A Review on the Potential Therapeutic Profile of Carica papaya Leaf Extract in the Management of Dengue Fever

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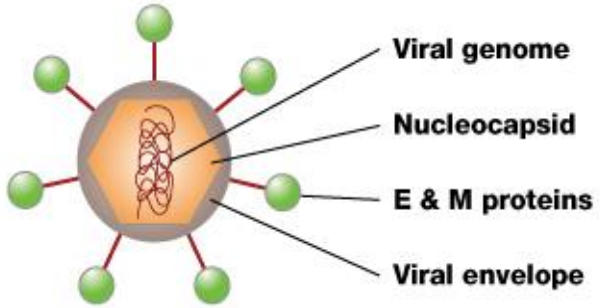
DAVANGERE

INTRODUCTION



- Acute viral infection
- Dengue viruses (DV): genus Flavivirus, family Flaviviridae
- Positive stranded encapsulated RNA virus
- 3 structural protein genes: C, M, E
- 7 NS protein genes

- Aedes aegypti mosquito transmission
- 1997 WHO classification of Dengue infection
  - Undifferentiated Fever
  - Dengue Fever (DF) and
  - Dengue Haemorrhagic Fever (DHF)
- 2009 WHO classification,
  - Uncomplicated
  - Severe

CLINICAL PRESENTATION

- Four main characteristic manifestations

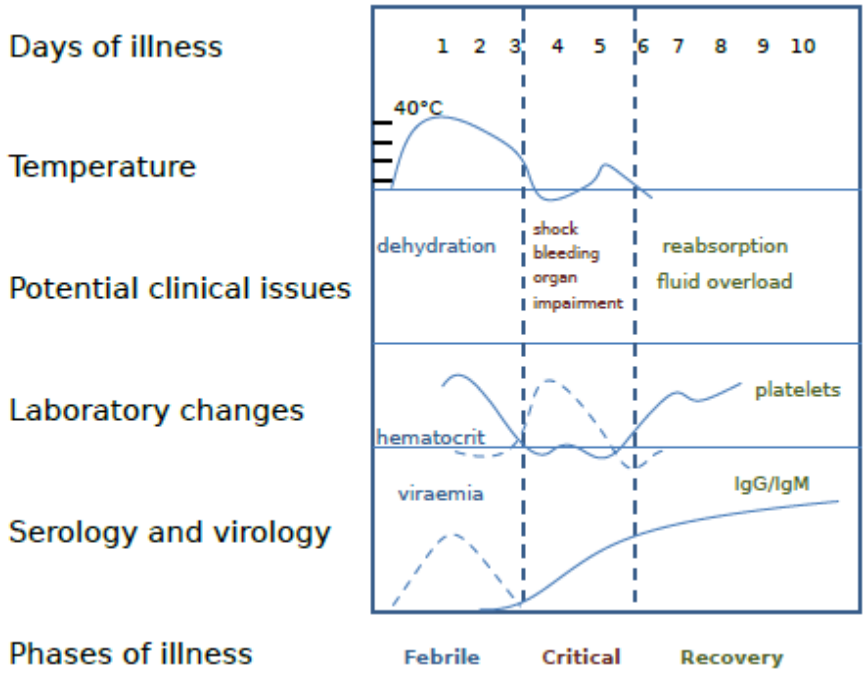
- Continuous high fever lasting 2-7 days;

- Haemorrhagic tendency;

- Thrombocytopenia (platelet count <100x109/L); and

- Evidence of plasma leakage

- Incubation period: 3 to 14 days

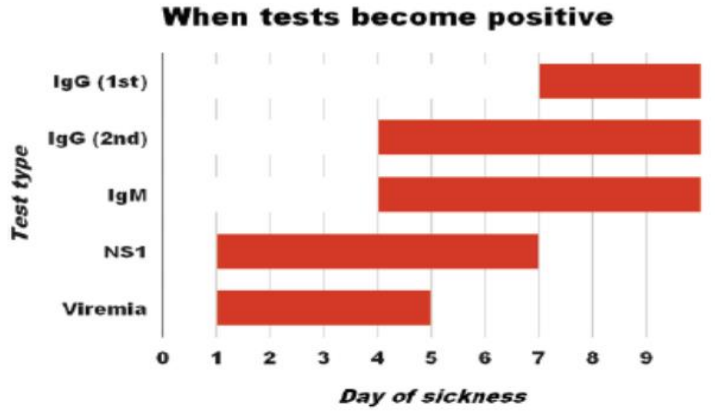


- After the incubation period, the illness begins abruptly
- Patients with moderate to severe disease, 3 phases
  - Febrile,
  - Critical and
  - Recovery
- **Individual risk factors:** secondary infection, age (young children) , ethnicity and possibly chronic diseases
- Associated problems

Diagnosis

- Typically made clinically
- A probable diagnosis is based on the findings of fever plus any 2 of the characteristic features
- The earliest change detectable on laboratory investigations
- Peripheral vascular collapse in children
- Warning signs are an important aspect for early detection

Laboratory tests



Graph of when laboratory tests for dengue fever become positive. Day zero refers to the start of symptoms, 1st refers to in those with a primary infection, and 2nd refers to in those with a secondary infection.[9]

- Diagnosis confirmed by microbiological laboratory testing
  - Virus isolation in cell cultures
  - Nucleic acid detection by PCR
  - Viral antigen detection (such as for NS1) or
  - Specific antibodies (serology)
- All tests may be negative in the early stages of the disease
- PCR and viral antigen detection are more accurate in the first seven days

Problem Statement

- Risk population: Over 2.5 billion people – over 40% of the world's population
- WHO estimation,
  - ✓ 50–100 million dengue infections and half a million DHF worldwide every year
  - ✓ Average case fatality rate ≈ 5 %
- Endemic in over 125 countries
- The exact extent of the problem not known

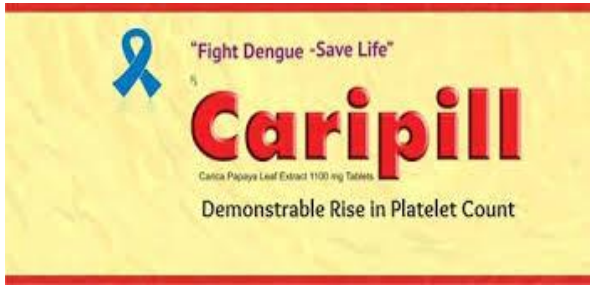
Currently available treatment modalities

- Treatment depends on the symptoms & severity
- IV fluids- titrated
- Blood transfusion initiated early in patients presenting with unstable vital signs
- Packed red blood cells or whole blood recommended
- Thrombocytopenia not addressed till it gets lowered down to levels less than 20000 /µl
- Reduction of mortality due to DHF from 20% to less than 1%
- Corticosteroid

- TPO agonists and mimetics like **Eltrombopag and Romiplastim**
- Dengue vaccine – under trial
- Alternatively other options need to be explored
- Considerations for alternate therapies
- **Traditional medicine**

Carica papaya (CP)

- Genus *Carica* of the plant family Caricaceae
- Cosmopolitan in distribution
- Leaves of Papaw are rich in anthraquinone and alkaloids like carpaine, a glucoside named carposide, flavonols and vitamins C and E



- TJ O'Hare and DJ Williams - 'Papaya As A Medicinal Plant'

anthelmintic activity, wound healing, antifertility properties, antifungal activity, antimalarial activity, antimicrobial activity, antiviral activity (dengue fever), anticancer and chemoprotection, anti-amoebic activity, diabetes and anti-hypertension

- Literature search: consistent results
- ***NADEEM SHEIKH, NEELAM YOUNAS & TASLEEM AKHTAR** on "**Effect of *Carica papaya* leaf formulation on Haematology and Serology of normal rat"** illustrated an exact mechanism of Thrombocyte formation
- Consumption for longer period: hepatotoxicity and risk for cardiovascular disease
- Probable action of Vitamin C
- In a clinical trials, 1100 mg TID of *Carica Papaya* leaf extract tablet (Caripill) for 5 days – significant increase in platelet count

- Sathasivam et al. (2009) – mice
- Ahmad et al. (2011), Hettige S. (2008), Yunita F (2012) and Soobitha Subenthiran (2013) – clinical trials
- NADEEM SHEIKH et al. **"Effect of *Carica papaya* leaf formulation on Haematology and Serology of normal rat" -** ↑ mean platelet count, MCH, MCV
- **"Identification of Secondary Metabolites Present in Carica Papaya L. Leaf Extract Found in Northern India by HPTLC & Other Test Procedures, its Significance and Role in Curing Dengue/DHF Disease"** by Dinesh Kumar et al. - physico-chemical and phytochemical evaluation

- TLC fingerprinting profile of different extracts → Secondary metabolites → Bioactive components separated from the co extractives → Secondary metabolites
- Flavonoids like quercetin, alkaloids like piperine, glycosides, saponins, tannins, terpenoids like triterpenoids, phytosterols and phenolics
- None any single ingredient/constituent or factor found responsible

Significance

- Better & viable option in fever associated with thrombocytopenia
- Palatable and appropriately formulated
- Fewer side effects
- Decreases the cost of hospitalization
- Cost effective
- More affordable and accessible
- Averting the mortalities

- International Anti dengue day - June 15th
- Intention to meet the achievable goals

CONCLUSION

- Serious public health problem worldwide
- Validation of traditional claims
- Discrepancy regarding its safety profile
- Cost effective - positive influence on the national economy
- Need for further studies on a large scale
- Considerations for nutraceutical and its potential as pharmaceutical

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