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Effect of *Papaya* Leaves Extract on Platelets Count and Hemoglobin Levels of Dengue Patients

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Abstract: The present study was conducted to investigate the effect of *Papaya* leaf extract on platelets count and hemoglobin levels in patients with dengue fever. Twenty adult patients admitted with diagnosis of dengue were purposively selected from a private hospital in Central India. These patients received standard symptomatic care for dengue fever. Ten patients who were willing to consume *Papaya* leaf extract were considered as experimental group and ten other patients were in control group. 50 ml/day *Papaya* leaf extract was given to the experimental group for four consecutive days and their platelets count and hemoglobin was monitored 24 hours for 4 days. The results indicated that the mean platelets count of the control group was 114200 $\pm$ 72568.44 /µL and of experimental groups was 70222 $\pm$ 67304.31 /µL on the day of admission. On the fourth day the platelets count of the control and experimental groups were 92900 $\pm$ 47103.79 /µL and 55500 $\pm$ 27399.31 /µL respectively. The mean platelets count of the experimental groups were significantly higher ($p = .044$) than the control group for the fourth day. The platelets count of control group showed a significant decrease on second ($p = .004$), third ($p = .003$) and fourth day ($p = .005$) as compared to the day of admission. Results further revealed that the mean hemoglobin levels of the control and experimental groups on the day of admission were 11.77 $\pm$ 0.48 mg/ and 11.34 $\pm$ 0.58 gm/dl respectively. On the fourth day the hemoglobin levels of the control and experimental

groups were 10.59 ± 0.40 mg/dl and 11.79 ± 0.46 gm/dl respectively. The mean hemoglobin level of the experimental and control group showed insignificant difference. A significant decrease in hemoglobin levels of control group was observed on the third (p= .002) and fourth days (p = .0003) as compared to the day of admission.

Keywords: *Papaya leaf extract, Platelets count, hemoglobin levels, Dengue fever*

INTRODUCTION

Dengue is the most important emerging viral disease of humans that in recent decades has become a major international public health concern. Dengue is found in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban area[1]. It is estimated that there are between 50 and 100 million cases of dengue fever (DF) and about 500 000 cases of dengue haemorrhagic fever (DHF) each year which require hospitalization[2]. Dengue viruses, mosquito-borne members of the *Flaviviridae* family, are the causative agents of dengue fever. Dengue fever is spread through the bite of an infected *Aedes aegypti* mosquito. The mosquito gets the virus by biting an infected person[3].

Thrombocytopenia is life threatening in many diseases particularly in dengue which is an escalating problem in the world**.** Of the available methods for treating thrombocytopenia, the treatment method mainly depends on the disease severity. Nevertheless, due to certain side effects and the costs involved, the availability of treatment for thrombocytopenia is limited[4].

The leaves of *Papaya* have been shown to contain many active components such as papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic-glucosides and glucosinolates that can increase the total antioxidant activity in blood and reduce lipid peroxidation level[5]. The alkaloids, flavonoids, saponins, tannin, and glycosides are related with anti-inflammatory activity. *Papaya* leaf extract was also found to have antibacterial effect[6], antitumor, and immunomodulator activities[5].

Studies have indicated that the juice of the leaves of the *Papaya* plant from the family *Caricaceae* could help to increase the platelet levels in these patients[7, 8, 9, 10, 11, 12]. In view of the above, the present investigation was carried out to study the effect of Papaya leaf extract on platelets count and haemoglobin levels of dengue patients.

MATERIALS AND METHODOLOGY

In all 20 adult patients admitted with diagnosis of dengue fever (DF) or dengue hemorrhagic fever (DHF) were purposively selected from a private hospital in central India. These patients received standard symptomatic care for dengue fever. Ten patients who were willing to consume *Papaya* leaf extract were considered as experimental group and ten other patients in control group. The oral consent was obtained from the experimental group. The procedure for preparing *Papaya* leaves extract was followed according to Hettige[7]. 50 ml *Papaya* leaf extract per day was given to the experimental group of patients for four consecutive days. The dosage was varied from case to case on basis of severity of dengue disease. In treatment, severe patients were given dosage of 10 ml per four hours, for average patients 10 ml for three hours and normal cases 10 ml per two hours.

The Platelets count and hemoglobin level of control and experimental groups were monitored for every 24 hours for 4 days. The data was analyzed using statistical tests viz., Mean, Standard Deviation, Independent and Paired‘t ‘ tests using Tool Pak of Microsoft Office 2007.

RESULTS AND DISCUSSION

The control group had six females and four males and the experimental group had five males and five females. The average age of control and experimental group was 43.20 ±14.06 and 44.90 ± 0.336 years respectively.

Platelets count of Control and Experimental Groups: The data according to the mean Platelets count of the control and experimental groups have been presented in **Table 1**.

Table 1: Mean platelets count (/µL) of the control and experimental groups

Day	Control Group		Experimental Group		**t value**	**P Value**
	Mean	SD	Mean	SD		
Day of Admission	114200	72568.44	70222	67304.31	1.405	.177
DAY 2	79600	59768.44	68400	41899.88	.485	.633
DAY 3	67700	46156.86	77900	45542.29	.497	.625
DAY 4	55500	27399.31	92900	47103.79	2.17	.044

The data presented in **Table 1** shows that the mean platelets count of the control group was highest on the day of admission (114200 ± 72568.44 /µL) and then started decreasing continuously till the fourth day and reached to the level of 55500 ± 27399.31/µL. In case of experimental group, the mean platelets count of the experimental groups was 70222 ± 67304.31/µL on the day of admission, further decreased on the second day (68400 ± 41899.88 /µL) but thereafter it started rising from the third day onwards and reached to the mean platelets count of 92900 ± 47103.79 /µL on the fourth day. The statistical analysis showed that the mean platelets count of the experimental groups was significantly higher (p =.044) than the control group for the fourth day. The difference between the mean platelets count of the control and experimental groups were insignificant (>0.05) for the rest of the days.

The increase in platelets count of the dengue patients consuming CP leaves extract has also been reported by several scientists[7, 8, 9, 12]. CP leaf extract has been found to accelerate the increase in platelets count, and shortened the hospitalization period[10]. A significant increase in the platelets count has been observed after oral administration of freshly prepared, mature leaf concentrate of C. *Papaya*. Both mature and immature leaves of C. *Papaya*, have the potential to be developed as a plant based therapeutic agent for thrombocytopenia[11]. Juice consumption during the course of dengue infection had the potential to induce the rapid production of platelets[12].

Comparison of Mean Platelets Count (/µL) within Days in Control and Experimental Groups: An attempt was made to compare the mean platelets count within control and experimental groups. The mean platelets count within control and experimental groups were compared and have been presented in **Table 2 and 3** respectively.

Table 2: The day wise comparison of mean platelets count (/µL) within control group

Control Samples		Mean	Std. Deviation	t value	P Value	Correlation	P Value
Pair 1	D/O/A	114200	72568.43	3.770	.004	.922	.001
	DAY 2	79600	59768.44				
Pair 2	D/O/A	114200	72568.43	3.927	.003	.895	.000
	DAY 3	67700	46156.85				
Pair 3	D/O/A	114200	72568.43	3.671	.005	.870	.001
	DAY 4	55500	27399.31				

It is evident from **Table 2** that the mean platelets count of the control group on the date of admission was highest as compared to all the consecutive days. The statistical analysis showed a significant decrease in mean platelets count on second (p = .004), third (p= .003) and fourth days (p = .005) as compared to the day of admission. The results further reveal high positive and significant correlations between the platelets count of the initial and consecutive days.

Table 3: The day wise comparison of mean platelets count (/µL) within experimental group

Experimental Group		Mean	Std. Deviation	t value	P Value	Correlation	P Value
Pair 1	D/O/A	70222	67304.30	0.091	.930	0.397	.256
	DAY 2	68400	41899.88				
Pair 2	D/O/A	70222	67304.30	0.358	.729	0.327	.356
	DAY 3	77900	45542.28				
Pair 3	D/O/A	70222	67304.30	1.007	.340	0.264	.461
	DAY 4	92900	47103.78				

The data presented in **Table 3** clearly shows that the mean platelets count of experimental group on the second day were lower than the mean platelets count of the day of admission. However for the third and fourth day, the mean platelets counts were higher than the day of admission. The statistical analysis did not show any significant difference between the mean platelets count of day of admission and of second (p= 0.930), third (p=0.729) and fourth day (p= 0.340). The Table further shows low positive and insignificant correlations between the platelet count of the initial and the consecutive days.

Hemoglobin Levels: The data according to the mean hemoglobin of the control and experimental groups have been presented in **Table 4.**

Table 4: Mean hemoglobin (gm/dl) of the control and experimental groups

Day	Control Group		Experimental Group		t Value	P value
	Mean	SD	Mean	SD		
Day of Admission	11.77	0.48	11.34	0.56	0.58	0.283
DAY 2	11.4	0.47	11.34	0.47	0.09	0.929
DAY 3	11.03	0.40	11.45	0.45	0.698	0.493
DAY 4	10.59	0.40	11.79	0.46	1.976	0.063

The data presented in **Table 4** shows that the mean hemoglobin level of the control group was highest on the day of admission (11.77 $\pm$ 0.48 gm/dl) and then started decreasing continuously till the fourth day and reached to the level of 10.59 ± 0.40 gm/dl. In case of experimental group, the mean hemoglobin levels of the experimental groups was 11.34 ± 0.58 gm/dl on the day of admission ,further remained same on the second day but thereafter it started rising from the third day onwards and reached to the mean hemoglobin level of 11.79 ± 0.46 gm/dl on the fourth day. The statistical analysis showed that the mean hemoglobin level of the experimental group and control group were insignificant. According to Shiekh *et al.*[4] the Mean Cell Hemoglobin (MCH) of rats treated with CP leaf formulation for seven days were significantly higher (15.2 ± 0.12), as compared to control receiving distilled water (14.2 ± 0.31). However hemoglobin levels showed insignificant increase in experimental group (13.43 ± 0.62) as compared to control group (12.83 ± 0.92).

Comparison of Mean Hemoglobin Levels within Days in Control and Experimental Groups: An attempt was made to compare the mean hemoglobin levels within control and experimental groups. The hemoglobin levels within control and experimental groups were compared and have been presented in **Table 5 and 6** respectively.

Table 5: The day wise comparison of mean hemoglobin (gm/dl) levels within control group

Control Samples		Mean	Std. Deviation	t value	P Value
Pair 1	D/O/A	11.77	0.48	1.632	0.136
	DAY 2	11.4	0.47		
Pair 2	D/O/A	11.77	0.48	4.105	0.002
	DAY 3	11.03	0.40		
Pair 3	D/O/A	11.77	0.48	5.67	0.0003
	DAY 4	10.59	0.40		

It is evident from **Table 5** that the mean hemoglobin level of the control group on the date of admission was highest as compared to the subsequent days. The statistical analysis showed an insignificant decrease

in mean hemoglobin levels on second (p = 0 .136), and significant decrease on the third (p= .002) and fourth days (p = .0003) as compared to the day of admission.

Table 6: The day wise comparison of mean hemoglobin (gm/dl) levels within experimental group

Experimental Group		Mean	Std. Deviation	t value	P value
Pair 1	D/O/A	11.34	0.55	0.00	1.00
	DAY 2	11.34	0.47		
Pair 2	D/O/A	11.34	0.55	0.50	0.623
	DAY 3	11.45	0.45		
Pair 3	D/O/A	11.34	0.55	1.95	0.082
	DAY 4	11.79	0.46		

The data presented in **Table 6** clearly shows that the mean hemoglobin levels of experimental groups on the first day and the second day were same (11.34 mg/dl). But for the third and fourth day, the mean hemoglobin levels were higher than the day of admission. Though there was rise in hemoglobin levels on third (11.45 mg/dl) and fourth day (11.79 mg/dl), the statistical analysis did not show any significant difference between them. It is evident from that the subjects in the experimental group that received extract can reach faster and higher increase in hemoglobin levels compared to the control group.

CONCLUSION

Papaya extract no doubt offers a cheap and possibly effective treatment for dengue. Various clinical and preclinical studies conducted have demonstrated a positive effect in dengue cases with thrombocytopenia. The study also demonstrates the same positive beneficial trend in increasing the platelets significantly on the fourth day of admission. However, large scale randomized clinical trials are necessary to further establish its pivotal role in the management of dengue.

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