Journal of Pharmaceutical Research International

33(48A): 137-141, 2021; Article no.JPRI.75492
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

A Study of D-Dimer Levels in Acute Febrile Non Covid Conditions in a Tertiary Care Hospital

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i48A33230
Editor(s):
(1) Dr. Syed A. A. Rizvi, Nova Southeastern University, USA.
(2) Dr. P. Veera Muthumari, V.V.Vanniaperumal College for Women, India.
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Reviewers:
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(3) Karthik Anand B, Vignana Bharathi Institute of Technology (V.B.I.T.), JNTUH, India.
Complete Peer review History: https://www.sdiarticle4.com/review-history/75492

Original Research Article

Received 20 September 2021
Accepted 28 October 2021
Published 06 November 2021

ABSTRACT

Introduction: Acute undifferentiated febrile illness (AUFI) is caused by a multitude of diverse pathogens, with significant morbidity and mortality in the developing world. This study aims to highlight the gaps in our understanding of the various differential diagnosis of acute febrile illness and their prognostic outcomes. In this study, We used d-dimer levels to arrive at a differential diagnosis in acute febrile illness and also used it as a biomarker of disease severity and prognostic outcome.

Materials and Methods: A prospective study was conducted at medicine department, Saveetha medical college and hospital, Thandalam, India for a period of 3 months from January 2020 - March 2020. Patients who presented to the medicine outpatient department with symptoms of acute febrile illness with non specific symptoms were registered after getting written consent in the study. The plasma concentration of D -dimer levels ,prothrombin time , APTT from which INR were measured. The duration of hospital stay of patients in study was recorded. The data collected was entered into an excel sheet and analysed using SPCC software.

Results: A total of 50 patients with acute febrile illness were enrolled in the study. Out of which 37 patients (74./. of patients) were found to have elevated D dimer levels.

These 37 patients with elevated D – dimer levels required longer duration of hospital stay, reflecting the need for more days for recovery.

Keywords: Covid; malignancy; pulmonary embolism; pregnancy and post puerperium; leptospirosis.

1. INTRODUCTION

Acute febrile illness which are characterised by malaise, myalgia and hyperpyrexia is a nonspecific manifestation of infectious diseases in the tropics [1-6]. The majority of acute febrile illnesses have non-specific symptoms such as fever, headache, and malaise that appear suddenly. Scrub typhus, murine typhus, spotted fever group rickettsia, Q fever, and leptospirosis are among the acute febrile illnesses that have originated or re-appeared in some locations during the Covid-19 pandemic. It's proven difficult to make an accurate and timely diagnosis in these cases of acute febrile illness. This can be linked to physicians' lack of knowledge in the newly developed area, as well as a lack of correct testing and possibly a lack of substantial experience in the re-appeared area [4-9]. As a result, sensitive and specific laboratory diagnostic assays are required to allow timely diagnosis and correct treatment with antibiotics of patients with this condition. In resource-limited settings, such as low-income nations like India, failure to reach a differential diagnosis in cases of acute febrile sickness leads to increased morbidity and mortality. The goal of this study is to bring attention to the gaps in our knowledge of the many differential diagnoses of acute febrile illness and their prognostic outcomes [10,11].

This study aims to highlight the gaps in our understanding of the various differential diagnosis of acute febrile illness and their prognostic outcomes. In this study, We used d-dimer levels to arrive at a differential diagnosis in acute febrile illness and also used it as a biomarker of disease severity and prognostic outcome.

2. MATERIALS AND METHODS

A prospective study was conducted at medicine department, Saveetha medical college and hospital, Thandalam, India for a period of 3 months from January2020 - March 2020, during the Covid-19 pandemic .

2.1 Inclusion Criteria

Patients who presented to the medicine outpatient department with symptoms of acute febrile illness with non specific symptoms like. Fever, headache, rash, vomiting, diarrhoea, malaise and body ache were registered after getting written consent in the study.

2.2 Exclusion Criteria

Patients who were diagnosed or had evidences suggestive of Covid -19, Pulmonary embolism, Disseminated intravascular coagulation, Pregnancy and post puerperium, Recent surgery, Cigarette Smoker, Malignancy, Congestive heart failure, Stroke ,Sickle cell disease, Arterial or venous thromboembolism, Acute coronary syndrome, Periphery artery disease, Haemorrhage, Atrial fibrillation were excluded from the study .

History and physical examination findings were recorded on a clinical record form. Blood samples were taken from all patients for baseline laboratory testing, such as complete blood count. The plasma concentration of D -dimer levels, prothrombin time, APTT from which INR were measured. The duration of hospital stay of patients in study was recorded. The data collected was entered into an excel sheet and analysedusing SPCC software.

3. RESULTS

A total of 50 patients with acute febrile illness were enrolled in the study. Out of which 37 patients (74./. of patients) were found to have elevated d dimer levels above 4200 ng/ml of D dimer units, increased Prothrombin time and activated partial thromboplastin clotting time. The remaining 13 patients were found to have normal D dimer levels, prothrombin time and activated partial thromboplastin time.

These patients had a differential diagnosis of typhoid fever, dengue,and other rickettsial diseases such as scrub typhus , Q fever, tularaemia and leptospirosis, dengue , malaria.

These 37 patients with elevated D – dimer levels required longer duration of hospital stay , reflecting the need for more days for recovery.

The patients with elevated D-dimer levels showed normal D dimer levels when repeat estimation of D dimer levels was done at the time of discharge.

Table 1. D- dimer levels in patients

	Normal D-Dimer levels	Elevated D dimer levels (>4200 ng /ml)	Total
Number of patients	13	37	50

Table 2. Differential diagnosis among the patients

Diagnosis	Number of patients
Scrub typhus	19
Dengue	10
Leptospirosis	6
Malaria	2
	37

4. DISCUSSION

Acute undifferentiated febrile illness (AUFI) is caused by a multitude of diverse pathogens, with significant morbidity and mortality in the developing world [10]. Acute febrile illness has been recognised as an important group of illness that is difficult to differentiate due to their similarity of symptoms and presentation with non specific symptoms. Acute febrile illness is a common cause of hospital admission, and although it is not recognised as a disease state by the World Health Organisation (WHO), its associated infectious causes contribute to substantial morbidity and death. Studies among adults with febrile illness who required hospital admission documented case fatality ratios that ranged from 5% to 24%. In low- and middle-income countries, where limited resources hinder diagnostic capacity, clinical management is infrequently supported by knowledge of the predominant local and regional etiologic pathogens. Declining transmission of malaria in many regions, combined with the increasing use of rapid diagnostic tests for malaria, has led to the increasing recognition of leptospirosis, rickettsial diseases, respiratory viruses, and arboviruses as etiologic agents of fevers. The studies also confirm the need for guidelines to respond to changes over time in the aetiology of febrile illness and in antimicrobial resistance of relevant pathogens [11].

Scrub typhus, Q fever, leptospirosis, dengue fever, and typhoid were the most common causes of acute febrile illness in our study. The coagulation cascade is activated in the majority of the diseases listed above, resulting in higher D dimer levels, prothrombin time, and INR. Hence , for a patient representing with acute febrile illness , D-dimer test has found to be of value-in arriving at differential diagnosis in acute febrile illness.

The coagulation system is activated in response to a variety of viruses, including the dengue virus. This response is most likely a host defence system designed to keep the infection from spreading. Acute viremia, on the other hand, can cause disseminated intravascular coagulation and consequent bleeding, which can lead to multi-organ failure and death. During viral infection, tissue factor appears to be the primary activator of the coagulation cascade. Endothelial cells infected with Dengue virus have higher TF expression. There are deleterious effects of over activation of the coagulation cascade during viral infection [12,13].

Scrub typhus can result in generalised vasculitis, which can lead to multiple organ dysfunction syndrome. Disseminated endothelial infection has been established as the key factor for scrub typhus and rickettsial disease. After infection, damage to vascular endothelial cells causes vasculitis, which is characterised by hemorrhagic symptoms. Damage to vascular endothelial cells also leads to perivascular leukocyte infiltration, endothelial proliferation, and microvascular thrombus development [14].

D-Dimer Assay is based on a latex enhanced immunoturbidimetric assay. D-Dimer proteins in the sample bind to the specific anti-D-Dimer antibody, which is coated on latex particles, and causes agglutination. The degree of the turbidity caused by agglutination can be measured optically and is proportional to the amount of D-Dimer in the sample.

D-dimer is a useful indicator of coagulation and fibrinolysis activation. The fibrinolytic breakdown of fibrin produces D-dimer. The presence of D-dimer (DD) indicates activation of the coagulation system, which is caused by the degradation of cross-linked fibrin and reflects clot formation and lysis. Thus, the D-dimer assay can be used to diagnose acute febrile sickness with coagulation system activation. D-dimer blood test presents elevated values as a response to inflammatory conditions seen in acute febrile illness, it also indicates that there is a hyper-coagulable state and secondary fibrinolysis in the body. These patients required longer hospital stays reflecting on the lengthened time of recovery needed. The estimation of D-dimer levels at the time of

discharge revealed that the levels returned back to normal. Though, they had elevated D dimer levels it wasn't related to thromboembolic episodes as in correlation with findings from investigations like venous doppler and echocardiogram. In order to detect rare thromboembolic consequences and organ failure, coagulation indicators such as DD and PT should be examined as early as possible.

5. CONCLUSION

In conclusion, the findings of this investigation revealed that individuals with acute febrile illness are likely to have hyper coagulation, and that hyper coagulation is linked to disease progression and clinical prognosis. D -dimer levels are of value in arriving at a differential diagnosis, hence start appropriate treatment and reduce morbidity in patients with acute febrile illness.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study protocol was approved by the Institutional ethics committee, of Saveetha medical college and hospital, Thandalam.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/75492