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Review

Assessment of the importance of platelet transfusion in patients with severe dengue: a systematic review

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ABSTRACT

Introduction: Dengue is one of the most important vector-borne viral diseases in subtropical and tropical regions. The World Health Organization (WHO) 2009 classified dengue into three groups: dengue without alarm signs, dengue with alarm signs, and severe dengue. According to the type of dengue, various managements have been proposed. The authors suggest that a predictive factor to avoid a poor prognosis in this disease is to keep platelet levels stable in the patient to prevent a fatal outcome. The aim of this paper is to analyze the efficacy of transfusion of platelet agents in the outcome of patients with severe dengue and thrombocytopenia.
Material and methods: A bibliographic search was carried out in the Medline, OVID, and Scielo databases from January 1, 2008, to April 31, 2023, using the MeSH terms.
Results: 7 articles were included in the systematic review. A wide range in age was found (18 to 79 years). A minimal number of studies detail the comorbidities of patients in their enrollment. Regarding platelet transfusion, the average number of platelet units used in the transfusion case was 5 (2 - 14). Transfusions of ABO identical and compatible pooled platelets transfusion were found to be more successful in increasing platelets. Almost all of the patients included in the studies had platelets <20,000 at enrollment. One study found a significant increase in platelets after transfusion, while the rest did not find it compelling. No mortality associated with platelet transfusion was recorded.
Conclusions: Prophylactic platelet transfusion is not recommended as a routine measure in patients with severe dengue and thrombocytopenia. The uncertainty highlights need to reach a specific consensus establishing the appropriate indications for platelet transfusion and what type of patients with dengue virus would be beneficial.

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Evaluación de la importancia de la transfusión de plaquetas en pacientes con dengue grave: una revisión sistemática

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RESUMEN

Introducción: El dengue es una de las enfermedades virales transmitidas por vectores más importantes en las regiones tropicales y subtropicales. La Organización Mundial de la Salud (OMS) en 2009 clasificó el dengue en tres grupos: dengue sin signos de alarma, dengue con signos de alarma y dengue grave. Según el tipo de dengue se han propuesto diversos manejos. Los autores sugieren que un factor predictivo para evitar un mal pronóstico en esta enfermedad es mantener estables los niveles de plaquetas en el paciente para evitar un desenlace fatal. El objetivo de este trabajo es analizar la eficacia de la transfusión de plaquetas en la evolución de pacientes con dengue grave y trombocitopenia.
Material y métodos: Se realizó una búsqueda bibliográfica en las bases de datos Medline, OVID y Scielo desde el 1 de enero de 2008 al 31 de abril de 2023, utilizando los términos MeSH.
Resultados: Se incluyeron 7 artículos en la revisión sistemática. Se encontró un amplio rango de edad (18 a 79 años). Un número mínimo de estudios detallan las comorbilidades de los pacientes en su inscripción. En cuanto a la transfusión de plaquetas, el promedio de unidades de plaquetas utilizadas en el caso de transfusión fue de 5 (2 - 14). Se encontró que las transfusiones de plaquetas combinadas ABO idénticas y compatibles tuvieron más éxito en el aumento de plaquetas. Casi todos los pacientes incluidos en los estudios tenían plaquetas <20 000 en el momento del reclutamiento. Un estudio encontró un aumento significativo de plaquetas después de la transfusión, mientras que el resto no lo encontró convincente. No se registró mortalidad asociada con la transfusión de plaquetas.
Conclusiones: La transfusión profiláctica de plaquetas no se recomienda como medida de rutina en pacientes con dengue grave y trombocitopenia. La incertidumbre pone de relieve la necesidad de llegar a un consenso específico que establezca las indicaciones adecuadas para la transfusión de plaquetas y qué tipo de pacientes con el virus del dengue serían beneficiosas.

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1. INTRODUCTION

Dengue is one of the viral diseases caused by one of the most important vectors in subtropical and tropical regions, affecting more than 390 million people annually [1]. During the last decades, the incidence of dengue has increased drastically, mainly due to the latest dengue outbreaks in geographically endemic areas and population growth towards tropical regions [2].

Dengue viruses, abbreviated as DENV, are of four types: DENV-1, DENV-2, DENV-3 and DENV-4. DENV belongs to the *Flaviviridae* family, and it has been described that the four types of DENV can circulate together and cause the same clinical picture. The dengue virus (DENV) transmission follows a human-mosquito cycle whose principal actor is the mosquito of the genus *Aedes spp* (*Aedes aegypti or Aedes albopictus*). When a female *Aedes* mosquito infected with DENV attacks a human, it introduces DENV to the person, and the cycle within the human begins. After this scenario comes the incubation period, which usually lasts between 3 to 10 days, after which the human being, now infected, begins to develop the disease [1, 3].

The World Health Organization (WHO) 1997 proposed a classification for this disease and divided it into three categories: dengue, dengue hemorrhagic fever, and dengue shock syndrome. Each of them had specific classification criteria that are currently no longer used. For the year 2009, the WHO decided to change the classification to the following categories: dengue without warning signs, dengue with warning signs, and severe dengue [1]. This last classification is currently used in the clinical and epidemiological fields for management and diagnosis. During the disease, two essential laboratory markers are proposed when evaluating dengue's evolution: hemoglobin and platelets. The total platelet count, in conjunction with hematocrit/hemoglobin, is widely used to monitor the progress of the disease [1, 4].

During DENV infection, three clinical phases can be differentiated: a febrile phase, a critical phase, and a recovery phase. The first phase is the febrile phase, lasting approximately 3 to 7 days. Two-thirds of patients develop a high fever ≥38.5 °C, headache associated with pain behind the eyes, and arthralgia. Nausea, vomiting, myalgia, and macular or maculopapular rash may also be seen and usually occur all over the body. This rash appears in approximately half of the cases. Other manifestations may include respiratory symptoms such as cough, rhinorrhea, and sore throat and gastrointestinal symptoms such as anorexia, diarrhea, and abdominal pain [1, 3, 5]. Hemorrhagic manifestations can occur in this phase, and the following phases and their clinical presentation are varied, for example, hematemesis, epistaxis, etc. It should be noted that hemorrhages are not associated with the presence of thrombocytopenia, but the presence of the latter increases the risk of developing them. This phase is where we can characteristically see the positive tourniquet test [1, 3, 5, 6]. Among the laboratory findings, we find a decrease in white blood cells and platelets (≤ 100,000/mm3); liver enzymes, especially AST, are usually elevated up to 5 times their normal value [1, 3]. Pay close attention to early signs of capillary leak, which can lead to severe dengue complications due to reduced intravascular volume and hypoxemia of the body's organs. At the laboratory level, an increase in hematocrit (by at least 20% from the initial value) and a significant reduction in the total platelet count are observed, indicating the presence of a capillary leak. Therefore, it is essential to monitor these indicators carefully to detect and address capillary leaks early on. [1, 3, 4, 7, 8].
The next phase is the critical phase, which lasts between 24 to 48 hours and does not usually occur in all cases of DENV infection; it commonly occurs when the fever begins to disappear, ending the febrile phase. In this phase, vascular leakage develops throughout the body, developing hemorrhages, shock, and multiple organ failure. Finding moderate or severe thrombocytopenia in this critical stage of the disease is prevalent [7, 8].
The last phase is the recovery phase, where the capillary leak and hemorrhages resolve, and everything returns to normal. Sometimes, a rash may appear for a few days but then disappear. This phase lasts between two to four days. Patients, upon recovery, may present a certain degree of fatigue for a few weeks until they fully recover; this does not mean they still have the disease [1, 3, 8].

Currently, the cornerstone of the therapeutic management of this disease is the rapid and effective restoration of circulating plasma volume through judicious administration of fluids since there are no definitive antiviral medications for the dengue virus. There is an area of uncertainty regarding the sensitivity and specificity of the criteria used for hospitalization and the optimal choice and timing of initiation of intravenous fluids. The recommended initial selection in the therapy of dengue shock syndrome is crystalloids, with the main options being normal saline solution (0.9%) and Ringer's lactate. What is sought with the correct administration of fluids is to improve central and peripheral circulation (reducing tachycardia, improving mean arterial pressure), restore perfusion in the organs, maintain a urinary flow greater than 0.5 ml/kg/h, and lower metabolic acidosis [1, 7].
During the management of severe dengue, a constant dilemma that baffles healthcare personnel is whether platelet transfusion should be performed in dengue patients with or without thrombocytopenia [9, 10]. This shows the importance of a specific consensus that delimits the indications for platelet transfusion in patients affected of dengue according to their classification: dengue without warning signs, with warning signs, and severe dengue [11-13]. The present research project is a systematic review whose main objective is to gather current evidence on the effectiveness of platelet transfusion (prophylactic or treatment) in patients who present thrombocytopenia in severe dengue and how it affects their outcome in the disease.

2. MATERIAL AND METHODS

We conducted this study which aims to gather current evidence on the effectiveness of platelet transfusion (prophylactic or treatment) in patients with thrombocytopenia and severe dengue and how it affects their outcome in the disease. We searched three electronic databases, Medline, OVID, and Scielo, from January 1, 2008, to April 31, 2023, using the MeSH terms. The search was limited to articles in English and Spanish. Titles and abstracts were examined to determine the relevance of the authors' information.
Two reviewers (JCFNA and AICR) independently screened the abstracts and selected the articles to assess the full-text articles (Table 1). Eligible studies were finalized by consensus among all authors. The results of this systematic review are reported following the recommendations established by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The PRISMA

diagram was made for data selection, as shown in Figure 1. No protocol was registered for this systematic review.

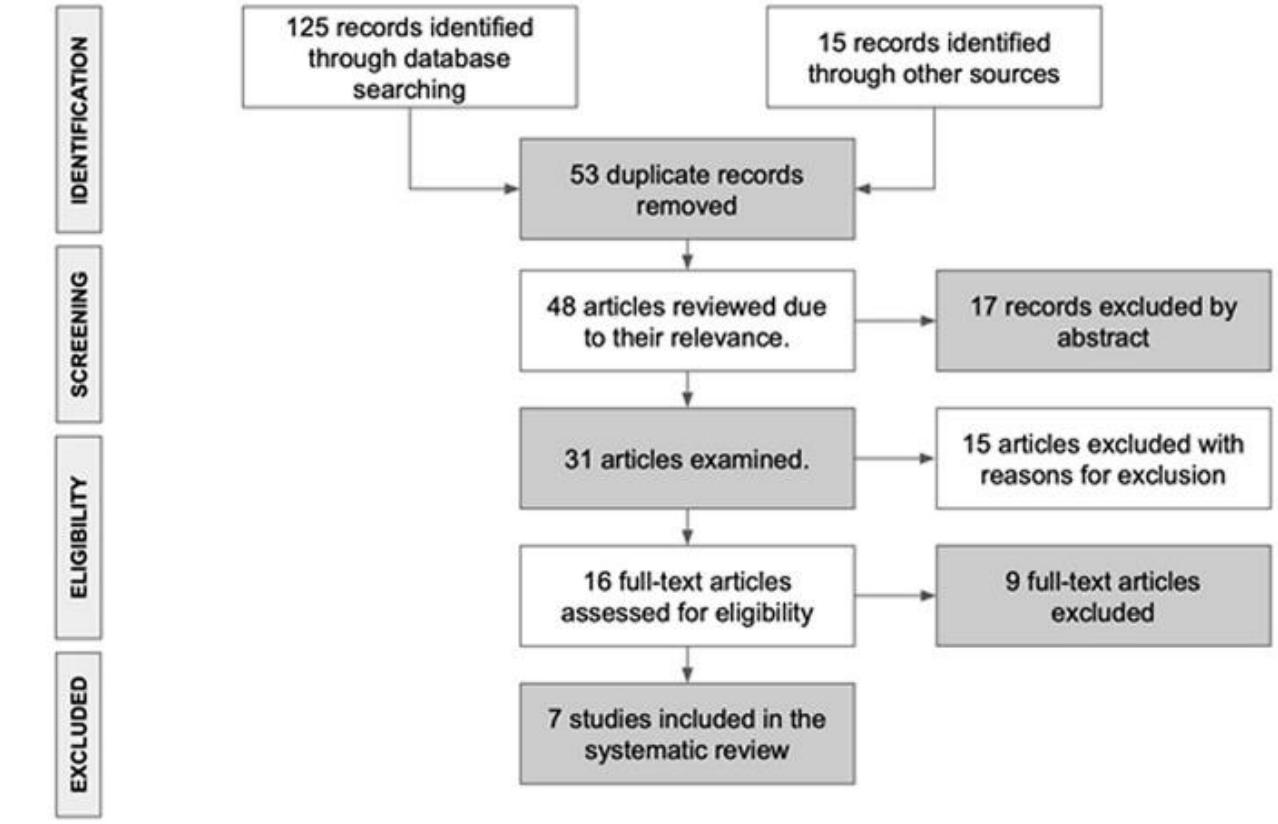

***Figure 1**: PRISMA diagram for data selection.*

3. RESULTS

1,564 patients were enrolled in the different studies and were also diagnosed with dengue. Most chosen studies specify the number of men and women enrolled. One study does not have data regarding the gender used, and it is estimated that of all the people in the studies reviewed, 715 were female, and 849 were male [14-20]. The age group of the enrolled people is not precisely specified; however, the age range of the target population is broad, ranging from 18 to 78 years old. Additionally, only two studies (David C. Lye, et al. (2009) and David C. Lye, Archuleta et al. (2017)) describe the most relevant sociodemographic characteristics (gender, age in years, and comorbidities) and clinical manifestations (fever, headache, myalgia, arthralgia, retroocular pain, nausea, vomiting, diarrhea, rash) (Table 2) [18, 20].

The population studied is divided into two groups: those patients who have received platelet transfusion and those who only received supportive treatment (restoration of plasma volume with crystalloids). Among the comorbidities found, essential hypertension, diabetes mellitus, and hyperlipidemia stand out. Fifty-two transfused patients had high blood pressure, while 40 non-transfused patients had high blood pressure. Twenty-nine patients who received platelet transfusion had diabetes, compared to 22 in the non-transfused group. Twenty-eight patients in each group had hyperlipidemia [18, 20]. It is worth mentioning that neither of the two selected studies included patients with ischemic disease (Table 3).

Of the studies reviewed, one proposes platelet transfusion as a treatment, while the rest propose it as prophylaxis to reduce complications such as bleeding and/or hemorrhages in patients with severe thrombocytopenia. Khan Assir, et al. (2013) used one (01) single donor unit of ABO identical plateletpheresis as prophylaxis. The platelet increase in their study was statistically significant; however, almost half of the patients did not respond to platelet transfusion. Likewise, it did not prevent the development of severe bleeding or shorten the time to cessation of bleeding in those who had it, and it was associated with significant side effects [16]. Prashantha, et al. (2014), in the group that received prophylactic platelet transfusion, the median number of platelet units transfused was five (05) with a range of two (02) to fourteen (14) units [14].

Table 1: Studies investigated platelet transfusion in patients with dengue

Study	Design	Intervention		Results				Conclusions	Assessment of study quality	E/G
		n	P/T	Platelets increase	Length of stay		Mortality			
					PT	NPT				
Bhat A, et al. (2016) [17]	Retrospective	203	P	In the group of patients who responded, the platelet count at 24 hours after the transfusion minus the initial platelet count was 25,000 (IQR 15,000 - 35,000), and 0 (IQR -9,000 - 3,000) platelets in those who did not respond.	NR	NR	**NR**	Identical and ABO-compatible platelet transfusions can prevent multiple transfusions to mitigate the risks of bleeding. It is cost-effective and avoids unnecessary transfusions.	Moderate	3/D
Lye DC, et al. (2009) [18]	Retrospective	256	P	The median platelet count increase at 24 hours in the arm that received the transfusion (7,103/mL) was lower than the median in the group that did not receive it (11,103/mL; OR: 1.00, 95% CI: 0.98 - 1.01; p = 0.26).	6 days	5 days	ICU: 7 patients Deceased: 1	There are no significant benefits of prophylactic transfusion among adult patients with dengue. This approach will save blood products and reduce patients' unnecessary exposure to transfusion risks.	Moderate	3/D
Lye DC, Archuleta S, et al. (2017) [20]	Randomized clinical trial	372	P	NR	NR	NR	13 adverse events (4 unrelated).	In adult patients with dengue and thrombocytopenia, prophylactic platelet transfusion was not superior to supportive therapy in preventing bleeding and could be associated with adverse events.	High	1+/B
Archuleta S, et al. (2020) [19]	Randomized clinical trial	372	P	The median time it took their patients to achieve a platelet count > 50,000/mL was similar between the two arms of their study.	Patients with a poor response to transfusion have a longer hospital stay.		No mortality was reported.	"Several independent predictors of poor platelet recovery have been identified in patients with dengue (advanced age, lower white blood cell count, and earlier clinical presentation). More research is needed to examine the pathophysiology and the role of thrombocytopenia and the risk of clinical bleeding in severe dengue."	High	1+/B
Prashantha B, et al. (2014) [14]	Retrospective	202	P	The platelet count in the group that received prophylactic platelets recovered to above 50,000/mL in 4.43 days, compared to 2.57 days in those who did not receive them (p < 0.0001).	5.13 days	3.68 days	17.4% of patients with TP experienced a sudden drop in white blood cell count	Prophylactic platelet transfusion in clinically stable patients with dengue was associated with a significant delay in platelet recovery and an increase in the duration of hospitalization, but it was not detrimental in terms of morbidity or mortality.	Moderate	3/D
Khan Assir MZ, et al. (2013) [16]	Randomized clinical trial	87	P	In the group of patients who received the transfusion, the mean was 34,780/mL ± 43,820 and a median of 22,000/mL (IQR 12,000 – 45,750), whereas in the group that did not 72receive it, the mean was 4,280/mL ± 10,360 and a median of 3,000/mL (IQR -2,000 – 9,000). The result was statistically significant (p < 0.001).	NR	NR	Three patients with adverse reactions and two deaths.	Platelet transfusion did not prevent the development of severe bleeding nor shorten bleeding duration and was associated with significant side effects. Therefore, platelet transfusion should not be performed in the management of dengue fever.	High	1-/C
Sundar V, et al. (2019) [15]	Retrospective	72	T	Platelet transfusion from random donors based on weight resulted in an average increase of 10,210 platelets/mL at 24 hours post-transfusion (p = 0.031); whereas those who received platelets from a single donor, platelets increased by a value of 22,874/mL (p < 0.001).	NR	NR	No mortality was reported.	Platelet transfusion, despite producing a 50-100% increase in platelet count, does not have a significant impact on clinical bleeding.	Moderate	3/D

PT: Platelet Transfusion,; NPT: No Platelet Transfusion,; P: Prophylaxis; T: Treatment,; NR: Not Reported; E: Evidence; G: Grade of recommendation.

Table 2: Clinical manifestations of the patients [18, 20]		
Clinical Manifestations	**Transfusion group**	**Control group**
Fever	233	203
Headache	135	122
Myalgia/arthralgia	141	120
Retroocular pain	29	16
Nausea	137	111
Vomiting	98	76
Rash	109	91

In their cohort, David C. Lye, et al. (2009) concluded that there were no significant benefits of prophylactic platelet transfusion in adult patients with dengue [18]. This same author, in 2017, in a clinical trial that compared prophylactic platelet transfusion and supportive management versus supportive management alone, found that in adult patients with dengue and thrombocytopenia, prophylactic platelet transfusion was not superior to supportive management to prevent bleeding and could be associated with adverse events. In the transfusion group, four (04) units of pooled platelets were used whenever platelets were below 20,000/mL, and supportive measures were bed rest, intravenous fluid therapy, and symptomatic medications for fever and pain [20].

Table 3: Comorbidities of the patients [18, 20]		
Comorbidities	**Transfusion group**	**Control group**
Diabetes Mellitus	29	22
Essential Hypertension	52	40
Hyperlipidaemia	18	28
Coronary artery disease	0	0

Several studies were carried out to analyze platelet transfusion's effect quantitatively. They measured the outcome by counting the number of platelets in the first 24 hours after the transfusion. Several studies in adult patients with dengue have shown that prophylactic transfusion did not significantly benefit thrombocytopenia or prevent complications such as bleeding. David C. Lye, et al. (2009) carried out a cohort in Singapore, where they recruited 256 patients with dengue without bleeding and with platelets < 20,000/ml, of whom 188 received prophylactic platelet transfusion. The median platelet count for patients who received and did not receive transfusion was 15 103/mL (OR: 1.02, 95% CI: 0.94 – 1.09; p = 0.87). The median increase in platelets in the arm that received the transfusion (7 103/ml) was lower than the median in the group that did not receive the transfusion (11 103/ml; OR: 1.00, 95% CI: 0.98 – 1.01; p = 0.26). The median time to platelet count > 50,000/ml was similar for transfused and non-transfused patients (3 days; OR: 1.05, 95% CI: 0.79 – 1.39; p = 0.59) [18]. The same author also conducted a randomized, open-label clinical trial in Singapore and Malaysia, where one arm of his study received prophylactic transfusion and supportive management. In contrast, the control group only received supportive management in patients with dengue and thrombocytopenia (<20,000/ml). He found that of 182 patients, 25% of those who received a prophylactic transfusion required a second transfusion on day 1.46 to maintain a count above 20,000/ml, and the rest achieved that goal only with the first transfusion [20]. Archuleta S., et al. (2020) describe that the median time it took their patients to achieve a platelet count > 50,000/mL was similar between the two arms of their study [19].

Varun Sundar (2019) describes that 74 dengue patients were analyzed through thromboelastography. Weight-based transfusion of platelets from random donors resulted in a mean increase of 10,210 platelets/ml at 24 hours post-transfusion (p = 0.031). Those receiving platelets from a single donor increased by 22,874/ml (p < 0.001). The initial number of platelets in the first group was 22,820±12,218/ml, while the second group was 16,760±7,220/ml. No significant improvement in clot strength on thromboelastography was observed in either group [15]. Another study was conducted by Prashantha, et al. (2014) in a group of patients with dengue without signs of hemodynamic instability (n = 202). The platelet count in the group that received prophylactic platelets recovered its value above 50,000/ml in 4.43 days versus 2.57 days in those who did not receive it (p < 0.0001) [14].

Khan Assir, et al. (2013) conducted a study in Pakistan in patients with dengue and thrombocytopenia < 30,000/ml (n = 87; of whom 43 received platelet transfusion). The median number of platelets at baseline in the group receiving prophylactic transfusion was 10,000/ml (IQR 8,000 – 15,000), while in those not receiving transfusion, it was 10,500/ml (IQR 9,000 – 17,700). In addition, the platelet increase was measured by subtracting the number of platelets at 24 hours minus the initial value, resulting in a 34,780/ml±43,820 and a median of 22,000/ml in the group of patients who received the transfusion. (IQR 12,000 – 45,750), while in the group that did not receive, the mean was 4,280/ml±10,360 and a median of 3,000/ml (IQR -2,000 – 9,000), the result was statistically significant (p < 0.001) [16]. Bhat Amoolya, et al. (2016) compared the type of platelets used in transfusion in patients with dengue and its impact. The platelet value initially in responders and non-responders to transfusion was 15,000 (IQR 12,000 – 20,000) and 16,000 (10,500 – 20,000), respectively. In the group of responding patients, the subtraction of the platelet count at 24 hours after transfusion minus the baseline platelet count

was 25,000 (IQR 15,000 – 35,000) and 0 (IQR – 9,000 – 3,000) platelets in those who did not respond [17].

Regarding mortality, all the studies conclude that there is no statistically significant difference between people who received platelets (as prophylaxis or treatment), and those who did not. In their cohort, David C. Lye, et al. (2009) detail that seven patients were admitted to the ICU, and one died; these eight patients had developed severe dengue. In the cohort, 1 (0.5%) patient of 188 developed massive bleeding (upper gastrointestinal bleeding from a pre-existing ulcer leading to death) in the group receiving prophylactic transfusion compared with 2 (2.9%) of 68 patients who did not receive ($p = 0.17$), in the last cases it was minor hemorrhage [18]. In 2017, David C. Lye conducted a randomized clinical trial where he recorded thirteen adverse events (of which four were concluded to be unrelated) in the transfusion group versus two events in the control group (both were considered unrelated to the study intervention) (AR 5.81%, 95% CI: –4.42 – 16.01; RR 6.26, 95% CI: 1.43 – 27.34; p=0.0064). Of the nine related adverse events, there were three cases of urticaria, one of maculopapular rash, one of pruritus, and one case of chest pain, while the others were one for anaphylaxis, one for TRALI (transfusion-related acute lung injury), and one for fluid overload. One of three patients with severe adverse events permanently discontinued platelet transfusion, but all patients fully recovered, and no deaths were reported [20].

In the study conducted by Varun Sundar, et al. (2019), no mortality was reported in their patients. They recorded two episodes of upper gastrointestinal bleeding after platelet transfusion, controlled without problems [15]. Khan Assir, et al. (2013) reported three patients (7%) with adverse reactions (anaphylactic reaction and hypotension) related to the transfusion and two deaths in the transfusion group. One death resulted from TRALI, while the other was excluded from the study because it occurred in the context of an older adult with cirrhosis and ruptured esophageal varicose veins. None of the patients who did not manifest bleeding at the beginning of the study presented de novo bleeding throughout the evaluation period [16]. Prashantha, et al. (2014) found no mortality in either of the two study arms. However, 17.4% of individuals who received transfusions experienced a notable decrease in leukocytes, indicating a mild immunological response to the transfusion. Nevertheless, this reaction did not significantly impact the patient's prognosis. There was no incidence of complications associated with the transfusion [14].

Archuleta S., et al. (2020) describe that the proportion of severe dengue cases in the two study groups was similar. He showed that patients who developed severe dengue from the beginning were less likely to have a poor response in the recovery of their platelet count if they received a prophylactic transfusion (OR 0.13, CI 95%: 0.02 – 0.97). In addition, it was also observed a poor recovery in their platelets if they did not receive the transfusion (OR 3.19, CI 95%: 0.35 – 29.16). Admission to the intensive care unit, development of any bleeding and severe bleeding did not vary significantly between patients who did or did not elevate their posttransfusion platelets. Patients with a poor response in platelet recovery were more likely to have bleeding if they received a prophylactic transfusion (OR 2.34, 95% CI: 1.18 – 4.63) and less likely if they did not receive the transfusion (OR 0.55, 95% CI: 0.28 – 1.12). He did not evaluate mortality in his study [19].

4. DISCUSSION

The use of platelet transfusion in managing severe dengue is a dilemma due to the associated risks. The articles reviewed measured the result by calculating platelet increase in the first 24 hours after transfusion. Some suggest the use of transfusion as part of the treatment, while others propose prophylactic transfusion to reduce complications in patients with severe thrombocytopenia and avoid fatal outcomes. The control group received supportive measures such as bed rest, fluid therapy, and medication [14-18, 25, 26].

Some records have shown that platelet levels increase significantly 24 hours after transfusion [16]. A study by Khan Assir et al. (2013) provides details on this, while Bhat Amoolya et al. (2016) found that ABO identical and compatible combined platelet transfusions are more successful in increasing platelet count compared to non-ABO compatible combinations [17]. However, B. Prashanta et al. (2014) found that non-transfused patients had faster platelet recovery and shorter hospitalization times [20].

Regarding mortality, all the studies reviewed conclude that there is no significant difference in mortality rates between patients who received platelet transfusion and those who did not, and no de novo bleeding was observed in participants without bleeding symptoms at the beginning of the study. However, severe transfusion reactions such as TRALI and anaphylactic shock were reported, as well as deaths in both study groups, which were not related to platelet transfusion [16, 20, 24]. Adverse events were observed in patients who received platelet transfusion in different studies, but there was no statistical difference in disease prognosis or outcome. This controversy emphasizes the need for a consensus on platelet transfusion indications in dengue patients according to WHO's proposed classification [1].

During the last decades, the incidence of dengue virus has increased dramatically in subtropical and tropical areas due to recent outbreaks in geographically endemic regions of the disease [2, 8, 12]. In 2023, Peru, an endemic country, suffered an outbreak of dengue with 98,760 cases (293 cases of severe dengue, 8,749 cases of dengue with warning signs, and 8,749 cases without warning signs) and 121 deaths. The most affected regions were Lima and Piura [1, 12, 13].

Thrombocytopenia is a condition that arises during DENV infection [1]. It is caused by temporary bone marrow suppression and increased destruction of platelets in the peripheral blood. DENV infection also causes accelerated platelet consumption due to the development of disseminated intravascular coagulation, platelet destruction due to increased apoptosis, platelet lysis through the complement system, and the intervention of antibodies [21-23]. Thrombocytopenia has multiple causes, including alteration of megakaryopoiesis through infection of hematopoietic cells and damage to the progenitor of platelet cell growth. Platelet count stability is critical to avoiding a poor prognosis for this disease. The mechanism for the abrupt drop in platelets is debated, with some suggesting it is associated with endothelial dysfunction due to the activation of monocytes and T cells. Complications of the virus may involve the heart, liver, kidneys, pleura, and lymphohistiocytosis. Supportive management, including oxygenation, hydration, and monitoring consciousness, is recommended. Various antiviral compounds are being investigated to combat the virus directly [1, 3, 7, 8, 21-24].

The decision to transfuse platelets in dengue cases follows clinical criteria according to the treating physician but does not follow an evidence-based guideline [27, 28]. Although there is still no protocol for managing and transfusion platelet agents, vaccination has been recognized as an essential pillar, in addition to vector control (repellents, mosquito nets, wastewater treatment), in the global approach to reducing the burden of dengue. However, developing a safe and effective vaccine against this disease has been challenging for over 75 years [10, 11, 27, 28].

The study has limitations in relying on secondary information from existing articles. The number of cases available for analysis is limited because the disease is concentrated in specific geographic regions, and only a tiny percentage of patients develop severe dengue and/or thrombocytopenia.

In conclusion, platelet transfusion does not improve disease prognosis in DENV-infected patients and is associated with increased adverse events. Routine prophylactic platelet transfusion is not recommended for patients with severe dengue and thrombocytopenia. However, there needs to be more consensus on the appropriate indications for platelet transfusion in patients with dengue virus, especially in endemic countries such as Peru, due to limited research on the potential benefits of this treatment. Vaccination against dengue is crucial to reduce the economic impact and morbidity caused by the disease.

5. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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