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Short Communication

# EVALUATION OF THE EFFICACY OF *CARICA PAPAYA* LEAF EXTRACT ON PLATELET COUNTS IN DENGUE PATIENTS

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# ABSTRACT

In Dengue fever thrombocytopenia is a major complication in all age groups. Treatment of dengue fever primarily includes symptomatic and intensive supportive care. Platelet transfusion is the only treatment and it is indicated only in severe cases. Carica papaya leaf extract (CPLE) are believed to have some role in increasing platelet counts hence this study was planned to evaluate the role of CPLE in improving dengue thrombocytopenia. Total 100 patients with dengue fever and thrombocytopenia matching inclusion criteria were included in the study. Control group consist of 50 age matched dengue patients. The patients were given CPLE (10 ml three times/ day) along with kiwi fruit without any other treatment. All the subjects were followed up and on the third day platelet and total WBC counts were estimated then results were compared with previous findings. Paired t-test in SPSS (version 15) was used to compare the mean values of the parameters in the study group before and after giving CPLE. The mean platelet count of study group before giving CPLE was 212210 $\pm$ 72257 cells/cumm and it was significantly increased to 275282 $\pm$ 78969 cells/cumm (*p*-value = 0.000). The mean WBC count was also increased in study group after giving CPLE as compared to control group. In conclusion, increased platelet count and WBC count were noted in the patients after giving CPLE as compared to control group. In conclusion, increased platelet count and skin rashes was observed in patients after giving kiwi fruits.

Keywords: Dengue, Thrombocytopenia, CPLE, Platelet count

# 1. INTRODUCTION

Dengue is an acute viral infection associated with thrombocytopenia, which is of great public health concern in India [1]. It is the foremost common arthropod borne viral illness transmitted by mosquitoes of species aedes [2]. In India *A. aegypti* is the main vector in most urban areas. Dengue and dengue hemorrhagic fever (DHF) are caused by virus serotypes DEN-1, DEN-2, DEN-3, and DEN-4 of the genus flavivirus which are closely associated with one another, but antigenically distinct [3].

India has over 67,000 cases of dengue fever in October 2019 [4]. WHO estimates an annual incidence of roughly 100 million infections, with approximately 500,000 people with dengue hemorrhagic fever (DHF) requiring hospitalization [5]. The clinical manifestation of dengue includes high grade fever, headache, arthalgia, retro orbital pain, back pain, myalgia, and flu like symptoms [6].

Carica papaya leaf extract (CPLE) has recently gained interest in the treatment of dengue because it improves

symptoms as well as platelet counts. Carica papaya leaves are being used in ayurvedic medicine since many years. Its use as an anti-inflammatory agent, for its woundhealing properties [7], antitumor as well as immune modulatory effects, and as an antioxidant is being studied. Safety studies for chronic, sub-acute, and acute toxicities were conducted on CPLE and demonstrated to be safe for human consumption based on the OECD guidelines [8]. Some of the genes have shown to influence platelet production, 12namely, arachidonate lipoxygenase (ALOX 12) and platelet-activating factor receptor (PTAFR) [9]. An upsurge in the activity of these genes is necessary for platelet production and activation. The ALOX 12 gene is intensely expressed in megakaryocytes, and it has shown to be accountable for the 12 hydroxyeicosatetraenoic acid (12-HETE) production of platelets in patients treated with CPLE extract [10]. On megakaryocytes, PTAFR gene is expressed, which indicates that it might be a precursor for platelet production [11]. Clinical evidence shows that C. papaya extract enhances the PTFAR activity around

13-fold and the ALOX 12 activity 15-fold [12] which is responsible for increased platelet production [13]. Hence, this study was taken up to assess the effect of carica papaya on dengue thrombocytopenia.

#### 2. MATERIAL AND METHODS

Total 100 dengue patients were included in this study group and control group consisted of 50 dengue patients. 5 ml venous blood was collected in a plain bulb (3 ml) and EDTA bulb (2 ml). Then Plain bulb was centrifuged at 2200 RPM for 10 minutes to separate serum. The serum sample was used to perform diagnostic tests for the detection of dengue. Detection of NS1 antigen and differential detection of IgM & IgG antibodies in patient's serum was carried out by using SD Dengue Duo kit method [14]. EDTA bulb was used for the determination of complete blood count, (the haemoglobin, platelet count, white blood cell count, and packed cell volume) was performed from sample on the five part auto haematology analyzer.

Study group patients of dengue fever with thrombocytopenia (1,50000 cells/ cumm) were given Carica papaya leaf extract i.e., 10 ml /3 times per day for adults and children 5 ml /3 times per day for 3 days along with one kiwi fruit. Carica papaya leaves extraction was prepared from fresh leaves using an extractor with addition of water. All the subjects were followed up daily for 3 days with monitoring platelet and WBC count and result was compared with previous one.

### 3. STATISTICAL ANALYSIS

Entire data obtained from this study was entered in Excel sheet. The Mean, Standard Deviation (SD) values was

Table 2: Platelet	Count	Observation
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calculated and data analysis was done by using SPSS software (version 15) [15]. Paired t-test was used to compare the mean values of the parameters in the study group before and after giving CPLE [15]. The p-value <0.05 was considered as statistically highly significant.

#### 4. **RESULTS**

A total of 100 patients suffering from dengue thrombocytopenia were recruited in to the study group and 50 dengue patients were included in control group. Out of 100 patients, 58 (58%) were male and 42 (42%) were female patients. All patients recruited were dengue NS1 (Ag) / IgM (Ab) or both positive.

Table 1: Gender wise distribution of patients of dengue fever

	Study group (n=100)	Control group (n=50)
Age ( in years)	30.56±12.65	25.1±11.96
Male	58 (58%)	30 (60%)
Female	42 (42%)	20 (40%)

Table 2 presents the mean platelet count of study group. The platelet count was significantly increased after 3 days [p-value  $0.00 \ (< 0.05)$ ] of giving CPLE in the study group. Symptoms of dengue i.e. high fever, vomiting, rashes etc. were also reduced. Increase in the mean platelet count was considered as the primary outcome, and increase in mean WBC counts was considered as the secondary outcome.

a	able 2: Flatelet Coult Observation				
-	Mean platelet count	Before giving CPLE	After giving CPLE	p-value	
_	Patients of dengue fever	212210±12727 cells/cumm	275282±27577 cells/cumm	0.000 (<0.05)	
_	Control	181281±21213 cells/cumm	183922±9899 Cells/cumm	0.000 (<0.05)	

### **Table 3: Total WBC count observation**

Mean WBC count	Before giving CPLE	After giving CPLE	p-value
Patients of dengue fever	4450±3288 cells/cumm	5479±1556 cells/cumm	0.000 (<0.05)
Control	4968±265 cells/cumm	$5141\pm112$ cells/cumm	0.000 (<0.05)

Table 3 represents the mean WBC count in control and study group of dengue patients. The WBC count was significantly increased after 3 days (p-value=0.00 (<0.05)) after giving CPLE and reduction in dengue symptoms, i.e. high fever was also observed.

#### 5. DISCUSSION

Studies conducted in adult patients with dengue have shown that CPLE had significant increases in the platelet count as compared to control group. Additionally there

was significant increase in the WBC counts in the study group as compared to the control group.

Our study conducted in patients with dengue has shown that CPLE had significantly increased the platelet count as compared to control group. Our results are correlated to those reported by Subenthiran et al that CPLE can increase platelet count in mice [16] and also in dengue fever patient as reported by a Gowda et al. [13] and Venugopal et al. [17] CPLE is shown to increase the expression of Arachidonate 12-lipoxygenase (ALOX12) and platelet activating factor receptor (PTAFR) gene responsible for platelet production [13]. Our results are also corroborative to those reported by Gowda et al. (2015) [13] that CPLE can increase platelet count in dengue fever patient and also similar with Yunita et al. (2012) [18], reported that the platelet counts rise more rapid in the intervention group. Abhishek et al. (2015) [19] noted that platelet counts appear to improve more rapidly following treatment with CPLE, and in several studies the platelet counts at day 3-5 seem to be higher in those who received CPLE compared to those who did not.

Additionally there was significant increase in the WBC counts in the study group as compared to the control group [20]. CPLE may have stimulating action at the myeloid stem cells in the bone marrow. Nwangwa et al. in their preclinical study documented an increase in the WBC count with the administration of Carica papaya leaf juice in mice [21] and clinical studies by Siddique et al. [21] corroborated the same in humans. The WBC values in both the groups showed an increasing trend after 3<sup>rd</sup> day onwards and can be correlated to the declining viraemia at this point of time.

There are very few studies available, regarding actual mechanism of beneficial effect of C. papaya leaf extract in dengue. In an "in vitro" study by Ranasinghe et al., the C. papaya leaf extract found to be associated with the improvement of erythrocyte membrane stabilization a study done by bioinformatics methods found that flavonoids of C. papaya leaf extract can inhibit a protease involved in viral assembly [22]. The leaf extract of C. papaya has antioxidant and free radical scavenging property which can help in the prevention of haemolysis and bleeding [23-26]. This is so far best available evidence for the use of C. papaya in dengue patients.

### 6. CONCLUSION

From our study it can be concluded that carica papaya leaf extract has a definitive role in improving the platelet count and shows reduction in symptoms as compared to control group. The WBC count was also increased significantly in dengue patients suffering thrombocytopenia as compared to control group. Carica papaya leaf extract was well tolerated among the patients as it has not any side effects therefore it is our strongest recommendation that it can be added as therapeutic agent in the management of dengue fever as supportive therapy along with allopathic therapy. It may improve the outcome in patients. Symptoms like muscles pain and skin rashes were also reduced after giving kiwi fruit. Therefore, it is our suggestion to add it as supportive therapy for better outcome of the patients. Our study provides beneficial information for dengue patients, however, further studies are needed to conduct in large number of dengue patients to explore the mechanism induced by carica papaya extract, which may be helpful to them as well as society in future.

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