



The Impact of Complementary Cupping Therapy on Immunity Changes (Interleukin-10) in Coastal Fishermen with Hypertension

Indriono Hadi^{1*}, Lilin Rosyanti¹, Ahmad¹, Alfi Syahar Yakub²

¹Department of Nursing, Poltekkes Kemenkes Kendari, Southeast Sulawesi, Indonesia

²Department of Nursing, Poltekkes Kemenkes Makassar, South Sulawesi, Indonesia

*Corresponding author: indrionohadi@gmail.com

ARTICLE INFO

Article History:

Received: 2024-10-11

Published: 2025-03-30

Keywords:

Complementary medicine;
Cupping Therapy;
Hypertension; Interleukin-10; Fishermen
Communities.

ABSTRACT

This study investigated the impact of complementary cupping therapy on immunity changes, specifically interleukin-10 (IL-10) levels, in coastal fishermen with hypertension. Forty participants, aged 20-50 years, were randomly allocated to either a cupping therapy intervention group or a placebo group. Blood pressure, pulse rate, and IL-10 levels were measured before and two weeks after the intervention. The cupping therapy procedure followed a six-step protocol, including informed consent, equipment preparation, point selection, scarification, and post-treatment care. Data were analyzed using paired and independent t-tests. The results showed a significant increase in IL-10 levels ($P=0.049$) and a significant decrease in systolic and diastolic blood pressure ($P<0.05$) in the hypertension group receiving cupping therapy. In contrast, no significant changes were observed in the normotensive group. The findings suggest that wet cupping therapy may enhance the immune system by increasing IL-10 levels and lowering blood pressure in hypertensive coastal fishermen. The underlying mechanisms may involve local inflammation, activation of the complement system, increased nitric oxide production, and stimulation of the autonomic nervous system. However, the limited sample size and potential methodological limitations warrant further high-quality trials to confirm these results. The study concludes that wet cupping therapy could serve as a viable complementary treatment for hypertension in fishing communities, but a comprehensive approach considering cultural, religious, and psychological perspectives is necessary to understand its full impact on individuals and society.



©2025 by the authors. Submitted for possible open-access publication under the terms and conditions of the Creative Commons Attribution (CC BY SA) license (<https://creativecommons.org/licenses/by-sa/4.0/>)

INTRODUCTION

Complementary medicine (CM) is a global healthcare method that is widely integrated into modern medical systems and is frequently used to treat a wide range of diseases and maintain health.¹ More than 70% of the population in developing countries uses complementary medicine systems. In rural areas, cultural beliefs and practices remain oriented towards self-care, conventional medicine, and consultation with traditional healers.² Traditional practices are based on a holistic approach to humans in their wider environment, serving as the fundamental framework of public health that encompasses aspects of religion, customs, and culture.³ The use of alternative therapies in the form of herbal preparations, complementary therapies, Quranic spiritual therapy and non-medical physical therapies is common.^{4, 5}

Among the primary sectors of the economy, the health of island communities is a priority due to the challenging working environment, which is fraught with dangers. Fishermen in maritime and coastal regions of Indonesia face various health issues that are significant health concerns.⁶ Environmental factors such as climate change, habitat alteration, air and water pollution, and the geographic isolation of coastal regions lead to significant health problems. Additionally, social factors like high poverty rates, unstable incomes, and limited access to healthcare and education are associated with detrimental health behaviors.^{7, 8} Fishermen are a group of people who require significant attention due to their stressful and hazardous work, presenting challenging physical conditions. They often experience separation and displacement from unhealthy and ideal personal habits. With a diverse lifestyle, they are susceptible to various diseases and have a high risk of chronic stress and its impact on health.⁹ Fishermen frequently rely on traditional therapy for treatment. Therefore, there is a need for attention to complementary and alternative medicine.¹⁰

In this study, the complementary therapy used was wet cupping therapy. Several studies have demonstrated the effectiveness of wet cupping therapy in improving health.¹¹ The specific mechanism of cupping therapy in providing its therapeutic effects involves the Taibah concept, which explains that this therapy operates similarly to the kidney filtration system. The kidneys filter hydrophobic materials through the glomeruli at normal pressure, while wet cupping filters both hydrophilic and hydrophobic materials through high-pressure filtration.¹²⁻¹⁴ Complementary medicine aims to enhance public health by preventing and treating diseases, providing treatment options to the community, and increasing the role of nurses in delivering healthcare.¹ The working process of cupping therapy involves cleansing through filtration and excretion of the skin, where humans have superficial tissue in the form of dermal fenestrated capillaries that help filter and cleanse blood adjusted to the pressure and size of the pores after being given external suction pressure. Physiologically, wet cupping therapy uses filtration and excretion principles for the blood cleansing process. The method works similarly to renal glomerular filtration.^{15, 16}

Cupping employs physiological principles to increase the efficiency of blood cleansing through filtration influenced by pressure, followed by the excretion process. This is more effective than chemical methods of blood cleansing, such as concentration-dependent dialysis. All of this is based on the taibah theory for the scientific basis of cupping therapy.^{15, 16} Cupping increases natural immunity and suppresses pathological immunity by reducing serum levels of autoantibodies, inflammatory mediators, and serum ferritin (which plays a role in autoimmunity). Additionally, cupping significantly reduces pain, reduces joint swelling, and treats diseases without side effects.¹⁷

Interleukin-10 (IL-10) is a pluripotent immunoregulatory cytokine that is very important for maintaining immune homeostasis and limiting autoimmunity with broad immunosuppressive activity in both innate and adaptive immunity. IL-10 enhances the differentiation, survival, and function of regulatory T cells but can directly inhibit the effector functions of Th1, Th2, and Th17 cells.¹⁸ IL-10 is an anti-inflammatory cytokine that is very important in controlling inflammatory responses and keeping the immune system in check after activation. IL-10 also functions to prevent excessive inflammation during infection and has been implicated in various autoimmune conditions.¹⁹ The novelty of this study lies in that until now there has been no research on cupping therapy's effects on changes in interleukin-10 levels.

METHODS

In accordance with the Declaration of Helsinki guidelines, ethical approval has been obtained from the Research Ethics Committee of Poltekkes Kemenkes Kendari (approval number LB.02.01; Ethics 030/2022), and each subject provided written consent. The research team discussed with the village head and the head of the Lalonggasumeeto village health center to prepare cupping therapy and collect respondent data according to the research criteria. The research team provided education on cupping therapy to the community and then recruited respondents. Those willing to participate in the study could register. The study was conducted

from May to August 2022 at the Lalongasomeeto District Health Center building. For two weeks, the Poltekkes Kemenkes Kendari research team collaborated with a certified professional cupping team from PBI (Indonesian Cupping Association).

Sample size and Randomization sampling methods

The participants in this study were male and female, aged between 20 and 50 years. The sampling method used randomization. Out of the 90 registered respondents, 50 were included in the hypertension group and 40 in the normotensive group, based on a randomization list generated. Random sampling was applied to both groups with a 1:1 allocation using a random block list created in Excel 2022. The results of the random sampling indicated 27 people from the hypertension group and 23 people from the normotensive group. After applying the inclusion and exclusion criteria, 40 respondents were collected: 20 for the group receiving cupping therapy intervention and 20 for the group receiving a placebo (vitamins). The use of placebo vitamins as a control in this study is very important to ensure that the research results obtained are accurate and not influenced by other factors.

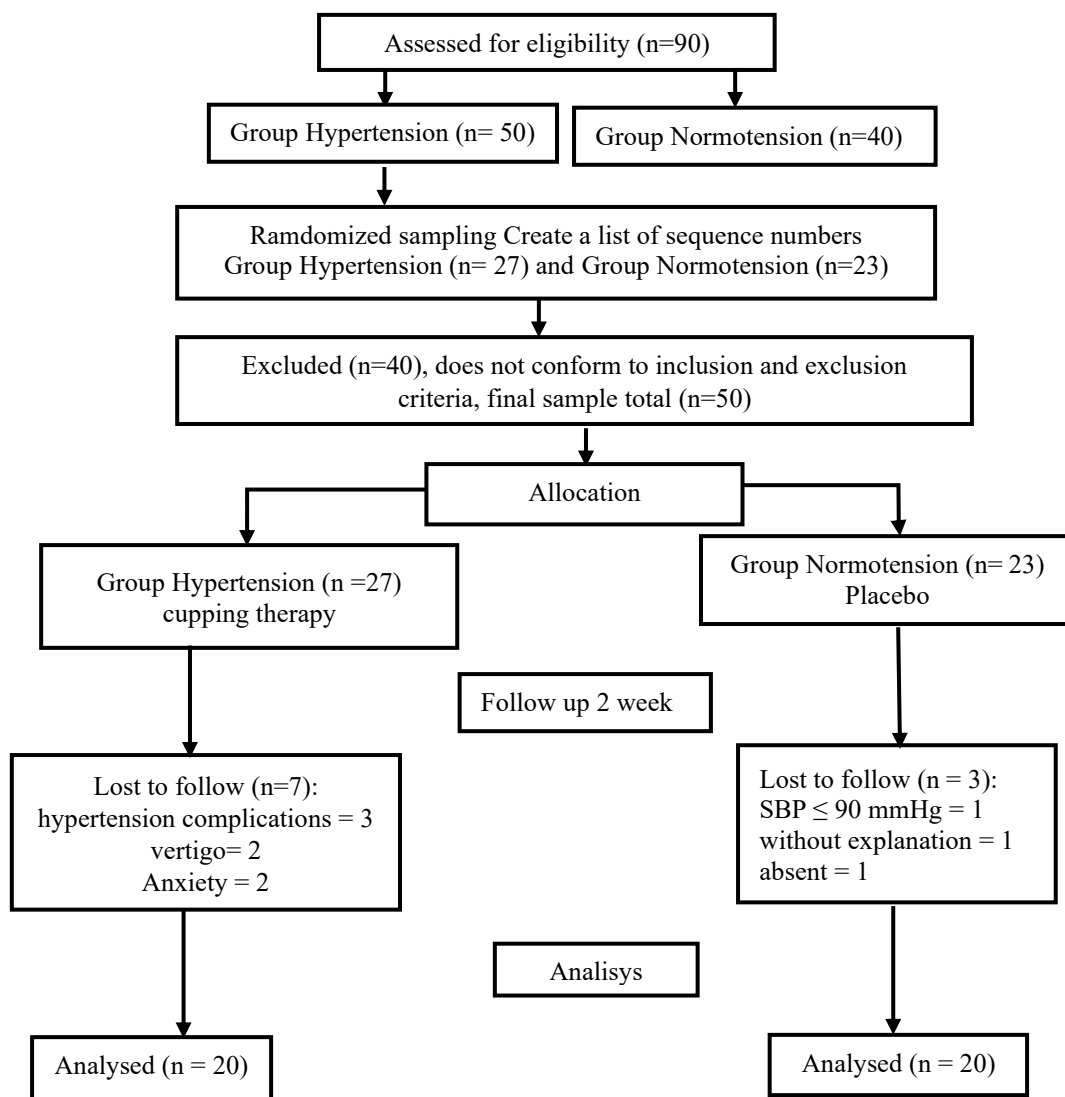


Figure 1. Research Flow Diagram

Clinical evaluation

Using a standard Omron HEM-7124 digital tensiometer, the respondents' blood pressure and pulse were measured twice: one week before and two week after cupping therapy. Measurements were taken while the respondents were sitting, after resting for 10 minutes. Blood sampling for IL-10 ELISA examination was conducted before and two week after cupping therapy. The ELISA kit employs the Sandwich-ELISA principle. The microplate is coated with specific antibodies for Human IL-10. Samples are added to the wells of the microplate and mixed with the specific antibodies. Subsequently, a biotinylated detection antibody specific to Human IL-10 and Avidin Horseradish Peroxidase (HRP) conjugate are added sequentially to each well and incubated. A substrate solution is then added. Only the wells containing Human IL-10, the biotinylated detection antibody, and the Avidin-HRP conjugate will develop a blue color. The enzyme-substrate reaction is halted by adding a stop solution, resulting in a color change to yellow. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 ± 2 nm. The OD value is proportional to the concentration of Human IL-10, allowing for the calculation of Human IL-10 concentration in the sample by comparing the sample OD with a standard curve. The measurements were conducted at the Microbiology Laboratory of Hasanuddin University, Makassar.

Cupping therapy procedure

The cupping session consisted of six steps. First, the respondent filled out an informed consent form, conducted interviews, and performed a health check on blood pressure, pulse rate, and blood sampling for IL-10. Wet cupping typically lasts approximately 30-40 minutes, adhering to aseptic technique requirements. The second step involves preparing sterilized cupping equipment, ensuring environmental cleanliness, and using personal protective equipment (PPE). Third, the therapist designated a specific point for cupping and disinfected the area using alcohol-betadine and olive oil. Next, the first cup was applied at the selected point, and the therapist created suction using two suctions for 3-5 minutes. Fourth, scarification (small shallow incisions) was performed using a 15-gauge sterile scalpel, making 10 incisions per cup location, each incision being 2-3 mm long and 0.1 mm deep to open the skin barrier and reach the fenestrated capillaries. Scarification was carried out by a professional therapist from the research team, and the cup was placed back on the skin for 30 seconds to 1 minute. External pressure suction cups help filter small molecules through fenestrated skin capillaries. Finally, the cupped skin was cleaned and disinfected.²⁰⁻²²

Data Processing and Analysis

IBM SPSS version 22 was employed to process and analyze the data. An independent t-test was utilized to determine whether the two groups had the same or significantly different mean values. In contrast, a paired t-test was used to compare the differences between the intervention groups before and after cupping therapy. The confidence interval level was set at 95% for $\alpha = 0.05$.

RESULT

This section presents the demographic characteristics of the study participants, divided into two groups: Group A (Cupping Therapy) and Group B (Placebo). The characteristics assessed include age, education level, occupation, and ethnicity. Table 1 summarizes the frequency, percentage, and mean \pm standard deviation (SD) for each variable across both groups.

Table 1. Means and Standard Deviations of the Characteristics of Fishermen Respondents

Variables	Group A (Cupping Therapy)			Group B (Placebo)		
	n	%	Mean \pm SD	n	%	Mean \pm SD
Age						
20-30 years	3	7.3	1.95 \pm .944	7	17.1	1.85 \pm .745
31-40 years	8	19.5		4	9.8	
41-50 years	9	22.0		9	22.0	

Variables	Group A (Cupping Therapy)			Group B (Placebo)		
	n	%	Mean \pm SD	n	%	Mean \pm SD
Education						
High School	7	17.1	1.85 \pm .745	3	7.3	1.50 \pm .760
Diploma	9	22.0		4	9.8	
Bachelor	4	9.8		13	31.7	
Occupation						
Fisherman	10	24.4	1.70 \pm .801	4	15.4	1.55 \pm .825
Housewife	6	14.6		10	38.5	
PNS (Public Servant)	4	9.8		7	26.9	
Ethnicity						
Tolaki	13	31.7	1.50 \pm .760	10	24.4	1.70 \pm .801
Bugis	4	9.8		6	14.6	
Java	3	7.3		4	9.8	

In Table 1, there is no significant difference among all groups in terms of age, education, occupation, and ethnicity.

Table 2. Statistical Test Values of Interleukin 10 ELISA in the Cupping Therapy Intervention Group

Group	Variable	(Mean \pm SD)		Std. error mean	P-Value
		Before	After		
(Cupping Therapy)	IL-10	5466 \pm 2852	7055 \pm 3111	753.73	0.049*

Uji paired sample T ; Nilai P = \leq 0,05

Based on the table above, the results of the paired sample T statistical test indicate that in the cupping therapy intervention group, there was a significant difference in the levels of interleukin 10 ELISA with a P-value of 0.049 ($P < 0.05$), suggesting a significant effect before and after cupping therapy. After the intervention, with an increase within the normal threshold, which indicates an increase in the immune system

Table 3: Distribution of Differences Between the Two Groups Before and After Cupping Therapy

Group	Variables	(Mean \pm SD)		Mean Difference \pm SD	P-Value
		Before	After		
Hypertensi	Systolic Blood Pressure	160.85 \pm 21.37	119.35 \pm 9.25	41.50 \pm 23.71	0.000*
	Diastolic Blood Pressure	86.35 \pm 9.16	78.20 \pm 4.29	8.15 \pm 8.83	0.001*
Normotensi	Systolic Blood Pressure	118.45 \pm 11.90	119.00 \pm 10.33	-0.55 \pm 6.21	0.697
	Diastolic Blood Pressure	77.15 \pm 4.39	76.40 \pm 6.047	0.75 \pm 3.35	0.330

Abbreviations: M: Mean, SD: Standard Deviation, P-Value (< 0.05): Significance level, Mean \pm SD: Mean difference (before-after), IL-10: Interleukin 10, TDS: Systolic Blood Pressure, TDD: Diastolic Blood Pressure

Table 3 displays the differences in blood pressure before and after cupping therapy. In the hypertension group, the average systolic blood pressure decreased from 160.85 \pm 21.37 to 119.35 \pm 9.25, and the average diastolic blood pressure decreased from 86.35 \pm 9.16 to 78.20 \pm 4.29, with a significant value (P-Value < 0.05). In contrast, the normotensive group showed no change in mean blood pressure values, with a P-value > 0.05 .

Table 4. Comparison of IL-10, Systolic Blood Pressure (TDS), and Diastolic Blood Pressure (TDD) Levels in Hypertensive and Normotensive Groups of Coastal Communities

Variables	t	df	Mean Difference	Sig. (2-tailed)	N
IL-10 Post Test	-3.393	26.26	-2584.650	0.002	40
TDS Pre Test	7.751	29.75	42.400	0.000	40
TDS Post Test	0.113	37.54	0.350	0.911	40
TDD Pre Test	4.048	27.28	9.200	0.000	40
TDD Post Test	1.085	34.29	1.800	1.286	40

Abbreviations: P-Value (< 0.05): Significance level, Mean difference (before-after), IL-10: Interleukin 10, TDS: Systolic Blood Pressure, TDD: Diastolic Blood Pressure

In Table 4, the comparison between the hypertensive and normotensive groups (n=40) in IL-10 levels, TDS, and TDD pre-test revealed significant differences with a P-value < 0.05. However, in the post-test for TDS and TDD, there were no significant differences with a P-value > 0.05.

DISCUSSION

In terms of demographics, the majority of respondents were fishermen, belonging to the Tolaki ethnic group, with a diploma education, and aged 41–50 years. Coastal areas are particularly vulnerable to the negative impacts of global warming due to the accumulation of influences from land and sea. Coastal fishermen are highly affected by stress and work fatigue because they are exposed to high psychosocial factors at work and face obstacles related to difficult working conditions.^{9, 23} Fishermen are the most vulnerable occupational group with unique characteristics that make them more susceptible to non-communicable diseases, particularly hypertension, as most of their time is spent at sea. Reported risk factors include physical activity at sea, stress factors, lack of sleep, poor dietary practices, tobacco use, alcohol consumption, and drug use, increased waist circumference, and higher BMI. Additionally, there is a relationship between BMI and body fat content according to body shape and proportion.²⁴ Hypertension is one of the global health problems influenced by many factors. Ideal blood pressure management and control require appropriate guidelines due to variations in each country influenced by race, dietary habits, lifestyle, and other factors.²⁵ The limitations and concerns in current hypertension care have led many hypertensive patients, especially in Asia, to turn to complementary therapies. Various approaches to treating hypertension have been carried out using complementary therapies, one of which is cupping therapy, which is effective in lowering blood pressure in hypertensive patients.²⁶

In this study, the mean and standard deviation values of blood pressure examinations, including Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), showed changes after cupping therapy. This is supported by several research findings, such as the relationship between complementary wet cupping therapy and decreased Systolic Blood Pressure in hypertensive patients.^{27, 28} Additionally, cupping therapy has been found to have an effect on hypertension.^{29, 30} An observational study on acute hypertensive patients observed that wet cupping therapy could lower systolic blood pressure by improving vascular compliance and vascular filling rate.³¹ Several studies on hypertensive patients using complementary and alternative therapies have shown that combining prescribed drugs with wet cupping therapy can lower blood pressure.³²⁻³⁴ Based on these results, cupping therapy can serve as supporting evidence in lowering blood pressure in hypertension and can be a complementary therapy to conventional therapy, helping to reduce the dose of antihypertensive drugs given.^{20, 22}

One of the findings of this study is the change in IL-10 levels following cupping therapy. The mean pre-intervention values of IL-10 (5466 ± 2852) increased to (7055 ± 3111) after the intervention, with an increase within the normal threshold. IL-10 is an anti-inflammatory cytokine crucial for controlling inflammatory responses and maintaining immune system balance after activation. It also functions to prevent excessive inflammation during infections and has been implicated in various autoimmune conditions. IL-10 production is triggered by inflammatory signals and can be produced by various immune cells, including T cells, B cells,

macrophages, and dendritic cells. Different mechanisms regulate IL-10 production in different cell types.¹⁹ Interleukin-10 (IL-10) is a multifunctional cytokine with strong anti-inflammatory properties. In a study, IL-10 limited the increase in RhoA/Rho-kinase signaling and vascular reactivity in arteries of hypertensive rats induced by angiotensin II (Ang II). IL-10 counteracts Ang II stress activity and vascular dysfunction associated with hypertension, partly through modulation of the RhoA-Rho kinase pathway. Strategies to increase IL-10 levels during hypertension may enhance the benefits of routine treatment.³⁵

Scientifically, cupping therapy can lower tissue blood pressure in the painful area and evacuate inflammatory agents and toxins, resulting in improved lymph and blood flow. However, studies on cupping therapy are still limited and influenced by cultural, social, and religious factors, but they produce positive effects.³⁶⁻³⁹ Cupping therapy can affect the immune system in various ways, such as inducing local inflammation, activating the complement system, and increasing levels of immune products like interferon. Additionally, there is an assessment of the effect of cupping on the patient's health level and hematological factors, which shows a decrease in blood hematocrit levels and hemoglobin levels to normal.^{15, 20} The Taibah mechanism theory in cupping therapy uses the physiological principle of renal glomerular filtration excretion. It purges blood excretion through skin capillaries, interstitial fluid of pathological substances, and evacuation of abscesses being the percutaneous excretory functions of cupping therapy. Cupping is reported to significantly cleanse the blood, increase natural immunity, assist pharmacological treatment, and treat various disease conditions.^{15, 21} Cupping therapy is useful in restoring body balance by strengthening the immune system, eliminating pathogenic factors, and improving blood circulation. It helps remove blood containing substances that are not needed by the body, thereby overcoming side effects and improving physical health.⁴⁰

In this study, there was an enhancement of the immune system with an increase in interleukin 10. The underlying scientific principle is that during cupping therapy, fine incisions are made on the skin (skin scarification), which increases the production of endogenous nitric oxide through the regulation of nitric oxide synthase (NOS) expression. mRNA regulation occurs and increases several-fold in the final stages of wound healing, peaking 24 hours after injury and persisting for several days in NOS protein expression (NOS mRNA). Nitric oxide plays a crucial role in antioxidant effects, vasodilator function, and antimicrobial effects.^{15, 16, 36} Another study on the mechanism of cupping therapy that enhances the immune system involves the pressure and suction of the cup, which increases blood volume and enhances capillary filtration rate, leading to the removal of filtered and interstitial fluids in the area. The filtered and sucked fluids contain substances related to disease, disease-causing agents, prostaglandins, and inflammatory mediators. Scalpel incisions enhance innate immunity by stimulating inflammatory cell migration and endogenous opioid release. This results in increased blood flow, elimination of toxins, restoration of neuroendocrine balance, increased oxygen supply, and tissue perfusion.¹²⁻¹⁴

Cupping therapy increases subcutaneous blood flow and stimulates the autonomic nervous system. The skin wounds caused by incisions stimulate autonomic, hormonal, and immune reactions associated with increased sympathetic and parasympathetic efferent nerve function to the somato-visceral reflex. Cupping therapy plays a role in activating the complement system and modulating the cellular part of the immune system. Overall, cupping affects changes in the biomechanical properties of the skin, increases the pain threshold directly in patients and healthy subjects alike, and reduces inflammation.^{38, 41, 42}

The results indicate that cupping therapy could be a viable treatment option; however, the evidence is restricted due to methodological limitations in the conducted trials. High-quality trials are required. Furthermore, the limited sample size is a concern, and it is essential to utilize larger and more representative samples to obtain more accurate research outcomes. Additionally, it is crucial to ensure that cupping therapy is administered in accordance with standards, maintaining aseptic practices consistent with medical procedures.^{20, 22, 43}

CONCLUSION

The results of this study suggest that wet cupping can lower blood pressure and enhance the immune system, making it a viable complementary therapy for fishing communities experiencing hypertension. To ensure the long-term benefits and sustainability of wet cupping therapy, further research is necessary to explore its mechanisms through various pathways. Additional studies on cupping therapy are required to understand potential side effects and contraindications, ensuring its safe and effective use. A comprehensive approach from cultural, religious, and psychological perspectives can provide a deeper understanding of its impact on individuals and society.

Acknowledgements: The author extends gratitude to all research respondents, the fishing communities in the coastal areas of Lalongasomeeto District, and the village government—particularly the sub-district secretary, the head of the health center, and all parties who assisted in this research. The author also thanks the leadership of Poltekkes Kemenkes Kendari, the cupping expert team, and all parties who provided assistance. Special appreciation is given to the financial support provided by the DIPA Poltekkes Kemenkes Kendari (PKUPT Scheme 2022), which enabled the completion of this research.

Conflict of Interest: The authors declare no conflicts of interest

REFERENCES

1. Mbizo J, Okafor A, Sutton MA, Leyva B, Stone LM, Olaku O. Complementary and alternative medicine use among persons with multiple chronic conditions: results from the 2012 National Health Interview Survey. *BMC Complement Altern Med*. 2018;18(1):281-.
2. Azaizeh H, Saad B, Cooper E, Said O. Traditional Arabic and Islamic Medicine, a Re-emerging Health Aid. *Evid Based Complement Alternat Med*. 2010;7(4):419-24.
3. AlRawi SN, Khidir A, Elnashar MS, Abdelrahim HA, Killawi AK, Hammoud MM, et al. Traditional Arabic & Islamic medicine: validation and empirical assessment of a conceptual model in Qatar. *BMC complementary and alternative medicine*. 2017;17(1):157-.
4. Satria D. Complementary and Alternative Medicine (CAM): Fakta atau Janji. *Idea Nursing Journal*. 2013;4(3).
5. Rosyanti L, Hadi I, Faturrahman T, Hidayat A. Changes in brain-derived neurotrophic factors in schizophrenic patients with spiritual psychoreligious therapy. *J Pak Med Assoc*. 2024;74(8):1458-63.
6. Kang SC, Lin CC, Tsai CC, Chang YC, Wu CY, Chang KC, et al. The Primary Care of Immigrant Workers and Their Associated Characteristics within A Taiwanese Fishing Community. *Int J Environ Res Public Health*. 2019;16(19).
7. Cabral H, Fonseca V, Sousa T, Costa Leal M. Synergistic Effects of Climate Change and Marine Pollution: An Overlooked Interaction in Coastal and Estuarine Areas. *Int J Environ Res Public Health*. 2019;16(15).
8. Azzeri A, Ching GH, Jaafar H, Mohd Noor MI, Razi NA, Then AY, et al. A Review of Published Literature Regarding Health Issues of Coastal Communities in Sabah, Malaysia. 2020;17(5).
9. Laraqui O, Manar N, Laraqui S, Ghailan T, Deschamps F, Laraqui CEH. Occupational risk perception, stressors and stress of fishermen. *Int Marit Health*. 2018;69(4):233-42.
10. Choi TY, Ang L, Ku B, Jun JH, Lee MS. Evidence Map of Cupping Therapy. *Journal of clinical medicine*. 2021;10(8):1750.
11. Ahmed SM, Madbouly NH, Maklad SS, Abu-Shady EA. Immunomodulatory effects of blood letting cupping therapy in patients with rheumatoid arthritis. *The Egyptian journal of immunology*. 2005;12(2):39-51.
12. Furhad S, Bokhari AA. Cupping Therapy. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2020, StatPearls Publishing LLC.; 2020.
13. Cao H, Han M, Li X, Dong S, Shang Y, Wang Q, et al. Clinical research evidence of cupping therapy in China: a systematic literature review. *BMC Complement Altern Med*. 2010;10:70.
14. Cao H, Li X, Liu J. An updated review of the efficacy of cupping therapy. *PloS one*. 2012;7(2):e31793.

15. El Sayed SM, Baghdadi H, Abou-Taleb A, Mahmoud HS, Maria RA, Ahmed NS, et al. Al-hijamah and oral honey for treating thalassemia, conditions of iron overload, and hyperferremia: toward improving the therapeutic outcomes. *J Blood Med*. 2014;5:219-37.
16. El-Shanshory M, Hablas NM, Shebl Y, Fakhreldin AR, Attia M, Almaramhy HH, et al. Al-hijamah (wet cupping therapy of prophetic medicine) significantly and safely reduces iron overload and oxidative stress in thalassemic children: a novel pilot study. *J Blood Med*. 2018;9:241-51.
17. Baghdadi H, Abdel-Aziz N, Ahmed NS, Mahmoud HS, Barghash A, Nasrat A, et al. Ameliorating Role Exerted by Al-Hijamah in Autoimmune Diseases: Effect on Serum Autoantibodies and Inflammatory Mediators. *International journal of health sciences*. 2015;9(2):207-32.
18. Zhang H, Kuchroo V. Epigenetic and transcriptional mechanisms for the regulation of IL-10. *Seminars in immunology*. 2019;44:101324.
19. MacKenzie KF, Pattison MJ, Arthur JS. Transcriptional regulation of IL-10 and its cell-specific role in vivo. *Critical reviews in immunology*. 2014;34(4):315-45.
20. Ilin Ir. Evaluation of Complementary Cupping Therapy in the Management of Hypertension and Triglyceride Levels in Coastal Fishermen Communities. *Public Health of Indonesia*. 2024;10(2):237-46.
21. Rosyanti L, Hadi I, Askrening A, Indrayana M. Complementary alternative medicine: Kombinasi terapi bekam dan murotal alquran pada perubahan tekanan darah, glukosa, asam urat dan kolesterol. *Health Information: Jurnal Penelitian*. 2020;12(2):173-92.
22. Hadi I, Rosyanti L, Askrening A, Herman H. Effect of Wet Cupping Complementary Therapy on Blood Changes in Active Smokers in Kendari City: A Quasi-Experimental Study. *Health Information : Jurnal Penelitian*. 2022;14(1):51-65.
23. Mulyasari G, Trisusilo A, Windirah N, Djarot IN, Putra AS. Assessing Perceptions and Adaptation Responses to Climate Change among Small-Scale Fishery on the Northern Coastal of Bengkulu, Indonesia. *ScientificWorldJournal*. 2023;2023:8770267.
24. Doddamani A, Ballala ABK, Madhyastha SP, Kamath A, Kulkarni MM. A cross-sectional study to identify the determinants of non-communicable diseases among fishermen in Southern India. *BMC Public Health*. 2021;21(1):414.
25. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. *Hypertension*. 2020;75(6):1334-57.
26. Wang J, Xiong X. Evidence-based chinese medicine for hypertension. *Evid Based Complement Alternat Med*. 2013;2013:978398.
27. Al-Tabakha MM, Sameer FT, Saeed MH, Batran RM, Abouhegazy NT, Farajallah AA. Evaluation of Bloodletting Cupping Therapy in the Management of Hypertension. *J Pharm Bioallied Sci*. 2018;10(1):1-6.
28. Zarei M, Hejazi S, Javadi SA, Farahani H. The efficacy of wet cupping in the treatment of hypertension. *ARYA Atherosclerosis*. 2012:145-8.
29. Aleyeidi NA, Aseri KS, Matbouli SM, Sulaiani AA, Kobeisy SA. Effects of wet-cupping on blood pressure in hypertensive patients: a randomized controlled trial. *Journal of integrative medicine*. 2015;13(6):391-9.
30. Aleyeidi N, Aseri K, Kawthar A. The efficacy of wet cupping on blood pressure among hypertension patients in Jeddah, Saudi Arabia: A randomized controlled trial pilot study. *Altern Integr Med*. 2015;4(183):10.4172.
31. Lee MS, Choi TY, Shin BC, Kim JI, Nam SS. Cupping for hypertension: a systematic review. *Clinical and experimental hypertension (New York, NY : 1993)*. 2010;32(7):423-5.
32. Ibrahim IR, Hassali MA, Saleem F, Al Tukmagi HF. A qualitative insight on complementary and alternative medicines used by hypertensive patients. *Journal of pharmacy & bioallied sciences*. 2016;8(4):284-8.
33. Baran AK, Demirci H, Budak E, Candar A, Akpınar Y. What do people with hypertension use to reduce blood pressure in addition to conventional medication–Is this related to adherence? *European Journal of Integrative Medicine*. 2017;13:49-53.
34. Rahmawati R, Bajorek BV. Self-medication among people living with hypertension: a review. *Family practice*. 2017;34(2):147-53.

35. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, et al. Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015. *Jama*. 2017;317(2):165-82.
36. Tagil SM, Celik HT, Ciftci S, Kazanci FH, Arslan M, Erdamar N, et al. Wet-cupping removes oxidants and decreases oxidative stress. *Complement Ther Med*. 2014;22(6):1032-6.
37. Mischak H, Apweiler R, Banks RE, Conaway M, Coon J, Dominiczak A, et al. Clinical proteomics: A need to define the field and to begin to set adequate standards. *Proteomics Clinical applications*. 2007;1(2):148-56.
38. Al Bedah AM, Khalil MK, Posadzki P, Sohaibani I, Aboushanab TS, AlQaed M, et al. Evaluation of Wet Cupping Therapy: Systematic Review of Randomized Clinical Trials. *J Altern Complement Med*. 2016;22(10):768-77.
39. Almainan AA. Proteomic effects of wet cupping (Al-hijamah). *Saudi Med J*. 2018;39(1):10-6.
40. Hadi I, Rosyanti L, Askrening A, Herman H. Pengaruh Terapi Komplementer Bekam Basah terhadap Perubahan Darah Rutin Perokok Aktif di Kota Kendari: Penelitian Kuasi Eksperimen. *Health Information : Jurnal Penelitian*. 2022;14(1):51-65.
41. Al-Bedah AMN, Elsubai IS, Qureshi NA, Aboushanab TS, Ali GIM, El-Olemy AT, et al. The medical perspective of cupping therapy: Effects and mechanisms of action. *J Tradit Complement Med*. 2019;9(2):90-7.
42. Arslan M, Yeşilçam N, Aydın D, Yüksel R, Dane S. Wet cupping therapy restores sympathovagal imbalances in cardiac rhythm. *J Altern Complement Med*. 2014;20(4):318-21.
43. Cramer H, Klose P, Teut M, Rotter G, Ortiz M, Anheyer D, et al. Cupping for Patients With Chronic Pain: A Systematic Review and Meta-Analysis. *J Pain*. 2020;21(9-10):943-56.