

## A STUDY OF PAPAYA EXTRACT IN THE TREATMENT OF LOW PLATELET COUNT IN MALARIA AND DENGUE CHILDREN BELOW 18 YEARS

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### ABSTRACT

#### BACKGROUND

The normal blood platelet count is 1,50,000-4,50,000/ $\mu$ L. Thrombocytopenia results from decreased production, increased destruction and/or sequestration. Although, the bleeding risk varies somewhat by the reason for the thrombocytopenia, bleeding rarely occurs in isolated thrombocytopenia at counts <50,000/ $\mu$ L and usually not until <10,000-20,000/ $\mu$ L. Coexisting coagulopathies as is seen in liver failure or disseminated coagulation, infection, platelet-inhibitory drugs and underlying medical conditions can all increase the risk of bleeding in the thrombocytopenic patient. Most procedures can be performed in patients with a platelet count of 50,000/ $\mu$ L. The level needed for major procedures will depend on the type of surgery and the patient's underlying medical state, although a count of approximately 80,000/ $\mu$ L is likely sufficient. Thrombocytopenia results from one or more of three processes- (1) Decreased bone marrow production; (2) Sequestration, usually in an enlarged spleen; and/or (3) Increased platelet destruction. In our country, malaria and dengue is quite prevalent and is known to cause the majority of morbidity and mortality, which is a direct result of thrombocytopenia. This study is done in order to check the efficacy of a papaya extract in these two diseases and thus in turn help save thousands of life, which are in the risk zone. Majority of the study on this topic was previously done in the adults, but none of the study came close to put an effort to what happens in the children or rather the paediatric group, which in our study is considered and studied. In the previous efforts, a plethora of diseases were considered, but in our study, it has been narrowed down to two diseases, which are rampant in this part of the world.

#### MATERIALS AND METHODS

This study was done in the Department of Paediatrics, Travancore Medical College at Kollam. The study was done in the patients who belonged to the paediatric age groups (range 9 to 18 years). The study consisted of children (30 in number) who were admitted in the hospital and confirmed to have thrombocytopenia, which was secondary to confirmed dengue or malaria. Patients were promptly examined after taking a detailed history session. The blood samples were sent to the lab. The disease was once again confirmed and thrombocytopenia was considered when three consecutive platelet count was taken and when the count was lessened by at least 10,000 platelets. The study was conducted from October 2014 to September 2015.

#### RESULTS

After treatment, only dengue patients responded significantly on the first day, although on the fifth day, it lacked the same pace of prognosis. After five days of treatment in both diseases, they responded very well and crossed the one and half lakhs mark.

#### CONCLUSION

This study effectively proves the efficacy of the papaya extract in the subsidiary treatment of the two rampant diseases. The study also suggests that the use of papaya extract has to be initiated at a very early stage as there is a significant association of the rise in the platelet count in the early phase of the disease.

#### KEYWORDS

Papaya Extract, Thrombocytopenia, Dengue, Malaria, Haemorrhage.

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#### BACKGROUND

The normal blood platelet count is 1,50,000-4,50,000/ $\mu$ L. Thrombocytopenia results from decreased production, increased destruction and/or sequestration. Although, the

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bleeding risk varies somewhat by the reason for the thrombocytopenia, bleeding rarely occurs in isolated thrombocytopenia at counts <50,000/ $\mu$ L and usually not until <10,000-20,000/ $\mu$ L. Coexisting coagulopathies, as is seen in liver failure or disseminated coagulation; infection; platelet-inhibitory drugs; and an underlying medical conditions can all increase the risk of bleeding in the thrombocytopenic patient. Most procedures can be performed in patients with a platelet count of 50,000/ $\mu$ L. The level needed for major procedures will depend on the type of surgery and the patient's underlying medical state, although a count of approximately 80,000/ $\mu$ L is likely



sufficient. Thrombocytopenia results from one or more of three processes- (1) Decreased bone marrow production; (2) Sequestration, usually in an enlarged spleen; and/or (3) Increased platelet destruction. In our country, malaria and dengue is quite prevalent and is known to cause the majority of morbidity and mortality, which is a direct result of thrombocytopenia.

An annual incidence of about 200 million cases of malaria and an estimated 6,55,000 deaths in 2010 was reported. It is definitely a global health problem.<sup>1</sup> Malaria is endemic in about 90 countries and India contributes anything in and around 70 to 75 percent of the total malaria cases in Southeast Asia.<sup>2</sup> Early diagnosis and frank treatment remains the key to the effective management of malaria.<sup>3,4,5</sup> The examination of thick and thin blood films under the light microscope was considered the gold standard in the diagnosis of malaria. It is informative and inexpensive and is usually the best in a developing country like ours, but it requires expertise and repeated smear examinations.<sup>6</sup> Polymerase Chain Reaction (PCR) is the most sensitive method, but it cannot be used for routine purposes as it is way too costly expenditure and the facility providing these kinds of services are scares in our country.<sup>6</sup> The time factor also to get these kinds of tests also plays an important role as prompt and immediate treatment has to be started. Haematological abnormalities have been observed in patients with malaria with anaemia and thrombocytopenia being the most common.<sup>7</sup>

The disease is caused by dengue viruses.<sup>8</sup> Dengue is found in tropical and subtropical regions around the world like and the fact that our country lies in the tropics means that the disease is rampant.<sup>9</sup> According to latest statistics, it is estimated that there are between fifty and one hundred million cases of dengue fever and about 5,00,000 cases of dengue haemorrhagic fever each year, which require hospitalisation.<sup>10</sup> Dengue fever is spread through the bite of an infected *Aedes aegypti* mosquito.<sup>11</sup> With each infection, the patient gets lifelong immunity to that particular serotype, but subsequent infection with a different serotype is possible.<sup>12</sup> Unfortunately, due to lack of adequate surveillance systems in the underdeveloped and developing countries, the exact extent of the problem are not known.<sup>13</sup> The problem is that it has a variety of presentations. It is estimated that there are currently 50-100 million cases of dengue, which including more than 5,00,000 reported cases of dengue haemorrhagic fever and dengue shock syndrome.<sup>14</sup> Dengue viruses are members of the Flaviviridae family, which is a single-stranded RNA viruses. The RNA encodes a single polyprotein, which is subsequently cleaved into three structural proteins.<sup>15,16</sup> The structural proteins include a capsid protein (C),<sup>17</sup> membrane protein (M) and an envelope protein (E).<sup>18</sup> The E protein is the major structural protein exposed on the surface of the viral particle. The E protein recognises the neutralising antibodies.<sup>19</sup> The nonstructural proteins are involved in viral translation, transcription and replication.<sup>20</sup> These proteins correlate with

viral titers and have been a useful tool in dengue infection diagnosis.<sup>21,22</sup> Because, it is expressed on the surface of infected cells, NS1 triggers host immune responses. Additionally, NS1 has been shown to display soluble complement-fixing activity.<sup>23</sup>

This study is done in order to check the efficacy of a papaya extract in these two diseases and thus in turn help save thousands of life, which are in the risk zone. Majority of the study on this topic was previously done in the adults, but none of the study came close to put an effort to what happens in the children or rather the paediatric group, which in our study is considered and studied. In the previous efforts, a plethora of diseases were considered, but in our study, it has been narrowed down to two diseases, which are rampant in this part of the world.

### AIMS AND OBJECTIVES

To study the effectiveness of the papaya extract in treating the thrombocytopenia that is encountered and is considered to be deadly in dengue and malaria in the paediatric age group.

### MATERIALS AND METHODS

This study was done in the Department of Paediatrics, Travancore Medical College at Kollam.

The study was done in the patients who belonged to the paediatric age groups (range 9 to 18 years).

The study consisted of children (30 in numbers) who were admitted in the hospital and confirmed to have thrombocytopenia, which was secondary to confirmed dengue or malaria.

Patients were promptly examined after taking a detailed history session. The blood samples were sent to the lab. The disease was once again confirmed and thrombocytopenia was considered when three consecutive platelet counts were taken and when the count was lessened by at least 10,000 platelets.

### Inclusion Criteria

1. Age of the patients was below 18 years.
2. Thrombocytopenia was considered when three consecutive platelet counts were taken and when the count was lessened by at least 10,000 platelets.

### Exclusion Criteria

1. Thrombocytopenia secondary to any of the other underlying pathologies was not considered.
2. Patients on anti-platelets drugs were not considered.

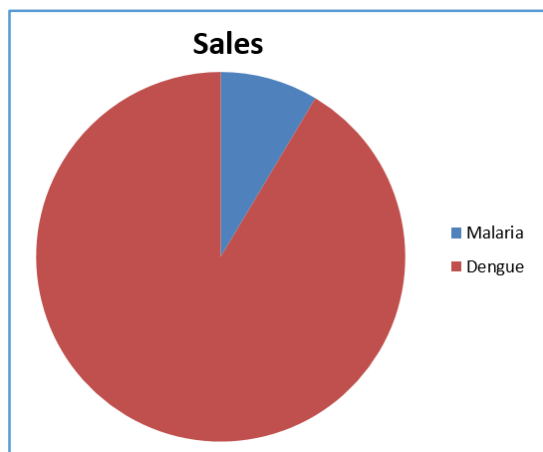
The patients were then administered 3-5 mL of papaya extract based upon the age in TID doses. The platelet counts were checked after giving the extract on day one, two, three, four and finally on day five.

All the statistics were done using the latest ANNOVA software 2016.

**RESULTS**

Disease Causing Thrombocytopenia	Thrombocytopenia	%
Dengue	21	70%
Malaria	9	30%

**Table 1. Number of Cases Found to be Suffering from Thrombocytopenia Due to Dengue and Malaria**



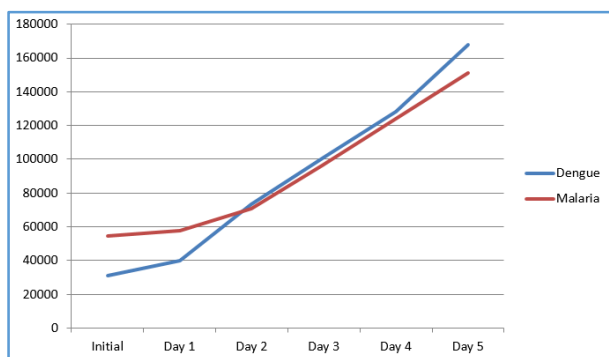
**Image 1. Number of Cases Found to be Suffering from Thrombocytopenia Due to Dengue and Malaria**

Disease Causing Thrombocytopenia	Mean Platelet Count	Standard Deviation
Dengue	31,300	16,100
Malaria	54,400	8,200

**Table 2. Mean Platelet Count in the Beginning**

Dengue	Platelet Count (Dengue)	Platelet Count (Malaria)
Initial	31,300	54,400
Day 1	39,800	57,500
Day 2	73,100	71,000
Day 3	10,100	96,800
Day 4	1,28,000	1,24,000
Day 5	1,68,000	1,51,000

**Table 3. Mean Platelet Count On Each Day After Treatment**



**Image 2. Mean Platelet Count On Each Day after Treatment**

Dengue initial response	
Mean platelet count	31,600
Second day platelet count (day 2)	73,100
Significance (P<0.05)	0.041

**Table 4. Test for Significance (Only the Report with p <0.05)**

**DISCUSSION**

After treatment, only dengue patients responded significantly on the second day, although on the fifth day, it lacked the same pace of prognosis. All other diseases after five days responded very well and crossed the one and a half lakhs mark.

In our study, the dengue contributed for 70% of cases and 30% of the cases were contributed by malaria.

The mean platelet count was found to be 31,300 with a standard deviation of 16,515 platelets in case of the dengue and 54,400 platelets with a standard deviation of 8,200 platelets.

There was a marked rise in the platelet count on day two of treatment and it is significantly associated with the rise of the platelets. After day 2, there is no difference in the rise in the platelet count when compared with the same as seen in the treatment of malaria.

When our study is compared with Gill MK et al,<sup>24</sup> the baseline in the initial part is reported to be in the range of 8,000-1,30,000 platelets. This may be due to the fact that in our study we have considered the patients after three samples and the patients considered in our study belong to the paediatric age group, whereas in their study, it is also the adults who were considered.

Disorders of production maybe either inherited or acquired. In evaluating a patient with thrombocytopenia, a key step is to review the peripheral blood smear and to first rule out "pseudothrombocytopenia," particularly in a patient without an apparent cause for the thrombocytopenia. Pseudothrombocytopenia is an in vitro artifact resulting from platelet agglutination via antibodies (usually IgG, but also IgM and IgA) when the calcium content is decreased by blood collection in Ethylenediaminetetraacetic (EDTA) (the anticoagulant present in tubes (purple top) used to collect blood for complete blood counts (CBCs)). If a low platelet count is obtained in EDTA-anticoagulated blood, a blood smear should be evaluated and a platelet count determined in blood collected into sodium citrate (blue top tube) or heparin (green top tube) or a smear of freshly obtained unanticoagulated blood such as from a fingerstick can be examined.

The long-term effects of the papaya extract and complete pharmacological aspects have not been studied and it is still in the early days of the infancy. It is right now used exclusively in the country. Apart from the extract, the other forms of papaya like the juice and the leaf extract has to be considered. In a country like ours, it would prove to a drug of boon as the two diseases considered above are rampant and a natural drug like this, which is abundantly available would be nothing short of a miracle. The study has

a lot of future as the safety of the drug in pregnancy and its long time side effects if any has to be proved. The pharmacovigilance has to be set and the doctors has to put in an effort to provide with the much awaited answers.

### CONCLUSION

The study shows successively the direct uses of the papaya extract in the treatment of dengue and malaria in the paediatric age group. The study also suggests that the use of papaya extract has to be initiated at a very early stage as there is a significant association of the rise in the platelet count in the early phase of the disease.

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