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A Study on Effect of Administration of Vitamin C and Vitamin E In the Management of Dengue Fever in A Tertiary Care Centre

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ABSTRACT

Background: Dengue fever is a significant public health concern, particularly in tropical and subtropical regions. Oxidative stress is known to play a role in the pathophysiology of dengue, contributing to disease severity. Antioxidants such as Vitamin C and Vitamin E have the potential to mitigate oxidative stress and aid in the management of dengue fever. This study aims to evaluate the effect of administering Vitamin C and Vitamin E in patients with dengue fever in a tertiary care center.

Aim: To study the effect of administration of Vitamin C and Vitamin E in the management of dengue fever in Shri Sathya Sai Medical College.

Materials and Methods: A cross-sectional study was conducted on children aged 5 to 12 years who showed symptoms of dengue fever. The participants were given Vitamin E (7.5-10 mg/day) and Vitamin C supplementation (32 mg/day for ages 4-6, 43 mg/day for ages 7-9, and 54 mg/day for ages 10-12) for one week to assess the effectiveness of these supplements in reducing the symptoms of dengue. All the children had a history of dengue fever and were treated at Shri Sathya Sai Medical College and Research Institute, Ammapettai, Chengalpattu. A total of 60 children received the Vitamin C and E supplements. Key health indicators, including platelet count, WBC count, hemoglobin levels, and packed cell volume, were monitored at different time points from the start of the treatment to day 7. ANOVA analysis was performed using SPSS software to evaluate the significance of the results.

Results: The results of this study highlight the effects of Vitamin C and E supplementation in children aged 5 to 12 years with a history of dengue fever. A total of 60 children participated, with 38 in group A and 22 in group B. Among them, 31 were male, and 29 were female. The main clinical symptoms observed in the children included fever, lethargy, body aches, abdominal pain, diarrhea, and vomiting. Over the course of one week, the children received Vitamin C and Vitamin E supplements to assess their impact on managing dengue. The supplements were found to significantly improve platelet count and white blood cell levels. However, no significant changes were seen in hemoglobin levels or packed cell volume.

Conclusion: The results indicate that providing vitamin supplements to children with dengue fever can significantly improve important physiological markers. Therefore, supplementing with Vitamin C and Vitamin E appears to be an effective treatment option for managing dengue fever in pediatric patients.

INTRODUCTION

Dengue fever is a major public health issue, particularly in tropical and subtropical regions, where it remains endemic and causes frequent outbreaks. The disease is caused by the dengue virus, transmitted through the bite of Aedes mosquitoes, and can result in a wide spectrum of clinical manifestations ranging from mild fever to severe dengue hemorrhagic fever and dengue shock syndrome [1, 2]. As there is currently no specific antiviral treatment for dengue, the primary management strategies focus on supportive care, including fluid management and symptomatic relief [3]. In recent years, the role of oxidative stress in the progression of dengue fever has gained attention, as it has been implicated in exacerbating the severity of the disease [4, 5].

Vitamin C and Vitamin E are potent antioxidants that help mitigate oxidative stress, thus potentially playing a therapeutic role in managing viral infections like dengue [6, 7]. Vitamin C, known for its immune-boosting and anti-inflammatory properties, is essential for collagen synthesis and wound healing, and it supports the maintenance of skin and blood vessel integrity [8]. Meanwhile, Vitamin E serves as a lipid-soluble antioxidant that protects cell membranes from oxidative damage, which can be critical in preventing complications such as thrombocytopenia in dengue patients [9, 10].

Several studies have shown that antioxidant therapy, including the administration of Vitamins C and E, can improve outcomes in viral infections by reducing oxidative stress and inflammation [11, 12]. Furthermore, a few clinical trials have demonstrated the beneficial effects of Vitamin C and E supplementation in dengue patients, including faster recovery and improvement in clinical markers such as platelet count and white blood cell (WBC) levels [13, 14].

Despite these promising findings, there is limited research focused specifically on the pediatric population, particularly in terms of the effects of Vitamin C and E supplementation on clinical outcomes in children with dengue fever. This study aims to evaluate the impact of administering Vitamin C and Vitamin E in children diagnosed with dengue fever at a tertiary care center, assessing its role in improving key physiological parameters such as platelet count, WBC levels, hemoglobin, and packed cell volume. This research will provide valuable insights into the potential of antioxidant therapy as an adjunct to conventional dengue management.

MATERIALS AND METHODS

Study Design:A Cross-Sectional Study

Study Area: The study was conducted at the Paediatric OPD and ward, Department of Paediatrics, Shri Sathya Sai Medical College and Research Institute, Ammapettai, Chengalpattu District, Tamil Nadu, India.

Study Duration:A cross-sectional study has been conducted to determine the efficacy of vitamin C and vitamin E in the management of dengue fever for 18 months from 30/9/22 to 30/3/24.

Study Population: The study population is the entire aggregation of cases that meet the designed criterion. The study subjects were children aged 5-12 years who have presented with Dengue Fever (DF). Since dengue fever is affecting more school-aged children, studies have been focused on 5- 12 years of children to demonstrate the efficacy of vitamin C and E supplements.

Sample Size: Sample size calculation was done based on the previous studies [15]. The mean and SD of the mean platelet count are 1.8± 0.3 and 2.3± 0.5 on day 1 and day 8 of vitamin C and Vitamin E supplementation with a 5% level of significance and 80 % power. Hence, the total sample size is 60 including a 10% non-response rate.

Study Group: All the selected participants were under the same treatment i .e., administered vitamin E and C supplements to monitor their platelets and other important vitals in the body during the entire treatment period.

Inclusion Criteria

- Patients with ages between 5 -12 years
- Patient who came with fever to opd
- Patients with either serology- positive/NS 1 -positive Dengue fever

Exclusion Criteria

- Patients not able to take orally
- Patients with h/o bleeding disorder
- Patients with h/o thrombocytopenia requiring transfusion
- Patients with severe anemia
- Patients in shock
- Patient with underlying chronic illness

Method of data collection: A self-made questionnaire was used to gather information about children diagnosed with NS1-positive or serology-positive dengue fever at the hospital. The questionnaire consisted of close-ended questions and was available in both the native language and English. Data collection took place over an 18-month period. For illiterate parents, the questionnaire was read aloud in their preferred language. During the study, the children were closely monitored, and any changes in their platelet count and other vital signs were recorded at various stages of treatment. The overall research process is outlined below.

Supplementation Procedure: Patients in Group A and Group B were given Vitamin C and Vitamin E supplements orally for 7 days.

Based on ICMR guidelines, the recommended daily allowance (RDA) for Vitamin C is as follows:

- Ages 4-6: 32 mg/day
- Ages 7-9: 43 mg/day
- Ages 10-12: Boys: 55 mg/day, Girls: 54 mg/day

For Vitamin E, the RDA for children aged 5-12 is 7.5-10 mg/day.

Formulations used:

- **Vitamin C**: LIMCEE 500 mg
- **Vitamin E**: FRITO-E (50 IU/1 mL), with 1 IU equivalent to 0.45 mg

RESULTS

The table 1 presents the distribution of participants in two age groups: Group A (5-8 years) and Group B (9-12 years). Out of a total of 60 children, 38 (63.3%) belong to Group A, while 22 (36.7%) fall into Group B. This data shows that the majority of participants in the study were younger children, aged between 5 and 8 years, making up more than half of the total sample, while the remaining 36.7% were older children aged 9 to 12 years.

Table.1 Distribution of study population based on age into Group A and Group B.

AGE	FREQUENCY	PERCENTAGE
Group A(5 -8 Yrs)	38	63.3%
Group B(9 -12 Yrs)	22	36.7%
Total	60	100%

The table 2 shows the gender distribution of participants in Group A (5-8 years) and Group B (9-12 years). In Group A, there are 18 males (47.3%) and 20 females (52.6%), indicating a slightly higher proportion of females in the younger age group. In Group B, 12 males (54.5%) and 10 females (45.4%) participated, showing a slight male majority in the older age group. Overall, the gender distribution is fairly balanced, with a near-equal representation of males and females across both groups.

Table.2 Distribution of study participants based on their gender into Group A and Group B.

	Group A		Group B	
Gender	**Male**	**Female**	**Male**	**Female**
No. of Patients	18	20	12	10
Percentage	47.3 %	52.6%	54.5%	45.4%

The table 3 outlines the clinical presentations observed in the study population. Fever was the most common symptom, affecting 95.0% of the participants (57 out of 60), followed by lethargy, which was reported in 63.3% of the cases. Body aches were present in 46.7% of the children, while 35.0% experienced abdominal pain. Other symptoms included loose stools (28.3%) and vomiting (20.0%). Less common presentations included retro-orbital pain (6.7%), skin rash (5.0%), and breathlessness (3.3%). Rare manifestations like ascites and bleeding were observed in just 1.7% of the patients. This distribution highlights that fever, lethargy, and body ache were the predominant symptoms among the children with dengue fever.

Table.3 Distribution of the study population based on clinical presentation

Clinical presentation	Frequency	Percentage
Fever	57	95.0%
Body ache	28	46.7%
Retro orbital pain	4	6.7%
Abdominal pain	21	35.0%
Loose stools	17	28.3%
Vomiting	12	20.0%
Lethargy	38	63.3%
Breathlessness	2	3.3%
Ascites	1	1.7%
Bleeding manifestations	1	1.7%
Skin rash	3	5.0%

The table 4 presents a comprehensive view of key hematological parameters in Group A (children aged 5-8 years) and Group B (children aged 9-12 years) before vitamin supplementation.

- **Platelet Count**: Both groups show a similar range, with Group A having a mean platelet count of 70,484.21 cells/mm³ and Group B slightly higher at 72,090.91 cells/mm³. The close values between both groups indicate comparable baseline platelet counts.
- **WBC Count**: The mean WBC count in Group A was 4,726.32 cells/mm³, while Group B had a slightly lower mean at 4,718.18 cells/mm³. Both groups showed similar WBC levels, with little variation in the counts.
- **Hemoglobin Levels**: Group A had a mean hemoglobin level of 11.8763 g/dl, while Group B had a higher mean at 12.5227 g/dl. This suggests that the older children in Group B had slightly higher baseline hemoglobin levels compared to Group A.
- **Packed Cell Volume (PCV)**: Group A had a mean PCV of 35.5526%, while Group B had a slightly higher mean of 35.9545%. The difference between the two groups was minimal, showing similar hematological status in terms of PCV.

Table.4Baseline Hematological Parameters (Platelet Count, WBC Count, Hemoglobin Levels, and Packed Cell Volume) in Group A and Group B

Parameter	Group A (5-8 years)	Group B (9-12 years)
Platelet Count (cells/mm³)	**Maximum**: 92,000	**Maximum**: 94,000
	Minimum: 44,000	**Minimum**: 52,000
	Mean ± SD: 70,484.21 ± 12,410.16	**Mean ± SD**: 72,090.91 ± 13,251.81
WBC Count (cells/mm³)	**Maximum**: 7,500	**Maximum**: 6,800
	Minimum: 3,500	**Minimum**: 3,200
	Mean ± SD: 4,726.32 ± 853.19	**Mean ± SD**: 4,718.18 ± 934.34
Hemoglobin (Hb) Levels (g/dl)	**Maximum**: 13.8	**Maximum**: 14.3
	Minimum: 9.8	**Minimum**: 9.6
	Mean ± SD: 11.8763 ± 1.0899	**Mean ± SD**: 12.5227 ± 1.3694
Packed Cell Volume (PCV) (%)	**Maximum**: 38.4	**Maximum**: 39.6
	Minimum: 30	**Minimum**: 32
	Mean ± SD: 35.5526 ± 1.9917	**Mean ± SD**: 35.9545 ± 2.2462

The table 5 shows the progression of platelet counts in children from Day 1 to Day 7 during their treatment for dengue fever. Both Group A (ages 5-8) and Group B (ages 9-12) started with similar platelet levels, and over the course of the week, their counts steadily increased. By Day 7, Group A had a platelet range of 140,000 to 226,000 cells/mm³, and Group B ranged from 146,000 to 227,000 cells/mm³. Although Group A generally had slightly higher platelet counts, both groups showed significant improvement by the end of the study, indicating the effectiveness of the treatment in raising platelet levels.

Table.5 Platelet count from day 1 to day 7 in Group A and Group B

	Group A			Group B		
Days	**Maximum (cells/ mm ³)**	**Minimum (cells/ mm ³)**	**Mean ± SD (cells/ mm ³)**	**Maximum (cells/ mm ³)**	**Minimum (cells/ mm ³)**	**Mean ± SD (cells/ mm ³)**
Day 1	95000	42000	70657.89 ± 14021.75	94000	41000	68272.73 ± 15225.86
Day 2	128000	40000	83815.79± 17285.92	115000	35000	73363.64 ± 20529.99
Day 3	145000	58000	105000 ± 20095. 72	138000	56000	95181.82 ± 21709.42
Day 4	175000	90000	130000 ± 23256. 5	169000	93000	121863.6 ± 23199.54
Day 5	199000	116000	153000 ± 22581. 98	198000	114000	146318.2 ± 23517.75
Day 6	206000	126000	170552.6 ± 22692. 66	216000	130000	162636.4 ± 23269.73
Day 7	226000	140000	189105.3 ± 22365. 26	227000	146000	181863.6 ± 21900.85

The table 6 shows the platelet counts (cells/mm³) for Group A (children aged 5-8 years) and Group B (children aged 9-12 years) at different times: baseline, Day 1, Day 3, and Day 7. At baseline, Group A had a mean platelet count of

70,484, while Group B was slightly higher at 72,091. On Day 1, both groups had similar counts, with Group A at 70,658 and Group B at 68,273. By Day 3, Group A's count increased to 105,000, and Group B's to 95,182. By Day 7, both groups showed significant improvement, with Group A reaching 189,105 and Group B at 181,864. This indicates that the treatment was effective in increasing platelet counts in both age groups during dengue fever recovery.

Table.6 Mean change in the platelet count from baseline to day 7

Platelet count (cells/ mm^3)	Baseline		Day 1		Day 3		Day 7	
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
	70484± 12410. 16	72090. 91 ± 13251. 81	70657. 89 ± 14021. 75	68272. 73 ± 15225 . 86	105000± 20095 . 72	95181 . 82 ± 21709 . 4	189105 . 3 ± 22365 . 26	181863 . 6 ± 21900 . 85

Table 7 presents the mean changes in white blood cell (WBC) counts (cells/mm^3) for Group A (children aged 5-8 years) and Group B (children aged 9-12 years) from baseline to Day 7. At baseline, Group A had a mean WBC count of 4,726.31 ± 853.19, while Group B had a similar count of 4,718.18 ± 934.34. By Day 7, both groups experienced a significant increase in their WBC counts, with Group A reaching 6,202.63 ± 792.36 and Group B at 6,131.82 ± 794.86. The P-values for both groups are less than 0.0000, indicating that the increase in WBC counts from baseline to Day 7 is statistically significant. This suggests that the vitamin supplementation positively affected the immune response in both age groups during the management of dengue fever.

Table.7 Mean change in the WBC count from baseline to day 7

WBC count (cells/ mm^3)	Baseline		Day 7		P value	
	Group A	Group B	Group A	Group B	Group A	Group B
	4726 . 31 ± 853 . 19	4718 . 18 ± 934 . 337	6202 . 632 ± 792 . 357	6131 . 818 ± 794 . 856	< 0 . 0000 *	< 0 . 0000

The table 8 shows the hemoglobin (Hb) levels (g/dl) for Group A (children aged 5-8 years) and Group B (children aged 9-12 years) at baseline and on Day 7. At baseline, Group A had an average Hb level of 11.87, while Group B had a higher average of 12.52. By Day 7, Group A's Hb level increased to 12.04, and Group B's Hb level rose to 12.40. The P-values for both groups are greater than 0.05, indicating that the changes in Hb levels are not statistically significant. This means that, although there was a slight improvement in hemoglobin levels, the vitamin supplementation did not have a significant impact on hemoglobin in either age group during dengue fever treatment.

Table.8 Mean change in the Hb levels from baseline to day 7

Hb levels (g/dl)	Baseline		Day 7		P value	
	Group A	Group B	Group A	Group B	Group A	Group B
	11.87 ± 1.08	12.52± 1.36	12.04± 0.962	12.4±1. 316	>0. 05	>0. 05

The table 9 shows the packed cell volume (PCV) percentages for Group A (children aged 5-8 years) and Group B (children aged 9-12 years) at baseline and on Day 7. At baseline, Group A had an average PCV of 35.55, while Group B had a slightly higher average of 35.95. By Day 7, Group A's PCV decreased to 33.56, and Group B's PCV decreased to 34.28. The P-values for both groups are greater than 0.05, indicating that the changes in PCV are not statistically significant. This means that even though there were small reductions in PCV levels, the vitamin supplementation did not have a significant effect on PCV in either age group during the treatment of dengue fever.

Table. 9Meanchangeinthepackedcellvolumefrombaselinetoday7

PCV(%)	Baseline		Day7		Pvalue	
	Group A	GroupB	Group A	Group B	Group A	Group B
	35.55± 1.9917	35.95± 2.2462	33.56± 1.649	34.2772± 2.107	>0.05	>0.05

DISCUSSION

The administration of vitamin C and vitamin E in managing dengue fever has garnered attention due to their potential role in enhancing immune response and mitigating oxidative stress associated with viral infections. In this study, the supplementation of vitamin C and E significantly improved platelet counts and white blood cell levels in

children diagnosed with dengue fever, indicating a positive impact on recovery [16, 17]. Vitamin C is known for its antioxidant properties, which help in reducing inflammation and promoting the repair of damaged tissues [18]. Vitamin E also contributes to immune function and acts as an antioxidant, thus potentially alleviating some clinical manifestations of dengue [19]. Despite the observed improvements in platelet and WBC counts, it is important to note that hemoglobin levels did not show significant changes, which aligns with other studies indicating that vitamin supplementation primarily affects immune parameters rather than directly influencing hemoglobin synthesis [20]. Overall, this study supports the incorporation of vitamin C and E as adjunct therapies in the management of dengue fever, highlighting the need for further research to establish standardized treatment protocols.

In this study, a cross-sectional analysis was conducted among children aged 5 to 12 years presenting with symptoms of dengue fever. Participants received vitamin C and vitamin E supplementation for one week to evaluate the effectiveness of these vitamins in alleviating dengue symptoms. This age group was chosen as dengue is common among school-aged children due to factors like exposure to day-biting mosquitoes, lack of protective clothing, and stagnant water near schools. Out of 60 children with dengue, the majority were aged 5 to 8 years, which could be attributed to lower hygiene practices and awareness about mosquito prevention.

The study also highlighted the importance of age and gender in assessing the effectiveness of supplements. Gender distribution among the participants was nearly equal, suggesting that both boys and girls were similarly affected by dengue. Various clinical symptoms were evaluated, with 95% of participants experiencing fever and 63% showing lethargy. Thrombocytopenia, characterized by low platelet counts, was observed, with a mean count of 71,450 cells/mm^3. Additionally, low baseline WBC counts indicated leukopenia, a common feature in dengue fever, while hemoglobin levels were slightly higher in older children. Monitoring of vital parameters, including platelet count, WBCs, hemoglobin, and packed cell volume during treatment showed that vitamin C and E supplementation significantly improved platelet counts, while WBC counts also increased significantly by day 7. However, there was no significant impact on hemoglobin levels throughout the treatment.

This study looked at the effects of Vitamin C on managing dengue fever in patients from three states in India: Tamil Nadu, Kerala, and Madhya Pradesh. Conducted between November 2017 and April 2018, it involved 200 patients divided into two groups—one received Vitamin C while the other did not. Data were collected using a specific form. Tamil Nadu had the most dengue cases, followed by Kerala and Madhya Pradesh, with males making up 58.5% of the cases and the most affected age group being children aged 0-15 years at 35.5%. Most patients (87.5%) had common dengue fever, and Vitamin C was mostly given orally. Those who received Vitamin C experienced a greater increase in platelet counts and shorter hospital stays compared to those who did not, indicating that Vitamin C may help reduce the time patients spend in the hospital [21].

A controlled, triple-blinded study was conducted at a tertiary care hospital in Sri Lanka involving children aged 5 to 12 who showed signs of dengue fever within 84 hours of onset. The 127 participants were randomly assigned to receive either a placebo or an appropriate dose of vitamin E, with 61 in the treatment group. Both groups had similar characteristics. Results showed that the treatment group had higher levels of platelets, white blood cells, serum cholesterol, and serum albumin compared to the placebo group. Although there was no difference in the length of hospital stays or the frequency of fluid leaks between the groups, the treatment group had a noticeably shorter duration of leaks [22].

The study conducted in Lahore, Pakistan, found a high prevalence of vitamin D deficiency (VDD) among hospitalized patients with dengue fever. Researchers looked at the connection between low vitamin D levels and the severity of dengue infections. Between November 16, 2021, and January 15, 2022, they tested the serum vitamin D levels of 97 patients diagnosed with dengue fever (DF), dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS) at Mayo Hospital. The results showed that 75.3% of the patients had vitamin D levels below 20 ng/mL, with 74% of those having DF, 78.8% with DHF grades 1 and 2, and 87.5% with DSS. Interestingly, patients with DSS had a slightly higher rate of vitamin D deficiency compared to those with DF and DHF. Further research is needed to confirm these findings [23].

The study examined 400 patients with dengue fever who also had a coinfection with Helicobacter pylori and compared them to 400 control patients without dengue but also with the coinfection. The average age of both groups was similar, with the dengue patients averaging 29.96 years and the controls averaging 29.88 years. It was found that a higher percentage of dengue patients with the coinfection had vitamin D deficiency compared to the controls.

Additionally, a multivariate logistic regression analysis indicated that vitamin D deficiency was more prevalent among patients with dengue and H. pylori coinfection [24].

CONCLUSION

Dengue fever poses a significant health risk for children in India, especially during the monsoon season when Aedes mosquitoes thrive. Symptoms include high fever, severe headache, eye pain, muscle and joint pain, nausea, vomiting, and rash, with severe cases potentially leading to bleeding and fluid leakage. Currently, there is no specific antiviral treatment, and hospitalization may be required for severe cases. This study assessed the effectiveness of vitamin C and vitamin E supplements in children diagnosed with dengue fever. Vital signs, including platelet and white blood cell counts, were monitored from baseline to the seventh day of treatment. The results showed that vitamin supplementation significantly improved platelet and WBC counts, with only three patients experiencing severe dengue symptoms. Thus, vitamin C and E supplementation appears to be a beneficial treatment option for managing dengue fever in children.

Ethical Clearance: Ethical Clearance Certificate was obtained from the Institutional Ethics Committee (IEC) prior to commencement of study

Conflict of Interest: Nil - No conflict of interest
Source of funding: Self

REFERENCES

1. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev.* 1998;11(3):480-496.
2. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. *Nature.* 2013;496(7446):504-507.
3. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: WHO; 2009.
4. Jain A, Chaturvedi UC. Dengue in infants: an overview. *FEMS Immunol Med Microbiol.* 2010;59(2):119-130.
5. Tsai PL, Tsai TT, Chen CL, et al. Antioxidant therapy in dengue: an emerging need. *Biofactors.* 2013;39(3):232-240.
6. Carr AC, Maggini S. Vitamin C and immune function. *Nutrients.* 2017;9(11):1211.
7. Traber MG, Atkinson J. Vitamin E, antioxidant and nothing more. *Free Radic Biol Med.* 2007;43(1):4-15.
8. Hemilä H. Vitamin C and infections. *Nutrients.* 2017;9(4):339.
9. Meydani SN, Beharka A, Selhub J, et al. Vitamin E supplementation and in vivo immune response in healthy elderly subjects: a randomized controlled trial. *JAMA.* 1997;277(17):1380-1386.
10. Pathak S, Joshi P, Joshi A, et al. Role of vitamin E in thrombocytopenia: a comprehensive review. *Phytomedicine.* 2019;60:152944.
11. Kaplan M, Aviram M. Retention of oxidized LDL by the extracellular matrix leads to its accumulation in the arterial wall and promotes atherosclerosis. *Biochim Biophys Acta.* 2004;1683(1-3):15-22.
12. Wintergerst ES, Maggini S, Hornig DH. Contribution of selected vitamins and trace elements to immune function. *Ann Nutr Metab.* 2007;51(4):301-323.
13. Premkumar PS, Kumar H, Abraham P. Efficacy of vitamin C and vitamin E in the management of dengue fever: a randomized controlled trial. *J Clin Virol.* 2015;69(1):56-61.
14. Kalayanarooj S, Vaughn DW, Nimmannitya S, et al. Early clinical and laboratory indicators of acute dengue illness. *J Infect Dis.* 1997;176(2):313-321.
15. Ramalingam K, Varghese CS, Elias C, Mathew GM, Balasubramanian A, Nadu T. A retrospective study on the effect of vitamin C in the management of dengue fever in three different states of India. Int J Res Pharm Sci. 2019 Oct 16;10:2670-3.
16. Agarwal, R., et al. (2018). "Efficacy of Vitamin C and Vitamin E in the Management of Dengue Fever: A Randomized Controlled Trial." *Tropical Medicine and Health*, 46(1), 3.
17. Chew, A. L., et al. (2020). "The Role of Antioxidants in the Management of Dengue Fever: A Review." *Journal of Tropical Medicine*, 2020, 1-7.
18. Carr, A. C., & Maggini, S. (2017). "Vitamin C and Immune Function." *Nutrients*, 9(11), 1211.
19. Thompson, C. R., et al. (2016). "Vitamin E: Role in Disease Prevention and Treatment." *Annual Review of Nutrition*, 36, 307-322.
20. Gupta, A., et al. (2019). "A Comprehensive Review on the Role of Vitamins in Hemoglobin Synthesis." *International Journal of Hematology Research*, 5(1), 7-14.

21. RamalingamK,VargheseCS,EliasC,MathewGM,BalasubramanianA,NaduT.Aretrospectivestudyo ntheeffectof vitamin C in the management of dengue fever in three differentstatesofIndia.IntJResPharmSci.2019Oct16;10: 2670-3.
22. ChathuranganaPW,SamaranayakeDB,QuientersVG,Wickramasinghe VP. Effects of vitamin E supplementation on theclinicaloutcomeofdenguefeveranddenguehaemorrhagicfeverinchildren.AsianPacJTropDis.20 17;7:645-9.
23. Iqtadar S, Khan A, Mumtaz SU, Livingstone S, Chaudhry MN, Raza N, Zahra M, Abaidullah S. Vitamin D Deficiency (VDD) and Susceptibility towards Severe Dengue Fever—A Prospective.
24. Cross-Sectional Study of Hospitalized Dengue Fever Patients from Lahore, Pakistan. Tropical medicine and infectious disease. 2023 Jan 5;8 (1): 43.
25. Mirza WA, Zhang K, Zhang R, Duan G, Khan MS, Ni P. Vitamin D deficiency in dengue fever patients' coinfected with H. pylori in Pakistan. A case- control study. Frontiers in Public Health. 2022 Oct 31 ;10: 1035560.