International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 19-12-2019; Accepted: 20-01-2020
www.medicalsciencejournal.com
Volume 6; Issue 2; February 2020; Page No. 145-149

Assessment of prevalence of thrombocytopenia in patients suffered from fever from Bihar region

Dr. Manoj Kumar Rai[1], Dr. Suman Prakash[2], Dr. Nagendra Mohan Sinha[3]
[1, 2] Junior Resident, Department of General Medicine, Nalanda Medical College and Hospital Patna, Bihar, India
[3] Assistant Professor, Department of General Medicine, Nalanda Medical College and Hospital Patna, Bihar, India
[*] Corresponding Author: Dr. Suman Prakash

Abstract
Fever is perhaps the most ancient hallmark of disease since the beginning of civilization itself, fever has been regarded as a prime clinical feature of illness. Fever is the body's response to variety of factors that is reflected in on increase body temperature above normal range. Platelets are fragment of the large megakaryocytes, produced in the bone morrow under influence of thrombopoetin, a chemical made by the liver and kidney. Each megakaryocyte makes about 4000 platelets. The platelets then enter circulation and have a life span of 7-10 days. They are cleaned from body by spleen and to lesser extent, the liver and bone morrow. A normal human platelet count ranges from 150,000 to 450,000 platelets per microlitre of blood. Thrombocytopenia defined as platelet count less than 150,000 per micro liter. Which is further divided in mild (100,000-150,000 per micro liter), moderate (50,000-100,000 per micro liter), sever (< 50,000 per micro liter). Hence based on above findings the present study was planned for Assessment of Prevalence of Thrombocytopenia in Patients Suffered from Fever from Bihar Region.
Total 50 cases of the patients suffered from fever with thrombocytopenia were enrolled in the present study. The present study was planned in Department of General Medicine, Nalanda Medical College and Hospital Patna, Bihar, India. Detailed examination of various systems was done. Routine investigation was done, the specific and special investigations were done as and when indicated.
The data generated from the present study concludes that thrombocytopenia is a challenging problem in clinical practice and is usually caused by infectious diseases. In this study, malaria is the most common cause of febrile thrombocytopenia closely followed by dengue fever, especially in epidemic scenarios. Other infections such as enteric fever, scrub typhus, chickungunya fever, viral hepatitis, leptospirosis and sepsis also contribute to cases of febrile thrombocytopenia but in lesser numbers.

Keywords: thrombocytopenia, fever, Bihar, etc

Introduction
Thrombocytopenia is a condition characterized by abnormally low levels of thrombocytes, also known as platelets, in the blood. A normal human platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. These limits are determined by the 2.5th lower and upper percentile, so values outside this range do not necessarily indicate disease. One common definition of thrombocytopenia requiring emergency treatment is a platelet count below 50,000 per microliter. Thrombocytopenia can be contrasted with thrombocytosis, an abnormally high level of platelets in the blood [1].
Thrombocytopenia usually has no symptoms and is picked up on a routine full blood count (or complete blood count). Some individuals with thrombocytopenia may experience external bleeding such as nosebleeds, and/or bleeding gums. Some women may have heavier or longer periods or breakthrough bleeding. Bruising, particularly purpura in the forearms and petechiae in the feet, legs, and mucous membranes, may be caused by spontaneous bleeding under the skin [2].
Eliciting a full medical history is vital to ensure the low platelet count is not secondary to another disorder. It is also important to ensure that the other blood cell types, such as red blood cells and white blood cells, are not also suppressed. Painless, round and pinpoint (1 to 3 mm in diameter) petechiae usually appear and fade, and sometimes group to form ecchymoses. Larger than petechiae, ecchymoses are purple, blue or yellow-green areas of skin that vary in size and shape. They can occur anywhere on the body [2].
A person with this disease may also complain of malaise, fatigue and general weakness (with or without accompanying blood loss). Acquired thrombocytopenia may be associated with the use of certain drugs. Inspection typically reveals evidence of bleeding (petechiae or ecchymoses), along with slow, continuous bleeding from any injuries or wounds. Adults may have large, blood-filled bullae in the mouth [8]. If the person's platelet count is between 30,000 and 50,000/mm3, bruising with minor trauma may be expected; if it is between 15,000 and 30,000/mm3, spontaneous bruising will be seen (mostly on the arms and legs) [3].
Laboratory tests for thrombocytopenia might include full blood count, liver enzymes, kidney function, vitamin B12 levels, folic acid levels, erythrocyte sedimentation rate, and peripheral blood smear. If the cause for the low platelet count remains unclear, a bone marrow biopsy is usually recommended to differentiate cases of decreased platelet production from cases of peripheral platelet destruction [4].
Thrombocytopenia in hospitalized alcoholics may be caused by spleen enlargement, folate deficiency, and, most

frequently, the direct toxic effect of alcohol on production, survival time, and function of platelets [5]. Platelet count begins to rise after 2 to 5 days' abstinence from alcohol. The condition is generally benign, and clinically significant hemorrhage is rare.

In severe thrombocytopenia, a bone marrow study can determine the number, size and maturity of the megakaryocytes. This information may identify ineffective platelet production as the cause of thrombocytopenia and rule out a malignant disease process at the same time [6].

Treatment is guided by the severity and specific cause of the disease. Treatment focuses on eliminating the underlying problem, whether that means discontinuing drugs suspected to cause it or treating underlying sepsis. Diagnosis and treatment of serious thrombocytopenia is usually directed by a hematologist. Corticosteroids may be used to increase platelet production. Lithium carbonate or folate may also be used to stimulate platelet production in the bone marrow [7].

Treatment of thrombotic thrombocytopenic purpura (TTP) is a medical emergency, since the associated hemolytic anemia and platelet activation can lead to kidney failure and changes in the level of consciousness. Treatment of TTP was revolutionized in the 1980s with the application of plasmapheresis. According to the Furlan-Tsai hypothesis [8], this treatment works by removing antibodies against the von Willebrand factor-cleaving protease ADAMTS-13. The plasmapheresis procedure also adds active ADAMTS-13 protease proteins to the patient, restoring a normal level of von Willebrand factor multimers. Patients with persistent antibodies against ADAMTS-13 do not always manifest TTP, and these antibodies alone are not sufficient to explain how plasmapheresis treats TTP [9].

Many cases of ITP can be left untreated, and spontaneous remission (especially in children) is not uncommon. However, counts of under 50,000 are usually monitored with regular blood tests, and those with counts of under 10,000 are usually treated, as the risk of serious spontaneous bleeding is high with such a low platelet count. Any patient experiencing severe bleeding symptoms is also usually treated. The threshold for treating ITP has decreased since the 1990s; hematologists recognize that patients rarely spontaneously bleed with platelet counts greater than 10,000, although there are documented exceptions to this observation [9, 10].

Thrombopoetin analogues have been tested extensively for the treatment of ITP. These agents had previously shown promise but had been found to stimulate antibodies against endogenous thrombopoietin or lead to thrombosis. Romiplostim (trade name Nplate, formerly AMG 531) was found to be safe and effective for the treatment of ITP in refractory patients, especially those who relapsed following splenectomy [11].

Discontinuation of heparin is critical in a case of heparin-induced thrombocytopenia (HIT). Beyond that, however, clinicians generally treat to avoid thrombosis [12]. Treatment may include a direct thrombin inhibitor, such as lepirudin or argatroban. Other blood thinners sometimes used in this setting include bivalirudin and fondaparinux. Platelet transfusions are not routinely used to treat HIT because thrombosis, not bleeding, is the primary problem. Warfarin is not recommended until platelets have normalized [13].

Bone marrow/stem cell transplants are the only known cures for this genetic disease. Frequent platelet transfusions are required to keep the patient from bleeding to death before the transplant can be performed, although this is not always the case [14].

Human Induced Pluripotent Stem Cell Derived Platelets is a technology currently being researched by the private sector, in association with the Biomedical Advanced Research and Development Authority (BARDA) and the U.S. Department of Health and Human Services that would create platelets outside the human body [15].

Thrombocytopenia affects a few percent of newborns, and its prevalence in neonatal intensive care units (NICU) is high. Normally, it is mild and resolves without consequences. Most cases affect preterm birth infants and result from placental insufficiency and/or fetal hypoxia. Other causes, such as alloimmunity, genetics, autoimmunity, and infection, are less frequent [16].

Thrombocytopenia that starts after the first 72 hours since birth is often the result of underlying sepsis or necrotizing enterocolitis (NEC). In the case of infection, PCR tests may be useful for rapid pathogen identification and detection of antibiotic resistance genes. Possible pathogens include viruses (e.g. Cytomegalovirus (CMV), rubella virus, HIV), bacteria (e.g. Staphylococcus sp. [17]. Enterococcus sp., Streptococcus agalactiae (GBS), Listeria monocytogenes, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Pseudomonas aeruginosa, Yersinia enterocolitica), fungi (e.g. Candida sp.), and Toxoplasma gondii. The severity of thrombocytopenia may be correlated with pathogen type; some research indicates that the most severe cases are related to fungal or gram-negative bacterial infection. The pathogen may be transmitted during or before birth, by breast feeding, or during transfusion. Interleukin-11 is being investigated as a drug for managing thrombocytopenia, especially in cases of sepsis or necrotizing enterocolitis (NEC).

Platelet disorders can involve either a decreased number of platelets (thrombocytopenia) or defective platelet function. Functional disorders of platelets can be inherited (rare) or acquired (common). Platelet aggregation tests are useful in differentiating various disorders of platelet function. In all cases of thrombocytopenia, the peripheral blood smear must be reviewed to confirm the thrombocytopenia. This review is crucial.

Spurious thrombocytopenia can occur due to aggregates forming in the specimen. In addition, dilutional thrombocytopenia may occur in situations of fluid replacement or blood component replacement without platelet support. Thrombocytopenia can be further divided into increased destruction or decreased production. Thrombocytopenia resulting from increased destruction occurs either by an immune mechanism or increased consumption.

Platelets are consumed intravascularly by the activation of the coagulation process (diffuse/disseminated intravascular coagulation [DIC]) or by deposition on damaged endothelial cells (microangiopathy). Production defects result from those diseases that cause bone marrow failure, such as aplastic anemia, infiltration by leukemia or another malignancy, fibrosis or granulomatous disorders, or tuberculosis. Causes of thrombocytopenia related to increased destruction include (1) immune thrombocytopenias (eg, autoimmune, alloimmune, drug-induced) and (2) increased consumption (eg, DIC, TTP).

Causes of thrombocytopenia related to decreased production include bone marrow depression and inherited disorders.

Genetic defects have been defined for 30 forms of inherited thrombocytopenia, but the underlying genetic or molecular mechanisms remain unidentified for nearly 50% of cases [18].

Fever is perhaps the most ancient hallmark of disease since the beginning of civilization itself, fever has been regarded as a prime clinical feature of illness. Fever is the body's response to variety of factors that is reflected in on increase body temperature above normal range. Platelets are fragment of the large megakaryocytes, produced in the bone morrow under influence of thrombopoetin, a chemical made by the liver and kidney. Each megakaryocyte makes about 4000 platelets. The platelets then enter circulation and have a life span of 7-10 days. They are cleaned from body by spleen and to lesser extent, the liver and bone morrow. A normal human platelet count ranges from 150,000 to 450,000 platelets per microlitre of blood. Thrombocytopenia defined as platelet count less than 150,000 per micro liter. Which is further divided in mild (100,000- 150,000 per micro liter), moderate (50,000-100,000 per micro liter), sever (< 50,000 per micro liter). Hence based on above findings the present study was planned for Assessment of Prevalence of Thrombocytopenia in Patients Suffered from Fever from Bihar Region.

Methodology

Total 50 cases of the patients suffered from fever with thrombocytopenia were enrolled in the present study. The present study was planned in Department of General Medicine, Nalanda Medical College and Hospital Patna, Bihar, India. Detailed examination of various systems was done. Routine investigation was done, the specific and special investigations were done as and when indicated.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Cases admitted with fever with thrombocytopenia.

Exclusion criteria: Patient presenting with thrombocytopenia without fever. A Diagnosed case of immune thrombocytopenic purpura. A Patient with thrombocytopenia already diagnosed to have haematological disorder/malignancy or on treatment with chemotherapy and other immunosuppressive agent. Â Diagnosed cases of platelet disorder and dysfunction. Â Patients on treatment with antiplatelet drugs and other drugs causing thrombocytopenia. Â Patients with cirrhosis and chronic liver disease.

Results & Discussion

Fever with thrombocytopenia is a distinct clinical entity and refers to a reduction in platelet count below 150 × 109 /L in association with fever. Thrombocytopenia is due to decreased production, increased destruction (immunogenic and non-immunogenic) or increased sequestration in spleen and patients with thrombocytopenia may experience bleeding manifestations like petechiae, epistaxis, gum bleeding, hematuria, gastrointestinal hemorrhage or intracranial bleeding.

Thrombocytopenia occurs due to decreased platelet production, which occurs in condtions such as vitamin B12 and folate deficiency, leukemia, sepsis (bacterial or viral infection) and hereditary disease. Thrombocytopenia may also occur due to increased destruction such as idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), paroxysmal nocturnal hemoglobinuria (PNH), systemic lupus erythematosus (SLE), antiphospholipid syndrome, post-transfusion purpura and hypersplenism. Drugs, which can cause thrombocytopenia are quinine, valproic acid, methotrexate, carboplatin, interferon, isotretinoin and heparin.

Table 1: Demographic Details

Age	No. of Cases
10 – 20 years	18
21 – 30 years	9
31 – 40 years	10
41 – 50 years	6
51 – 60 years	4
61 & above years	3
Total	50
Sex	
Male	32
Females	18
Total	50

Table 2: Causative Disease

Disease	No. of Cases
Dengue	21
P. vivax malaria	16
P. Falci malaria	7
P. vivax malaria + P. Falci malaria	3
Enteric Fever	3
Total	50

Table 3: Lowest Platelets count

Disease	Lowest Platelets count
Dengue	10000 – 13000
P. vivax malaria	20000 – 28000
P. Falci malaria	12000 – 25000
Enteric Fever	50000 – 90000

Thrombocytopenia is the very common finding in septicemia and is an independent prognostic marker. In a study conducted by Lee *et al*. on 53 patients with septicemia thrombocytopenia was observed in 57% patients and DIC in 35% patients [19]. The etiology of thrombocytopenia in sepsis is multifactorial. It is commonly associated with DIC and is caused by splenic destruction of immune complex coated platelets, platelet adherence to damaged vascular surfaces and by direct platelet toxicity caused by microorganisms [20]. It is also probably related to impaired production of platelets from within the bone marrow, active phagocytosis of megakaryocytes and other hematopoietic cells by monocytes and macrophages hypothetically due to stimulation with high levels of macrophage colony-stimulating factor (M-CSF) in sepsis and platelet consumption due to ongoing generation of thrombin. Dengue is the most common arbovirus disease worldwide and occurs in tropical countries. Thrombocytopenia is an important finding and has got predictive as well recovery parameter of dengue fever/dengue hemorrhagic fever/dengue shock syndrome (DF/DHF/DSS).

Thrombocytopenia in DF is caused by bone marrow suppression (i.e., decreased platelet synthesis and increased immune-mediated destruction of platelets) [21].

The pathogenesis of thrombocytopenia in dengue fever is not clearly understood. Increased peripheral destruction of antibody coated platelets is strongly suspected as the possible mechanism. Other modes include acute bone marrow suppression leading to amegakaryocytic condition, mild DIC like presentation and enhanced platelet destruction by the reticuloendothelial system [22].

The causes for thrombocytopenia are varied and range from idiopathic, infectious to malignancies. Patients with acute febrile illnesses in a tropical country like India usually have an infectious aetiology and may have associated thrombocytopenia. Infections like malaria, dengue and typhoid are some of the common causes of fever with thrombocytopenia. Patients having thrombocytopenia with fever many times do not have bleeding manifestations. Hence study of correlation between platelet counts and hemorrhagic manifestations will help us to know the correct time for infusion of platelets, thus avoiding unnecessary platelet transfusion Pseudo thrombocytopenia is false low platelet count and is suspected when there is no bleeding despite very low platelet count [23].

Dengue is a mosquito-borne viral infection, which spreads rapidly [24, 25]. It is caused by 4 serotypes DENV–dengue virus (DENV1, DENV2, DENV3, and DENV4) Dengue fever, dengue hemorrhagic fever, and dengue shock syndrome; which is one among the lethal illness [26]. This disease leads from a relatively minor febrile illness to a life-threatening condition. Infection is the most common cause of thrombocytopenia. Thrombocytopenia associated with fever helps to narrow the differential diagnosis and management of fever [27]. It also helps to know the various complications of thrombo-cytopenia and its management. The aedes aegypti mosquitos are the one, which spreads the lethal illness named dengue and dengue viruses are also called as arboviruses [28]. These mosquito breeds in water holding receptacles such as desert coolers, vases, discarded containers, coconut husks, or old tires or in plants close to human dwellings. The accumulation of infection is both man and mosquito [29]. 70% of the 96 million apparent infections occur in Asia, in which India is making up to one-third of the total. In spite of abundant efforts to control the mosquito populations, dengue fever has arisen, extend and established itself vastly. The most serious complication of the infection is Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). Individuals of all ages and both sexes are susceptible to dengue fever [30]. It is accompanied by high fever, headache, dehydration, anorexia, muscle and joint pain, etc. Some patients also have a macular rash, lymphadenopathy, and palatal vesicles. Epistaxis and scattered petechiae are commonly seen in uncomplicated dengue. Preexisting gastrointestinal lesions may bleed during the acute illness [31, 32].

Bleeding manifestations associated with thrombocytopenia were commonly seen among dengue cases. Deterioration in the clinical condition of the patient, at the time of defervescence is a strong pointer towards dengue fever. Vomiting, pain abdomen and bleeding manifestations were the common warning symptoms noted in this series. A rapid decline in platelet count with rising hematocrit heralds the onset of capillary leak. Platelet transfusions were carried out as per WHO guidelines. In most DHF/DSS cases, platelet transfusions do not influence the incidence of severe bleeding. In the epidemic scenario, there is a widespread panic among the general public with a demand for platelet transfusions, which is sometimes perpetrated by ill-informed medical practitioners. There is a need to create public awareness campaigns as well as conduct workshops to update doctors regarding the latest management guidelines. Treatment costs for DHF/DSS cases could be reduced if these unnecessary platelet transfusions are avoided. In most other infections, thrombocytopenia was transient and asymptomatic, usually in the mild to moderate range and resolved with treatment of underlying condition.

Conclusion

The data generated from the present study concludes that thrombocytopenia is a challenging problem in clinical practice and is usually caused by infectious diseases. In this study, malaria is the most common cause of febrile thrombocytopenia closely followed by dengue fever, especially in epidemic scenarios. Other infections such as enteric fever, scrub typhus, chickungunya fever, viral hepatitis, leptospirosis and sepsis also contribute to cases of febrile thrombocytopenia but in lesser numbers.

References

1. Schafer AI. "Thrombocytosis". N. Engl. J Med. 2004; 350(12):1211-9. doi:10.1056/NEJMra035363. PMID 15028825.
2. Bhatia MPS. "B.E. Project on Platlet Count Using Image Processing Techniques" (PDF). BTP Report, 2014. Retrieved 30 November.
3. Rosdahl, Caroline Bunker; Kowalski, Mary T. Textbook of Basic Nursing. Lippincott Williams & Wilkins, 2008. ISBN 9780781765213. Retrieved 2015-05-01.
4. "How Is Thrombocytopenia Diagnosed? - NHLBI, NIH". Www.nhlbi.nih.gov. Retrieved 2015-05-19.
5. Lieber Charles S. Medical and Nutritional Complications of Alcoholism: Mechanisms and Management. Springer Science & Business Media, 2012. ISBN 9781461533207.
6. Hillyer Christopher D, Abrams Charles S, Shaz Beth H, Roshal Mikhail, Zimring James C, Abshire Thomas C, *et al*. Transfusion Medicine and Hemostasis: Clinical and Laboratory Aspects. Elsevier, 2009. ISBN 9780080922300. Retrieved 2015-05-01.
7. Lawrence Peter F, Bell Richard M, Dayton Merril T. Essentials of General Surgery. Lippincott Williams & Wilkins, 2012. ISBN 9780781784955.
8. Chapman Kent, Seldon Michael, Richards Ross. "Thieme E-Journals - Seminars in Thrombosis and Hemostasis / Full Text". Seminars in Thrombosis and Hemostasis. 2012; 38(1):47-54. doi:10.1055/s-0031-1300951. PMID 22314603.
9. "How Is Thrombotic Thrombocytopenic Purpura Treated? - NHLBI, NIH". Www.nhlbi.nih.gov. Retrieved 2015-05-20.
10. Thrombocytopenic Purpura: New Insights for the Healthcare Professional, 2013. Edition: Scholarly Paper. Scholarly Editions. 2013-07-22. ISBN 9781481662420.
11. "Idiopathic thrombocytopenic purpura (ITP): Medline Plus Medical Encyclopedia". Www.nlm.nih.gov. Retrieved 2015-05-20.

12. "Nplate (romiplostim) for subcutaneous injection". Www.fda.gov. Retrieved 2015-05-02.
13. Warkentin Theodore E, Greinacher Andreas. Heparin-Induced Thrombocytopenia. CRC Press, 2007. ISBN 9781439826423.
14. Ahmed I, Majeed A, Powell R. "Heparin induced thrombocytopenia: diagnosis and management update". Postgraduate Medical Journal. 2007; 83(983):575-582. doi:10.1136/pgmj.2007.059188. ISSN 0032-5473. PMC 2600013. PMID 17823223.
15. Smit-Sibinga C. Th. Neonatology and Blood Transfusion. Springer Science & Business Media, 2010. ISBN 9780387236001.
16. Clark Douglas. "New technology may aid emergency preparedness". Homeland Preparedness News, 2019. Retrieved 2019-10-23.
17. Roberts I, Murray NA. "Neonatal thrombocytopenia: causes and management". Archives of Disease in Childhood: Fetal and Neonatal Edition. 2003; 88(5):F359-64. doi:10.1136/fn.88.5.F359. ISSN 1468-2052. PMC 1721612. PMID 12937037.
18. Balduini CL, Melazzini F, Pecci A. Inherited thrombocytopenias-recent advances in clinical and molecular aspects. Platelets. 2017; 28(1):3-13.
19. Lee KH, Hui KP, Tan WC. Thrombocytopenia in sepsis: a predictor of mortality in the intensive care unit. Singapore Med J. 1993; 34(3):245-6.
20. Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, *et al*. Shirley Parker Levine - Miscellaneous causes of thrombocytopenia. In: Wintrobe's Clinical Haematology. Vol. 2, 10th edition, Lipincott Williams: Philadelphia, 1999, p.1623-9.
21. Jayashree K, Manasa GC, Pallavi P, Manjunath GV. Evaluation of platelets as predictive parameters in dengue Fever. Indian J Hematol Blood Transfus. 2011; 27(3):127-30.
22. Stasi R, Provan D. Management of immune thrombocytopenic purpura in adults. Mayo Clin Proc, 2004; 79:504-22.
23. Bichile SK. Chapter 16 Platelet Disorders In: Munjal YP, Sharma SK, Agrawal AK, Gupta P, Kamath SA, Nadkar SA, Singal RK, Sundar S, Varma S, Pangtey GS, Prakash A, Shah SN editors API textbook of medicine 9th edition Jaypee Brothers, 2012, 987.
24. Tamibmaniam J, Hussin N, Cheah WK. Proposal of a clinical decision tree algorithm using factors associated with severe dengue infection. PLoS ONE, 2016; 11:1-10.
25. Medagoda K, Gunathilaka SB, De Silva HJ. A case of self-limiting coombs' negative hemolytic anemia following dengue shock syndrome. Ceylon Med, 2003; 48:147-8.
26. Verma R, Jatav VK, Sharma S. Identification of inhibitors of dengue virus (DENV1, DENV2 AND DENV3) NS2B/NS3 serine protease: a molicular docking and simulation approach. Asian J Pharm Clin Res, 2015; 8:287-92.
27. Whitehorn J, Farrar J. Dengue. Br Med Bul, 1995; 95:161-73.
28. Khan DM, Kuppusamy K, Sumathi S, Mrinalini VR. Evaluation of thrombocytopenia in dengue infection along with seasonal variation in rural melmaruvathur. J Clin Diagn Res, 2014; 8:39-42.
29. Garg S, Arora R, Kakkar N. Fever and petechiae in a middle aged male. Labmedicine, 2007; 38:23-5.
30. Tayade MR, Shinkar DM, Patil PB, Saudagar RB. Emerging therapy for dengue. Int J Curr Pharm Res, 2018; 10:1-4.
31. Kulkarn D, Sharma B. Dengue fever-induced cold-agglutinin syndrome. Ther Adv Infect Dis, 2014; 2:97-9.
32. Dutta D, Kuila P, Chatterjee D, Das S. Co-infection of brucella and dengue virus. Asian J Pharm Clin Res, 2017; 10:299-301.