Correlation of Temperature with Platelet Count and Total Leukocyte Count in Dengue: Findings from a Secondary Data Analysis

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Abstract

Background: Dengue fever annually affects almost 100 million people globally with 2.5 billion people at risk of developing dengue fever. The symptoms of dengue fever begins with flu like illness and may lead to severe manifestations such as bleeding, sudden loss of consciousness and even loss of life. The treatment of the infection is decided on the basis of severity of clinical features and level of fluids in the body.

Objective: To assess the correlation of temperature with platelet count and total leukocyte count in patients of dengue fever.

Methods: A secondary data analysis of a randomized controlled trial on the effects of silymarin on hepatic enzymes and clinical manifestation of dengue fever was carried out including only the patients in the placebo group of the trial. The correlation of temperature with platelet count and total leukocyte count was assessed using Spearman's correlation coefficient. The significance level was set at 0.05.

Results: The study results revealed that the temperature was significantly negatively correlated with total leukocyte count on day 3 only (p=0.026). Furthermore, in patients with fever duration of 5 to 7 days it was significantly negatively correlated with platelet count on day 3 only (p=0.002) whereas in patients aged 40 years or above it was significantly negatively correlated with total leukocyte count on day 3 only (p=0.025).

Conclusion: Raised temperature was found to be significantly negatively correlated with total leukocyte count on day 3 only. Moreover, stratified analysis showed it to be significantly negatively correlated with platelet count on day 3 in patients with longer duration of fever and with total leukocyte count on day 3 in patients aged 40 years or above. Further evaluation of the study findings with a larger sample size is recommended.

Key words: Correlation, temperature, platelet count, total leukocyte count, dengue, secondary data analysis

Introduction

A mosquito induced viral infection; dengue fever annually affects almost 100 million people globally with 2.5 billion people at risk of developing dengue fever. [1] It has four viral strains i.e. DEN-1, DEN-2, DEN-3, and DEN-4. [2] Majority of the cases of dengue fever have been estimated to be caused by DEN-2 and DEN-3 viral strains.[3, 4]The symptoms of dengue fever begins with flu like illness and may lead to severe manifestations such as bleeding, sudden loss of consciousness and even loss of life. [5] Fever usually persists for one week while within first two days patients feel warmth and redness on face or neck with red spots under the skin. [6] Its clinical manifestations include headache, fever, skin rashes, leucopenia and arthralgia. Dermatological manifestations occur in almost 50% of cases and begin just after patient appears to be afebrile. [6, 7]Bleeding occurs more frequently in patients with severe thrombocytopenia. [8]

Dengue fever and dengue hemorrhagic fever are diagnosed on the basis of clinical and epidemiological parameters. The treatment plan depends upon detection of IgM and IgG antibodies in the patient's blood whereas ELISA is used to differentiate between primary and secondary dengue infections. [9] For rapid diagnosis of the dengue virus, NS1 antigens are detected in the

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patient's blood. [10]The treatment of the infection is decided on the basis of severity of clinical features and level of fluids in the body. Patients with hemorrhagic manifestations such as petechiae, gum-bleeding, epistaxis etc. require platelet transfusion. [8]

Dengue is prevented by mosquitoes control and by protecting the subjects from mosquito bite. [11]Viral prevention strategies include properly disposing off waste, up gradation of water storage system and proper usage of repellents. [9] There is no recommended vaccine yet for the eradication of the virus though a new live attenuated tetravalent vaccine is undergoing clinical trials. [12]

To the best of author's knowledge, local data evaluating any potential association of fever with platelet count and total leukocyte count in the context of dengue fever are limited at best. The current study was therefore designed to assess the correlation of temperature with platelet count and total leukocyte count in patients of dengue fever by means of a secondary data analysis.

Methods

After taking ethical approval, a secondary data analysis of a randomized controlled trial on the effects of silymarin on hepatic enzymes and clinical manifestation of dengue fever was carried out. The trial was conducted at Ziauddin Hospital, Clifton, and Karachi. For the sake of current study, only the patients in the placebo group of the trial (n=46) were included in the analysis. These patients, aged 18 to 70 years, had been diagnosed clinically with a positive serological test. The relevant data were analyzed on SPSS version 20. After checking normality, the correlation of temperature with platelet count and total leukocyte count was assessed using Spearman's correlation coefficient. The significance level was set at 0.05.

Results

In a total of 46 patients the mean level of platelet count at 1st, 2nd 3rd, 4th and 5th day was observed to be 82.28±44.62 x 10^3, 74.45±37.7 x 10^3, 77.53±43.12 x 10^3, and 93.59±58.69 x 10^3, 99.0±77.11 x 10^3 cells/cumm respectively. Similarly the mean of leukocyte count was observed to be 3.7±1.62 x 103, 4.4±2.69 x 10^3, 5.53±3.02 x 10^3, and 5.97±3.33 x 10^3, 6.25±3.06 x 10^3 cells/cumm respectively. The study results revealed that the temperature was not significantly correlated with platelet count whereas it was significantly correlated with total leukocyte count on day 3 only (ρ= -0.329, p = 0.026) (table 1).

The study results revealed that in patients with fever duration of up to 4 days the temperature was not significantly correlated with either platelet count or total leukocyte whereas in patients with fever duration of 5 to 7 days it was significantly correlated with platelet count on day 3 only (ρ=-0.681, p= 0.002) (table 2).

The study results also showed that in patients aged <40 years the temperature was not significantly correlated with either platelet count or total leukocyte whereas in patients aged 40 years or above it was significantly correlated with total leukocyte count on day 3 only (ρ= -0.576, p = 0.025) (table 3).

Table 1: Correlation of Temperature with Platelet Count and Total Leukocyte Count

Variables (n=46)	Platelet Count		Total Leukocyte Count	
	P	p	ρ	P
Day 1 Temperature	-0.146	0.331	0.068	0.654
Day 2 Temperature	-0.174	0.246	-0.199	0.186
Day 3 Temperature	-0.177	0.239	-0.329	0.026
Day 4 Temperature	-0.152	0.314	-0.279	0.061
Day 5 Temperature	-0.070	0.643	0.023	0.881

Table 2: Correlation of Temperature with Platelet Count and Total Leukocyte Count Stratified for Fever Duration

Variables	Fever Duration of up to 4 Days (n=28)				Fever Duration of 5 to 7 Days (n=18)			
	Platelet Count		Total Leukocyte Count		Platelet Count		Total Leukocyte Count	
	P	p	ρ	p	P	P	ρ	p
Day 1 Temperature	-0.189	0.335	0.087	0.659	0.096	0.704	0.097	0.701
Day 2 Temperature	-0.211	0.28	-0.134	0.497	-0.092	0.716	-0.296	0.233
Day 3 Temperature	0.118	0.548	-0.343	0.074	-0.681	0.002*	-0.280	0.26
Day 4 Temperature	0.053	0.79	-0.357	0.062	-0.357	0.146	-0.135	0.593
Day 5 Temperature	-0.324	0.093	0.056	0.779	0.227	0.366	0.065	0.799

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Table 3: Correlation of Temperature with Platelet Count and Total Leukocyte Count Stratified for Age

Variables	Age<40 Years (n=31)				Age 40 Years or Above (n=15)			
	Platelet Count		Total Leukocyte Count		Platelet Count		Total Leukocyte Count	
	P	p	ρ	p	P	P	ρ	p
Day 1 Temperature	-0.164	0.378	0.128	0.494	-0.082	0.77	-0.101	0.721
Day 2 Temperature	-0.350	0.054	-0.210	0.256	0.205	0.465	-0.207	0.458
Day 3 Temperature	-0.233	0.207	-0.172	0.354	0.043	0.878	-0.576	0.025*
Day 4 Temperature	-0.119	0.523	-0.228	0.218	-0.182	0.517	-0.341	0.214
Day 5 Temperature	-0.086	0.644	0.062	0.74	….	….	….	….

Discussion

The study results revealed that the temperature was not significantly correlated with platelet count whereas it was significantly negatively correlated with total leukocyte count on day 3 only (p<0.05). Furthermore, in patients with fever duration of up to 4 days the temperature was not significantly correlated with either platelet count or total leukocyte whereas in patients with fever duration of 5 to 7 days it was significantly negatively correlated with platelet count on day 3 only (p<0.05). Moreover, in patients aged <40 years the temperature was not significantly correlated with either platelet count or total leukocyte whereas in patients aged 40 years or above it was significantly negatively correlated with total leukocyte count on day 3 only (p<0.05).

As expected, the study results revealed a negative correlation of temperature with the platelet count and total leukocyte count of the dengue patients, albeit only on day 3 which was an interesting finding in itself. Unfortunately, a thorough literature search did not reveal any pertinent published data to make a meaningful comparison of the study results.

In the management of dengue fever, platelet transfusion is considered when patients manifest bleeding problems such as petechiae, gum-bleeding, epistaxis etc. which occur more frequently in patients with severe thrombocytopenia. [8] Moreover, a large cross-sectional study from Pakistan in 2010 reported that while a low total white cell count was seen more commonly in patients with dengue fever as compared to dengue hemorrhagic fever (p=0.020), Neutropenia (p=0.019) and monocytosis (p=0.001) were found to be more common in the latter group. [13]

Literature shows that decisions taken using simple clinical and hematological parameters can predict diagnosis and prognosis of dengue fever in the early phase of illness. [14] If it can be unequivocally established that raised temperature in dengue hemorrhagic fever is inversely correlated with platelet count and total leukocyte count, it could be used as a marker, apart from bleeding manifestations, of the need to start platelet transfusion, or prophylactic antibiotics for that matter, though literature not always recommends prophylactic antibiotics in such cases. [15] In emergency situations where detailed hematological analysis requires time which a patient doesn't always have, such a marker can prove to be of great value in the timely management of such patients.

Conclusion and Recommendation

The study results revealed raised temperature to be significantly negatively correlated with total leukocyte count on day 3 only. Furthermore, stratified analysis showed it to be significantly negatively correlated with platelet count on day 3 in patients with longer duration of fever and with total leukocyte count on day 3 in patients aged 40 years or above. Further evaluation of the study findings with a larger sample size is recommended.

Conflict of Interests

The authors report no conflict of interests.

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