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Integrated homeopathy approach in treating thrombocytopenia associated with dengue in a tertiary care hospital

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Abstract

Background: As per the report by the National Centre for Vector Borne Disease Control of India, Dengue cases in 2023 reached nearly 10 million in India. Randomized trials haven't identified an effective therapy for Dengue. The homeopathic medical repertory lists 16 medicines for management of Dengue. Recognized by the WHO, homeopathy has managed dengue symptoms effectively. Thus, this study aimed to assess homeopathic medicines' impact as adjunctive therapy for Dengue-related thrombocytopenia.

Methods and Materials: This study was a prospective, two arm, single centre, interventional study conducted from October 2020 to February 2022 at Homeopathy Department of a tertiary care centre in Thane, Maharashtra, India. A total of 130 patients were enrolled in the study, 65 patients in each group (Control and Intervention Group). Data parameters included monitoring of daily temperature, pulse rate, respiratory rate, daily platelet counts, CRP levels, concurrent medical conditions, and corresponding medications. Additionally, clinical features such as fever, cough, cold, body aches, headache, nausea, diarrhoea, purpura, and any instances of bleeding (rectal or vaginal) were documented. All statistical data were analysed by IBM SPSS software v.16.0 and were expressed as mean \pm SD.

Results: In the control group, mean hospitalization lasted 5.57 days, with a mean pulse rate of 82.14 beats per minute, respiratory rate of 19 breaths per minute (bpm), mean fever duration of 2.65 days, and mean platelet rise of 1.09 lacs/cumm. In contrast, the interventional group had a shorter hospitalization of 4.48 days, higher pulse rate (89.43 bpm), respiratory rate (22.50 bpm), lower fever duration (1.36 days), and mean platelet rise of (1.15 lacs/cumm). Fluid transfusion requirement was higher in the control group (9.23%) than the interventional (1.54%), however there was not statistically significant correlation observed.

Conclusion: Homeopathic approach in dengue associated thrombocytopenia has shown better clinical outcomes by reducing requirement for platelet transfusion.

Keywords: Dengue, thrombocytopenia, homeopathy, platelets, fever

Introduction

Dengue, the prevalent mosquito-borne viral illness globally, accounts for approximately 50 million infections annually. While the case fatality rate in the South-East Asian region stands at 1%, it escalates to 3-5% in Myanmar, India, and Indonesia [1]. According to the report from the National Centre for Vector Borne Disease Control of India, the total incidence of Dengue in India in 2023 was nearly 10 million cases, with Maharashtra exhibiting a notably higher prevalence [2]. The incidence of Dengue has shown a consistent rise over the past 50 years, attributed to factors such as global trade, increased travel, urban expansion, population growth, and climate fluctuations. These elements create favourable environments for the proliferation of Dengue vectors and viruses [3].

Dengue shows various blood-related symptoms, with thrombocytopenia being a prominent diagnostic marker, present in 79% to 100% of cases. This condition increases the risk of bleeding and further complications [4, 6]. According to WHO guidelines, platelet transfusion is recommended for dengue patients experiencing Haemorrhage, regardless of thrombocytopenia, and also as a preventive measure for those with a platelet count below 10,000/mm³ in the absence of active bleeding [9]. However, platelet transfusion can cause side effects which can be life-threatening, such as anaphylactic reactions, Transfusion-related acute respiratory syndrome (TrALI), post-transfusion purpura, haemolytic reactions, non-haemolytic febrile reactions, transfusion-associated circulatory overload (TACO), sepsis,

hypotensive reactions, critical infections, air embolism, hypocalcaemia, hyperkalaemia, and hypothermia [38]. The rate of platelet transfusion among dengue patients varies widely, ranging from 7% to 50%, as documented in studies conducted in Trinidad and Tobago, India, Taiwan, and Singapore [5]. Platelet transfusions are common in adults, ranging from 22% to 50% across different settings. However, about 23% of patients may not require them, indicating possible overuse or inappropriate usage [7]. A worldwide survey among physicians revealed a diversity of approaches regarding the use of platelet prophylaxis in dengue patients, highlighting significant variations in clinical practice. This states a notable gap in evidence-based guidelines in this specific area [8].

Controlling dengue is difficult due to factors like four virus serotypes causing severe illness independently, limited understanding of its pathophysiology, no specific treatments or vaccines available, and challenges in vector control. Despite decades of trials, there's no specific treatment, the management focuses on supportive care and fluid therapy [10, 11]. While the latest WHO guidelines offer detailed clinical algorithms for fluid management, maintaining proper fluid balance remains pivotal in managing severe dengue and preventing complications such as vascular leakage and shock [12]. No specific therapy has been shown to be effective in the treatment of any of the manifestations of dengue in a randomized controlled trial [15-21].

Homeopathic medicine has been recommended for therapeutic purposes in dengue since the 19th century [22]. The homeopathic medical repertory includes a list of 16 medicines specifically indicated for dengue [23]. Homeopathy, as recognized by the WHO, has been utilized effectively for the prevention and treatment of various infectious diseases, such as influenza and diarrhoea. Additionally, it has been noted to play a significant role in alleviating the symptoms of dengue fever [1]. *Eupatorium perfoliatum* is one of the most frequently indicated medicines in dengue fever. Moreover, the clinical observations from 2021 dengue fever cases documented by the teams assigned by the Council across different hospitals in Delhi indicate that *Eupatorium perfoliatum* is emerging as a key therapeutic agent [24]. Research conducted to assess the effectiveness of homeopathic treatment for dengue fever has yielded promising results, with evidence emerging from various regions worldwide. For instance, in Brazil, there was an 81.5% reduction in dengue incidence following the administration of a single dose of the homeopathic remedy *Eupatorium perfoliatum* [25]. Additionally, in 2012, a double-blind, placebo-controlled randomized trial was undertaken involving dengue patients who received the same homeopathic complex. This study aimed to assess the efficacy of the homeopathic intervention during a dengue epidemic. Results indicated that the intervention group experienced improvement in various symptoms, including headache, fever, and myalgia [22]. In Pakistan, a homeopathic complex comprising 10 medicines, including *Bryonia alba*, *Rhus Toxicodendron*, *Gelsemium sempervirens*, *Aconitum napellus*, *Eupatorium perfoliatum*, *China boliviana*, *Hamamelis*, *Citrullus colocynthis*, *Crotallus horridus*, and *Phosphorus*, was administered to 25 patients with dengue fever. The mean values of various criteria in both the homeopathic and standard treatment groups were compared. Encouragingly, better results were observed in blood values within a week of prescription

compared to those receiving standard maintenance therapy [26]. A study conducted in India, in which 138 patients received a homeopathic medicine along with standard of care and 145 patients received only standard of care, the results suggest a positive role of adjuvant homeopathy treatment in reducing thrombocytopenia due to dengue [27]. In Cuba, a group of 25,000 dengue-positive patients received treatment with a homeopathic complex consisting of medicines *Bryonia alba*, *Eupatorium perfoliatum*, *Gelsemium sempervirens*, and Dengue nosode. Remarkably, no severe symptoms were reported post-administration, and none of the patients required intensive care beyond 3 to 5 days of entering the Intensive Care Unit. Furthermore, hospital stays were notably reduced from an average of 7-10 days to 3-5 days. This evidence suggests that homeopathy may be effective not only in preventing dengue but also as an adjunct therapy, particularly in diminishing the severity of the disease and shortening hospital stays [26]. These findings underscore the need for further research in this area, focusing on selecting appropriate medicines for prevention or treatment during epidemic outbreaks.

Therefore, the current study was conducted with the primary objective of comparing and evaluating the impact of homeopathic medicines as adjunctive therapy in managing thrombocytopenia associated with dengue fever. Additionally, the secondary objectives included assessing and comparing the necessity for platelet transfusion, duration of hospitalization in both treatment groups.

Materials and Methods

This study was a prospective, two arm, single centre, interventional study conducted from October 2020 to February 2022 at Homeopathy Department of a tertiary care centre in Thane, Maharashtra, India. This study was approved by the Institutional Ethics Committee (IEC) (BMR/36/2020).

The patients of all genders between age group of 5 years to 75 years who tested positive for Dengue NS1 Antigen (Non-Structural protein) were included in the study. And the patients who were known cases of Idiopathic Thrombocytopenic Purpura (ITP) or iatrogenic thrombocytopenia were excluded from the study.

A sample size of 130, of which 65 patients were enrolled in each group. Post obtaining voluntary consent, the eligible patients were randomised using computer generated randomization in either control (standard of care-allopathy) or intervention group Homeopathy treatment and standard of care-allopathy). The homeopathy medicines prescribed in interventional group was according to the symptomatology and indications observed.

The standard of care procedure for dengue involved analysing various data parameters, including daily temperature, pulse rate, respiratory rate, daily platelet counts, CRP levels, concurrent medical conditions, and corresponding medications. Additionally, clinical features such as fever, cough, cold, body aches, headache, nausea, diarrhoea, purpura, and any instances of bleeding (rectal or vaginal) were documented.

The numeric data was summarized by descriptive statistics like; n, Mean \pm SD, median. Before applying for any statistical test, a normality test was performed. The categorical data was summarized by frequency count and percentage. All statistical data were analysed by IBM SPSS software v.16.0 and were expressed as mean \pm SD.

Results

Table 1: Demographic details

Sr. No.	Parameters	Group	Distribution	N	%
1.	Age	Intervention	Below 18 years	1	1.54%
			18 to 28 years	22	33.85%
			29 to 38 years	25	38.46%
			39 to 48 years	12	18.46%
			Above 49 years	5	7.69%
		Control	Below 18 years	19	29.23%
			18 to 28 years	11	16.92%
			29 to 38 years	17	26.15%
			39 to 48 years	6	9.23%
			Above 49 years	12	18.46%
2.	Gender	Intervention	Male	42	64.62%
			Female	23	35.38%
		Control	Male	33	50.77%
			Female	32	49.23%

Table 2: Association of symptoms of dengue in both the groups

Sr. No.	Parameters	Control (N=65)	Intervention (N=65)	P-Value
		Mean	Mean	
1	Duration of Hospitalization (Days)	5.57	4.48	0.47
2	Pulse Rate (Beats per minute)	82.14	89.43	0.54
3	Respiratory Rate (Breaths per minute)	19.7	22.50	0.61
4	Fever (no. of days)	2.65	1.36	0.34
5	Rate of increase in Platelet counts (lacs /cumm)	1.09	1.15	0.44
6	Requirement of platelet Transfusion	6	1	0.115

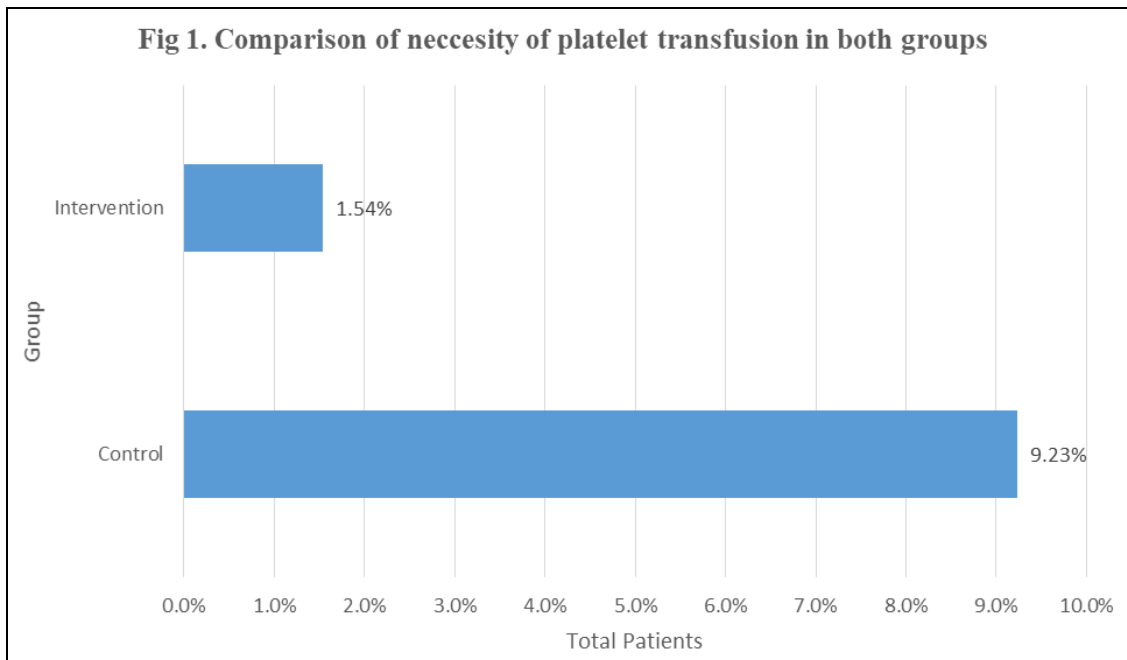


Fig 1: Comparison of necessity of platelet transfusion in both groups

In this study, 130 patients were enrolled, with 65 patients allocated to each group. The intervention group primarily comprised individuals in age group of 29 to 38 years (38.46%), closely followed by those within the age group of 18 to 28 years (33.85%), with only one participant under 18 years old. Conversely, the majority of participants in the control group were below 18 years old (29.23%), followed by participants in age group of 29 to 38 years (26.15%). The study observed a predominance of male participants in both the intervention and control groups, comprising 64.63% and 50.77%, respectively (Table 1).

In the control group, the mean number of days of hospitalization was 5.57, with a mean pulse rate of 82.14 beats per minute, a mean respiratory rate of 19 breaths per minute, an average of 2.65 days of fever, and a mean rise in platelet count of 1.09 lacs/cumm.

In contrast, the interventional group exhibited a shorter mean hospitalization duration of 4.48 days, a higher mean pulse rate of 89.43 beats per minute, an increased respiratory rate of 22.50 breaths per minute, a mean fever duration of 1.36 days, and a mean rise platelet count of 1.15 lacs (Table 2).

The requirement for fluid transfusion was notably higher in the control group, accounting for 9.23% of participants, compared to only 1.54% in the interventional group (Fig 1). However there is no statistical significant found between requirement of fluid transfusion when compared in both the groups (Table 2).

Discussion

A 2017 study on dengue outbreaks in India found that Punjab, Haryana, Rajasthan, Gujarat, and Kerala experienced the majority of outbreaks during the monsoon or post-monsoon period from September to November. Factors contributing to dengue expansion include unplanned urbanization, environmental changes, host-pathogen interactions, and population immunology. Currently, dengue management relies on symptom-based approaches, with ambiguity around antiviral therapy [26, 29, 30]. Platelet transfusions also vary widely in different disease severity stages, with associated risks such as transfusion reactions and the potential transmission of blood borne infections [28]. A review of homeopathic literature revealed numerous mentions of homeopathic remedies such as *Aconitum napellus* (Monkshood), *Belladonna* (Deadly Nightshade), *Bryonia alba* (Wild Hops), *Eupatorium perfoliatum* (Thoroughwort), *Gelsemium* (Yellow Jasmine), and *Rhus toxicodendron* (Poison Ivy) for the treatment of symptoms associated with dengue fever [31]. In the current study, patients in the intervention group were administered the following homeopathic medicines base on homeopathic literature: *Eupatorium perfoliatum*, *Cinchona officinalis*, *Gelsemium sempervirens*, *Bryonia alba*, *Arnica montana*, and *Ferrum metallicum*. For patients with severe symptoms, additional prescriptions included *Nux vomica*, *Carbo vegetabilis*, and *Carica papaya 6c*. Female patients experiencing profuse bleeding during Dengue fever and menstrual cycles were provided with *Hamamelis virginica Q* and *Millefolium Q* as supplementary treatment. The treatment provided in the present study is consistent with the treatment regimen designed to treat dengue-related thrombocytopenia as outlined in a study conducted in Delhi. This regimen includes the use of *Crotalus horridus*, *Phosphorus*, *Nux vomica*, *Pulsatilla nigricans*, and *Pyrogen* [27].

Research investigating the efficacy of homeopathic treatment for dengue fever has yielded promising results worldwide. In Brazil, a single dose of the homeopathic remedy *Eupatorium perfoliatum 30C* reduced dengue incidence by 81.5%, indicating its potential effectiveness in managing the disease [32]. Moreover, a double-blind, placebo-controlled randomized trial demonstrated improvements in various symptoms, such as headache, fever, and myalgia [22].

In an Indian study assessing the efficacy of homeopathic medicine in treating dengue fever, the intervention group experienced shorter hospitalization periods compared to the control group [34]. Randomized controlled study in Indonesia observed that platelet counts increased more rapidly and were significantly higher in the intervention group, leading to shorter hospitalization durations (3.48 ± 0.6 days vs. 5.38 ± 0.67 days, $p < 0.05$) compared to the control group with intervention of (*Carica Papaya*) CP leaf extract capsule (CPC 550 mg, two capsules three times daily) [33], results of this study are in similar lines with the current study where the mean hospitalization duration in the intervention group

(4.48 days) was shorter than that in the control group (5.57 days) (Table 2).

Adjunct homeopathy could significantly shorten the time for fever clearance, thereby reducing the need for antipyretics [35]. Similarly, the present study found a decrease in fever duration among patients in the interventional group, with an average of 1.36 days in interventional group when compared to 2.65 days in the control group; however, this difference was not statistical significance (Table 2). This observation parallels findings from a two-arm study conducted in the USA, where the mean fever duration in the intervention group was 2.57 days compared to the placebo control group, yet no statistically significant difference was observed [29].

In a series of studies across India and Pakistan, various treatments for Dengue Fever were investigated, including *Carica Papaya* (CP) leaf extract tablets and homeopathic remedies. In a randomized controlled trial conducted in India, researchers investigated the impact of CP leaf extract tablets on average platelet counts among patients diagnosed with Dengue Fever. The study found a significant increase in mean platelet counts five days after treatment initiation in the intervention group compared to the control group [36]. Additionally, a study conducted in Pakistan demonstrated that patients who received combined homeopathic treatment experienced an increase in platelet count after six days, in contrast to patients who received standard allopathic treatment [36]. A study conducted in Delhi, India, revealed that there was a statistically significant greater rise in platelet count on the first day of follow-up in the group receiving homeopathic treatment along with standard care compared to those receiving standard care alone. Furthermore, patients in the homeopathic treatment group reached a platelet count of 100,000/mm³ nearly two days earlier than those in the standard care alone group [38]. The findings of this studies align with present study, where the mean rate of platelet rise in the intervention group was 1.15 lacs/cumm in comparison to 1.09 lacs/cumm in the control group. However, despite this consistency, no statistically significant correlation was found between the intervention and control groups in the present study (Table 2).

A study conducted in Delhi revealed that among patients who received homeopathic treatment alongside standard care, 42.3% required platelet transfusion, while 57.6% of patients in the standard care group needed transfusion. However, no statistically significant differences were observed between the two groups [38]. A 2016 study conducted in India revealed that platelets were transfused in 28% of patients in the intervention group and 46% in the control group ($p < 0.01$). The period of hospitalization was longer in the control group ($p < 0.01$) [37]. The current study's findings align with those of the previous study. In the present study, 9.23% of patients in the control group required platelet transfusion, whereas only 1.54% of patients in the intervention group required it (Figure 1). However, no statistical significance was observed between the groups (Table 2).

The study has few limitations for consideration. Firstly, the sample size was relatively small, potentially constraining the generalizability of the findings. Despite randomization, there existed an imbalance in age distribution among the study cohorts, notably with a higher prevalence of individuals below 18 years old in the control group compared to just 1 participant below 18 years in the interventional group. Additionally, it's essential to

acknowledge that as part of the hospital's standard care protocol for increasing the platelet counts, patients in the control group received a medication containing carica papaya, this can be a potential source of bias that could impact the interpretation of the results.

Conclusion

Evidence supports the effectiveness of homeopathic treatment in dengue patients, resulting in notable improvements in thrombocytopenia and a reduced need for platelet transfusions, thereby minimizing adverse transfusion effects. This suggests a promising future for integrating homeopathic management into the standard care for dengue infections. Moreover, there is an opportunity for conducting more comprehensive studies with larger sample sizes to validate the additional benefits that homeopathy offers in dengue treatment. Given the potential complications associated with transfusions, homeopathy presents a safe and effective avenue for naturally enhancing blood counts and reducing the need for transfusions. Further focused investigations in this area are warranted to fully harness the potential of homeopathic medications.

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Conflict of Interest:

Not available

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Not available

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