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Clinical Profile of Patients with Fever and Thrombocytopenia

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Abstract: The present study included 160 patients of fever with thrombocytopenia conducted at tertiary care hospital in department of medicine between Oct, 2014 March, 2016. Study aim is to evaluate the clinical profile of patients with fever and thrombocytopenia, attending tertiary care hospital. Male to female ratio in the present study was 2.3:1. The patients age ranged from 15-70 years with mean age of 32.53 (\pm 15.23) years. Out of 160 cases, mortality noted in 12 (7.5%) cases, out of them 5 were of dengue, 3 were of malaria, 3 were of viral fever (unspecified) and 1 was of sepsis. Deaths were due to multiorgan failure in all the 12 cases.

INTRODUCTION

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates (Larson *et al.*, 1982). Seen first as a disease but later recognized as an accompaniment to a variety of disease entities, fever is an easily noted and reliable marker of illness (Nolan and Fitzgersld, 1987). Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is such a common manifestation of illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history (Woodward, 1997).

Timely recognition and treatment of the underlying condition, platelet transfusions are required to prevent fatal outcomes. Hence, a need for study to know the clinical profile and complications of fever with thrombocytopenia.

Aims and objectives

Aim: To evaluate the clinical profile of patients with fever and thrombocytopenia, attending tertiary care hospital.

Objectives: To study the association of thrombocytopenia with fever and its clinical outcome.

Literature review: The histogenesis of platelets from megakaryocytes was first described by John Wright in 1910. Adelson E described platelets as sponges in the year 1961. Behnke O described the electron microscope structure of platelet membrane in the year 1968. Quantitation of the platelets in the peripheral smear was first described the year 1968. Behnke and Foerer in 1968 demonstrated two distinct populations of platelets that arise from two distinct populations of megakaryocytes. Jackson *et al.* in 1984 reported change in the protein content of megakaryocytes as they mature. Sternberg PE, Levin in 1989 described the mechanics of platelets production. A megakaryocytes can give rise as many as hundred to several thousand platelets. In order to maintain a relatively constant internal body temperature, fine balance between heat loss and heat production must be maintained, so that, any increase or decrease of one is promptly compensated by a similar increase or decrease of the other. Maintenance of body temperature within a normal range is accomplished by a number of

physiological process, involving both chemical and physical heat transfer. The operation of these mechanisms is integrated at various levels in the central nervous system. Heat production takes place through physiological oxidation of food materials in the body, combustion of carbohydrates, fats and proteins. The contribution of various organ systems to the total heat production varies greatly according to circumstances. During physical work one generates much additional heat in the muscles. Heat production in the muscular systems is of special importance in temperature regulation because it is adopted to maintain uniform body temperature being readily increased or decreased according to the need. Heat is lost from the body by three channels. They are skin, lungs and excretions mainly through radiation, conduction, convection and evaporation (Kasper *et al.*, 2005; Guyton and Hall, 2001).

In order to maintain a relatively constant internal body temperature, fine balance between heat loss and heat production must be maintained so that any increase or decrease of one is promptly compensated by a similar increase or decrease of the other. Maintenance of body temperature within a normal range is accomplished by a number of physiological processes, involving both chemical and physical heat transfer. The operation of these mechanisms is integrated at various levels in the central nervous system (Kasper *et al.*, 2005; Guyton and Hall, 2001). Heat production takes place through physiological oxidation of food materials in the body; combustion of carbohydrates, fats and proteins. The contribution of various organ systems to the total heat production varies greatly according to circumstances. During physical work one generates much additional heat in the muscles. Heat production in the muscular systems is of special importance in temperature regulation because it is adopted to maintain uniform body temperature being readily increased or decreased according to the need. Heat is lost from the body by three channels. They are skin, lungs and excretions mainly through radiation, conduction, convection and evaporation (Kasper *et al.*, 2005; Guyton and Hall). Thermoregulation is controlled by a continuum of neural structures and connections extending from the hypothalamus and limbic system to the lower brain stem and reticular formation, to the spinal cord and to the sympathetic ganglia. Because the preoptic region is sensitive to its own temperature and controls virtually all thermoregulatory responses, it is often described in terms of a negative feedback loop in a control system that regulates around a set-point temperature. It integrates central and peripheral thermal information, apparently responding to such information by shifting the pre optic set point temperature. Nervous system controls both heat production and heat loss in the following way. Cerebrum makes little contribution in thermoregulation. Conversely

when the body temperature falls below normal, the thermosensitive cells become less excited which now elicits opposite signals decreasing the rate of heat loss and increasing the rate of heat production, thus increasing the body temperature towards normal. Lesions of the anterior hypothalamus abolish these reactions and lead to loss of power to withstand high temperature (Dinarellow, 2015; Boulant, 2003; Bernheim *et al.*, 2006). The response to reduced temperature is controlled by posterior hypothalamus. Lesions of the posterior part lead to subnormal temperature. Shivering centre is also situated in the posterior part of the hypothalamus which exerts its effect by controlling autonomic nervous systems and ductless glands. Only a few thermal responses are mediated by parasympathetic system, e.g., salivary secretion, secretions of glands of the pharynx and respiratory tract, and local vasodilatation that follow physical activity. Greater part of the generalized thermal response in visceral effectors is due to sympathetic control (constriction of peripheral vessels, erection of hair, sweating and cutaneous vasodilatation).

Spinal cord is the connecting path between heat regulating centers in the hypothalamus, peripheral thermoreceptors and effector organs, the cervical part of the sympathetic outflow which regulates peripheral circulation and heat regulation. Effect of section of spinal cord depends on the level. When the section of the cord is made above or thorough the level of sympathetic outflow, gross disturbance of temperature regulation appears. Transection of spinal cord from the level of the upper thoracic segments downwards abolishes sweating and shivering below the level of transection. Muscle tone alone is the only source of heat production. CNS maintains muscle tone by continuous discharge of impulses to the muscles via the motor fibers. Shivering impulses from the shivering centre are not transmitted via sympathetic system but via the motor fibers of cerebrospinal system. Gram positive bacteria lack LPS, but contain peptidoglycan, lipoteichoic acid and a group of rhamnose glucose polymers. The basic structure responsible for peptidoglycan pyrogenicity is muramyl peptide. Gram positive bacteria release exotoxins which can also cause fever. Exotoxins act by binding to major histocompatibility complex class 1 molecules on antigen presenting cells which is then able to bind to T-cell receptor, which then becomes activated and release TNF and 1 L^{-1} . The ability of exotoxins to activate large numbers of T-cells has led to its designation as superantigen.

MATERIALS AND METHODS

Prospective observational non interventional study was performed in patients admitted with fever with

thrombocytopenia in tertiary care hospital. All patients presenting with fever with thrombocytopenia were taken up for study during the period of October, 2014-March, 2016. All patients were investigated with hemogram and PS, BSL, RFT, HIV and they were included only if their LFT, RFT, HIV were normal. Clinical profile was checked everyday till the patient was discharged. Specific investigations were done as per clinical diagnosis of the patient.

RESULTS AND DISCUSSION

The present study includes 160 patients who were admitted for acute febrile illness with thrombocytopenia at tertiary care hospital, between October, 2014 to March, 2016.

The majority (78.75%) of patients were <40 years, followed by 13.75% were in the age group of 41-60 years and 7.5% were >61 years (Table 1). The duration of fever in the present study ranged from 1-20 days with mean duration 5.51(±3.24)days. The duration of fever was maximum in 1-5 days (Table 2).

Fever was most common symptom, followed by headache (30.6%), vomiting (18.7%), abdominal pain (6.8%), breathlessness (4.3%), rash (3.7%), joint pain (3.1%), myalgia (1.8%) (Table 3) The present study included 160 patients of fever with thrombocytopenia in which males were more affected than females; 70 % were male and 30% were females and the ratio being 2.3:1.

Table 1: Age distribution among the study population

Age distribution in years	No	Percentage
<40	126	78.75
41-60	22	13.75
>61	12	7.50
Total	160	100.00

Mean age was 32.53 (+15.23) years

Table 2: Duration of fever on presentation in the present study

Days	n = 160	Percentage
1-5	104	65.00
6-10	48	30.00
11-15	6	3.75
>15	2	1.25

Table 3: Symptom at ology among the study population

Symptoms	No	Percentage
Fever	160	100.0
Headache	49	30.6
Vomiting	30	18.7
Pain abdomen	11	6.8
Breathlessness	7	4.3
Joint pain	5	3.1
Myalgia	3	1.8
Rash	6	3.7
Bleeding	0	0.0

In a study of fever associated thrombocytopenias by Nair, etc., 34 the male to female ratio was 2.3:1. The patients' age ranged from 15-70 years with mean age of 32.53(±15.23) years. In the present study the maximum prevalence of fever with thrombocytopenia in the age group of <40 years was about 78.8%. The least number of patients were in ≥61 year age group with only 7.5 % of it. All the patients in the study presented with fever. The duration of fever in the present study ranged from 1-20 days with mean duration 5.51(±3.24) days. The duration of fever was maximum in 1-5 days. Other than fever, patients presented with multiple other symptoms, headache was the most common symptom in 30.6% of patients after fever. Other prominent symptoms were vomiting (18.7%), pain abdomen (6.9%) and rash (3.7%), joint pain (3.1%), myalgia (1.9%). Most commonly detected signs in the present study were pallor (7%), splenomegaly (3.1%), hepatomegaly (2.5%), jaundice (3.1%). The commonest cause was viral fever (unspecified), 45% with present study. The other etiologies were dengue fever (36.25%), malaria (11.9%), septicemia (5%), leptospirosis (1.9%).

CONCLUSION

Febrile illness patients should be investigated for platelet count whether they have bleeding manifestation or not. Strong probability of dengue fever or other common causes like viral fever and leptospirosis should be kept in mind in any case of fever and thrombocytopenia as decreased platelet count could be severe without external manifestation. Vigilance and awareness is needed in the management of cases of fever with thrombocytopenia, since multiorgan dysfunction and death can occur in some cases.

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