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CHICKEN POX ASSOCIATED THROMBOCYTOPENIA IN ADULTS

Nadir Ali, Masood Anwar,* Irfan Majeed** and Waheed Uz Zaman Tariq***

ABSTRACT

Objective: To determine the frequency and magnitude of thrombocytopenia associated with chicken pox in adults.

Design: Observational descriptive study.

Place and Duration of Study: Combined Military Hospital, Attock, from July 2003 to June 2004.

Patients and Methods: All patients of age 15 years and above with history of fever, followed by appearance of the typical vesicular chicken pox rash, were inducted after informed consent. Two milliliters of whole blood was collected on day 1 of admission, and blood counts were performed. Patients were admitted and given 800 mg oral acyclovir, 5 times/day, for 7 days, in addition to symptomatic treatment. Patients were followed till 8 weeks.

Results: A total of 410 patients of chicken pox were received, out of which 270 were included. Age of patients ranged between 15 and 40 years with median age of 21 years. Platelet count on the day of admission ranged between $29 \times 10^9/L$ to $513 \times 10^9/L$, mean platelet count $178 \times 10^9/L$. Platelet count $< 150 \times 10^9/L$ was detected in 80/270 (30%) patients. Platelet count in thrombocytopenia patients was from $29 \times 10^9/L$ to $149 \times 10^9/L$ with mean $121 \times 10^9/L$. Thrombocytopenia recovered within 02 weeks in 78/80 (97%) patients. In 2 patients, thrombocytopenia recovered in 3 weeks. None of the patients developed purpuric spots, ecchymosis or bleeding manifestations.

Conclusion: Thrombocytopenia in chicken pox is a common entity. Platelet count remains above $25 \times 10^9/L$, which is usually not associated with bleeding manifestations. None of the patients in this series developed purpura. No specific pattern of total leukocyte counts was predictive of the progression or regression in platelet count.

KEY WORDS: *Thrombocytopenia. Chicken pox. Varicella-zoster.*

INTRODUCTION

Chicken pox is a viral infection caused by Varicella-zoster virus (VZV); a herpes virus. It is acquired by inhalation of virus laden aerosols arising from respiratory secretions of patients in the late incubation period. The disease is characterized by appearance of classic lesions that can be described as "oval teardrop on an erythematous base" or a dew drop on a rose petal.¹⁻³ Skin lesions initially appear on the face and trunk, beginning as red macules, progressing over 12-14 days to become papular, vesicular, pustular and finally crusted. The lesions predominate in central skin areas and proximal upper skin extremities with relative sparing of distal and lower extremities. Characteristically, all stages of lesions can be seen simultaneously. Associated fever is usually of low grade but occasionally it may be as high as $106^\circ F$.^{3,4} Most of the victims are children. In United States, only 5-10% are adults above 15 years of age, while in tropical climates, varicella may be more common in older children.⁵

Nearly 1 in 50 cases of varicella are associated with complications, which include Reye's syndrome, cerebellar ataxia, arthritis, thrombocytopenia, purpura fulminans, and secondary bacterial infections.⁶ There are likely to be two pathogenetic mechanisms: one "infectious" with thrombocytopenia during the period of viraemia; the other "post infectious" with thrombocytopenia continuing for

weeks and months.⁷ Mechanisms involved in platelet reduction are not well understood. ^{51}Cr -labeled platelet studies suggest marked platelet destruction. IgG and IgM anti-platelet antibody on platelets has been demonstrated, suggesting involvement of immune mediated mechanisms.⁸ Thrombocytopenia may be detectable before the characteristic rash appear, suggesting direct destruction of platelets. Immune thrombocytopenia (ITP) is a rare association of chicken pox which appears as delayed complication.^{9,10}

The chicken pox infection is more serious in adults and complications are relatively more common in adult contacts as compared to children.⁵ Thrombocytopenia (TP) is considered a common hematological complication of chicken pox infection, however, haemorrhagic manifestations are rare.

The aim of this study was to find out the frequency and magnitude of thrombocytopenia associated with chicken pox in adults.

PATIENTS AND METHODS

It was an observational study carried out from July 2003 to June 2004 in Combined Military Hospital, Attock. All patients aged 15 years and above with history of fever, followed by appearance of the typical vesicular chicken pox rash, were inducted after informed consent. To exclude the possibility of atypical measles, disseminated herpes simplex, and Cocksackievirus infection; patients with morbilliform lesions, with hemorrhagic component or rash, prominent on legs/body creases, were excluded from study. A brief clinical history and examination was recorded. Two milliliters of whole blood was collected in K_2 EDTA to final concentration

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1.5 mg/ml, and blood counts were performed on Sysmax-KX 32 automated hematology analyzer. In case platelet count was below $150 \times 10^9/L$, it was verified by peripheral blood smear examination. All patients were admitted in isolation ward and were given oral acyclovir 800mg, 5 times/day for 7 days in addition to symptomatic treatment. Platelet count was performed twice weekly till counts were within range of $150\text{--}400 \times 10^9/L$. Patients were discharged when asymptomatic. Patients were followed till 8 weeks with platelet counts at 02 week interval. Statistical analyses in descriptive statistics were performed on SPSS 10.0 programmer.

RESULTS

A total of 410 patients with chicken pox were received out of which 270 (65.8%) were included in the study. Age of patients ranged between 15 and 40 years with median age of 21 years, 267 were male and 3 were female. Complete blood counts of all patients are shown in Table I. Platelet count on day of admission ranged between $29 \times 10^9/L$ to $513 \times 10^9/L$, mean platelet count $178 \times 10^9/L$. Total leukocyte count (TLC) varied between $2.4 \times 10^9/L$ to $13.10 \times 10^9/L$. Grossly, the total leukocyte count increased with increase in platelet counts and vice versa. Absolute neutrophil count varied between $1.0 \times 10^9/L$ to $10.8 \times 10^9/L$. There was a similar correlation of absolute neutrophil count with platelet count as TLC with platelet count. Absolute lymphocyte count varied between $0.72 \times 10^9/L$ to $6.60 \times 10^9/L$. The absolute lymphocyte count with platelet was roughly in direct proportion to platelet count. Absolute monocyte count varied between $0.04 \times 10^9/L$ to $1.82 \times 10^9/L$. There was a similar correlation of absolute monocyte count

Table I: Blood cell counts of all adult patients of chicken pox (n=270).

Parameter	Minimum ($\times 10^9/L$)	Maximum ($\times 10^9/L$)	Mean ($\times 10^9/L$)	2-SD ($\times 10^9/L$)
Platelet count	29.00	513.00	178.00	55.00
TWBC	2.4	13	6.26	1.95
ANC	1.0	10.8	3.33	1.27
ALC	0.72	6.6	2.37	1.1
AMC	0.04	1.82	0.3	0.22

TWBC: Total white blood cell count; ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; AMC: Absolute monocyte count.

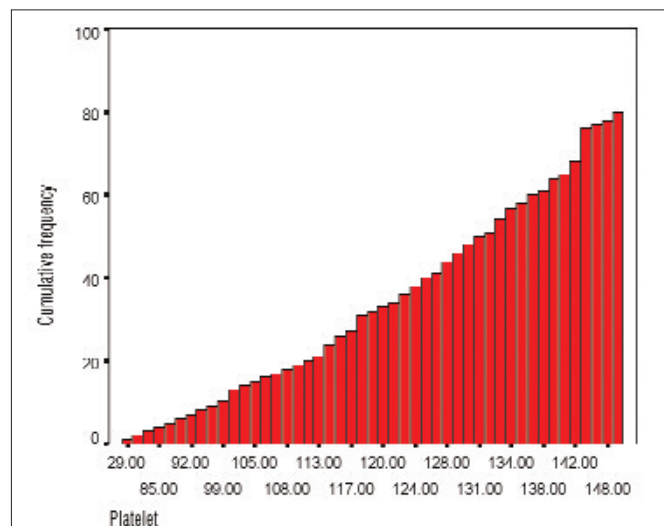


Figure 1: Distribution of platelet counts ($\times 10^9/L$) in chicken pox (n=270).

with platelet count as of lymphocyte count with platelet count. Platelet count $< 150 \times 10^9/L$ was detected in 80/270 (30%) patients, these were labeled as thrombocytopenia patients. Platelet count in thrombocytopenia patients varied from $29 \times 10^9/L$ to $149 \times 10^9/L$, mean platelet count $121 \times 10^9/L$, median $90 \times 10^9/L$, and 2 SD $17 \times 10^9/L$. Figure 1 shows the distribution and the cumulative frequency of platelet count, in most of the patients platelet count was above $50 \times 10^9/L$. Thrombocytopenia recovered within 02 weeks in 78/80 (97%) patients. In 2 patients thrombocytopenia recovered in 3 weeks. None of the patients developed purpuric spots, ecchymosis or bleeding manifestations in 08 week follow-up.

DISCUSSION

Thrombocytopenia is commonly seen in Varicella-zoster, Epstein-Barr virus, cytomegalovirus, hepatitis C virus, hepatitis B virus, Dengue virus, and with Crimean Congo Hemorrhagic virus (CCHF) infections. In Pakistan, it has been reported in CCHF, Dengue virus, Hepatitis C virus, Hepatitis B virus, and in chicken pox. Thrombocytopenia is also a common hematological finding in malaria which is a common entity in our set up and presents initially with features common to viral illnesses.¹¹⁻¹² In viral infections, TP can be mild, self-limiting and may remain unrecognized. Alternatively, the counts may drop to cause serious life threatening bleedings. In Dengue virus infection and CCHF, it may be the most important finding and predictor of hemorrhagic manifestations. Serious life threatening bleeding has been reported in CCHF, Dengue fever and chicken pox. Most of the viral infections are initially associated with fever, body aches and with varying degree of similar features. Finding thrombocytopenia in association with fever, even if it is well within safe limits, warrants further investigation. Once the etiological factor is known, the severity of TP can be predicted and a follow-up can be suggested.¹³

Chicken pox, once regarded as a benign self-limiting infection is no longer true. Serious life threatening bleedings has been reported with chicken pox in addition to other complications.¹⁴ The disease is more severe and complications are more frequent in adolescents, adults and in non-immune population.¹⁵ In a case reported by Bhatti *et al.*, chicken pox associated with Hepatitis B virus was fatal.¹⁶ However, in the study of Bari *et al.*, none of the patients out of 60, developed serious complications, while the TP was a common hematological finding.¹⁷ 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. Because of the subtleties of many viral illnesses, the frequency with which active infection produces ITP may be underestimated. Follow-up of platelet counts during acute infectious phase of chicken pox and for many weeks afterward should be suggested. There are no predictive markers that can identify the patients who are more likely to develop complications in acute infectious phase or ITP later on.¹⁸ Older children, adult contacts, immunocompromised patients, and patients on steroid therapy are at risk to develop complications in acute infectious phase.¹⁹ However, patients without risk factors are also prone to develop complications, thus acyclovir treatment can be started without discrimination that might reduce complication rate significantly.²⁰

Thrombocytopenia usually develops early in the disease process. The precise frequency of thrombocytopenia associated with chicken pox in adults is not known. In the study of Rivest *et al.*, it was 22.5% in children.²¹ In the reported study, it was 30% in adults, frequency being similar to children. In the series reported by Bari *et al.*, none of the 60 patients developed serious complications or bleeding manifestations. Probably thrombocytopenia associated with chicken pox is not severe enough to manifest clinically.^{22,23}

There was no specific correlation of platelet count with neutrophil, lymphocyte or monocyte counts in this study. A rough correlation of low total leukocyte count and neutrophil count with low platelet count suggests mechanisms involved in neutropenia general to all viral diseases. Similarly, a rise in lymphocyte count suggests reactive process to viral infections.^{24,25} No specific pattern of total leukocyte count, neutrophil count, lymphocyte or monocyte count was predictive of the progression or regression in platelet count.

Thrombocytopenia can appear before the appearance of characteristic rash of chicken pox.⁹ There are no unequivocal ways to distinguish immune thrombocytopenia (ITP) from other thrombocytopenias, even with state-of-the-art tests including anti-platelet antibodies, thrombopoietin, glyocalicin, and platelet reticulocyte counts; diagnosis is established by ruling out the other systemic processes.²⁶ If chicken pox infection is not considered, a diagnosis of ITP can lead to over enthusiastic steroid therapy.^{9,27} Patients on steroid therapy are at risk to develop serious complications of chicken pox.²¹ Thus, it is important to take history of contact, and a complete physical examination for rash to rule out chicken pox prior to starting the steroid therapy in thrombocytopenia.

CONCLUSION

About 30% adult patients with chickenpox develop thrombocytopenia. Platelet count remains above $25 \times 10^9/L$ which is usually not associated with bleeding manifestations. None of the patients developed idiopathic thrombocytopenic purpura. No specific pattern of total leukocyte count, neutrophil count, lymphocyte or monocyte count was predictive of the progression or regression in platelet count. Further comprehensive studies are suggested to study the pattern and frequency of thrombocytopenia in adults.

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