxygen as an adjunctive therapy. *Turk J Pediatr* 2004;46:256-8.
25. Bussel JB. Overview of idiopathic thrombocytopenic purpura: New approach to refractory patients. *Semin Oncol* 2000;27:91-8.

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