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Review Article

Exploring the efficacy of al-hijamah (wet cupping) in managing hypertension and dyslipidemia among indonesian population: a meta-analysis

Justika Usmadhani Aulya[1*], Asri Rizqi Matondang[2], Farahdina Farahdina[3], Ferdian Rizaliansyah[4], Nur Samsu[5], Jonny Karunia Fajar[6]

[1] Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.
[2] Faculty of Medicine, Universitas Diponegoro, Semarang Indonesia.
[3] Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.
[4] Faculty of Medicine, Airlangga University, Surabaya, Indonesia.
[5] Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.
[6] Brawijaya Internal Medicine Research Center, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.

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ABSTRACT

Background: In Indonesia, wet cupping therapy has been thoroughly investigated as a treatment for hypertension and dyslipidemia. Nevertheless, the outcomes across these studies are contradictory.
Objectives: To appraise the effectiveness of wet cupping therapy in the management of hypertension and dyslipidemia among the Indonesian population.
Methods: We examined papers sourced from Google Scholar, the Indonesian Scientific Journal Database, and Garba Rujukan Digital until September 5, 2020. These papers investigated blood pressure and lipid profile levels both pre- and post-wet cupping treatment. The collective data underwent Z-test analysis to assess associations.
Results: In total, we included 26 papers examining the correlation between wet cupping therapy and blood pressure, as well as 16 papers assessing lipid profile levels. Our combined analysis revealed significantly reduced systolic blood pressure (MD: 13.86; 95% CI: 10.01, 17.71), diastolic blood pressure (MD: 6.31; 95% CI: 3.84, 8.79), and lower total cholesterol levels (MD: 21.56; 95% CI: 10.32, 32.80]) in the post-treatment group compared to the pre-treatment group. However, we were unable to elucidate the impact of wet cupping therapy on the concentrations of low-density lipoprotein and triglyceride.
Conclusions: Wet cupping therapy exhibits potential efficacy in reducing blood pressure and total cholesterol levels among individuals in Indonesia.

1. Introduction

Hypertension and dyslipidemia, being the principal risk factors for non-communicable diseases culminating in cardiovascular events, have collectively accounted for more than 9.4 million deaths worldwide.[1] The global prevalence of hypertension and dyslipidemia among adults is approximately 1.13 billion and 29.7 million, respectively.[1,2] It is predicted that this figure will rise to 29.2% by the year 2025.[1] In Indonesia, the prevalence rates of hypertension and dyslipidemia are documented at 34.1% and 35.9%, respectively.[3] While the management of hypertension and dyslipidemia was well-established, its implementation in our country faced cultural challenges. Therefore, alternative approaches were deemed necessary for effective management. Given that the majority of our population was Muslim, exploring management options rooted in Islamic medical history, such as wet cupping therapy, was considered.

The practice of wet cupping therapy originated from ancient Egyptians around 1550 BC. Initially utilized for various conditions like polycythemia, vertigo, dysmenorrhea, headache, migraine, and drug intoxication, its use expanded over time to encompass musculoskeletal diseases, cardiovascular disorders, inflammatory diseases, and metabolic disorders, with documented effectiveness.[4] While the precise mechanism of wet cupping therapy remains debatable, over the last three decades, it has demonstrated encouraging results in the treatment of hypertension, dyslipidemia, and a range of other conditions.[5,6] Moreover, in terms of mitigating risk factors associated with cardiovascular diseases, wet cupping therapy is thought to offer clinical benefits because of its proposed detoxification mechanism. This involves extracting harmful substances from the blood, including lipid substances that are hydrophobic and not easily eliminated through renal pathways but may be excreted through the skin.[7] Wet cupping therapy has been extensively utilized in countries including Egypt, China, Greece, the Middle East, and Europe.[4] The majority of reports suggested that wet cupping therapy yielded favorable clinical outcomes for managing hypertension and dyslipidemia.[5,6] Moreover, previous meta-analyses have validated its effectiveness.[8-10] In our country, wet cupping therapy underwent extensive study, with research conducted in twenty-five regions. However, the results among these studies were conflicting.

* Corresponding author at: Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.
E-mail address: justika.drjuu@gmail.com (J.U. Aulya).

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Our study sought to appraise the efficacy of wet cupping therapy in managing hypertension and dyslipidemia among the Indonesian population using a meta-analysis methodology. The objective was to provide clarity on the inconsistent findings regarding the effects of wet cupping therapy on blood pressure and lipid profiles.

2. Methods

Study Design

From August to September 2020, we conducted a systematic review and meta-analysis to investigate the impact of wet cupping therapy on blood pressure and lipid profile levels among the Indonesian population. Published papers sourced from Google Scholar, the Indonesian Scientific Journal Database (ISJD), and Garba Rujukan Digital (GARUDA) were utilized to determine mean differences and 95% confidence intervals (95% CI). Our meta-analysis adhered to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines.[11]

Search strategy

We conducted searches for pertinent papers within the primary Indonesian scientific databases (GARUDA, ISJD, and Google Scholar) until September 5, 2020. We utilized keywords adapted from the Medical Subject Headings (MeSH) including ["hypertension" OR "blood pressure" OR "hipertensi"] AND ["wet cupping" OR "cupping therapy" OR "bekam" OR "al-hijamah"] AND ["hypercholesterolemia" OR "hiperkolesterolemia" OR "Profil lipid" OR "dyslipidemia"]. The search was confined to articles published in English and Bahasa Indonesia. Additionally, the reference lists of potentially related articles were manually searched to discover further pertinent studies.

Eligibility criteria

Articles meeting the specified criteria were included if they were prospective clinical studies examining blood pressure and lipid profile levels before and after wet cupping treatment, and if they provided adequate data for effect estimate calculation. Conversely, articles were excluded if they fell into any of the following categories: unrelated topic, review articles, letters to the editor, editorials, commentaries; if they contained incomplete data; if they were duplicate publications; or if they were deemed to be of low quality.

Quality assessment

The evaluation of paper quality in our analysis involved utilizing the Newcastle-Ottawa Scale (NOS).[12] The assessment of paper quality was carried out independently by two authors, JUA and JKF. The assessment comprised three components: paper enrollment (4 points), comparison between groups (2 points), and evaluation of exposure (3 points). Interpretation of the assessment results was categorized as good (score≥7), moderate (score 5-6), or poor (score≤4). Papers rated as poor quality were excluded from the analysis. Any inconsistencies between the authors were resolved through discourse.

Data extraction

Two independent authors conducted data extraction using a pilot form. The extracted data included the author names, publication years, locations (cities), sample sizes (pre- and post-intervention), case settings, participant ages, genders, and blood pressure and lipid profile levels before and after intervention.

Outcome measure

In our current study, wet cupping therapy served as the predictor covariate. The outcome measures encompassed blood pressure and lipid profile levels (total cholesterol, low-density lipoprotein, and triglycerides) before and after the application of wet cupping therapy.

Statistical analysis

Prior to examining the association and effect estimates between wet cupping therapy and blood pressure and lipid profile levels, we conducted an assessment to ascertain potential publication bias and heterogeneity. Heterogeneity within the included studies was evaluated through the Q test and $\chi 2$ (I2). Heterogeneity was considered present if the p-value was less than 0.10 and I2 exceeded 50%, prompting the adoption of a random-effects model. Conversely, if the p-value exceeded 0.10 and I2 was less than 50%, it indicated no significant heterogeneity among studies, thus warranting the utilization of a fixed-effect model.[13] To evaluate publication bias, we utilized the Egger test alongside funnel plots. A p-value below 0.05 was indicative of potential publication bias.[14] We determined the association between wet cupping therapy and blood pressure and lipid profile levels using a Z-test, while effect estimates were derived from the cumulative mean difference.[15] Data synthesis and analysis were conducted using Review Manager (Revman Cochrane Collaboration, London, UK) version 5.4 and Comprehensive Meta-Analysis (CMA, New Jersey, USA) version 2.1 by two independent authors (JUA & JKF). Any discrepancies were resolved through discussion between the two authors.

3. Results

Eligible studies

In total, our study encompassed 26 papers investigating the association between wet cupping therapy and blood pressure, and 16 papers examining the correlation between wet cupping therapy and lipid profile levels. Within these, 16 papers focused on total cholesterol, while three each centered on LDL and triglycerides. These papers were sourced through searches on GARUDA, ISJD, and Google Scholar, and were screened against predefined eligibility criteria. Initially, a total of 414 papers related to wet cupping therapy for hypertension and 61 papers on wet cupping therapy for lipid profiles were identified. Of these, 382 hypertension-related papers and 34 lipid profile-related papers were excluded due to irrelevant titles and abstracts. Additionally, among the hypertension papers, one review paper and two papers with incomplete data were excluded, while among the lipid profile papers, four dissertations and four papers lacking sufficient data for mean difference and 95% CI calculation were excluded. Figure 1 depicts the flowchart detailing paper selection in our meta-analysis. The fundamental characteristics of the papers analyzed in our study are outlined in Table 1 for blood pressure and Table 2 for lipid profile.

Data synthesis

We analyzed a collective of 26 papers documenting the impact of wet cupping on blood pressure.[16-41] Our pooled calculation found that lower systolic (mean difference: 13.86 mmHg [95% CI: 10.01-17.71], p = 0.0001) (Fig. 2) and diastolic (mean difference: 6.31 mmHg [95% CI: 3.84 – 8.79], p = 0.0001) (Fig. 3) blood pressure were observed after wet cupping therapy compared to before treatment. Regarding lipid profile, among the 16 papers assessing the effect of wet cupping therapy, our findings showed lower total cholesterol levels (mean difference: 21.56 mg/dL [95% CI: 10.32 – 32.80], p = 0.0002) (Fig. 4) in the post-treatment group compared to the pre-treatment group.[16,20,42-55] However, we were unable to clarify the effect of wet cupping therapy on the levels of LDL (mean difference: -4.38 mg/dL [95% CI: -11.32 – 2.56], p = 0.2200) [50-52] and triglycerides (mean difference: 8.68 mg/dL [95% CI: -19.83 – 37.20], p = 0.5500) [47,50,53]. The summary of the impact of wet cupping therapy on blood pressure and lipid profile levels is presented in Table 3.

Source of heterogeneity

Variability was observed in the covariates of systolic and diastolic blood pressure, necessitating the use of a random-effects model for cumulative association and effect estimates. Similarly, heterogeneity was observed in total cholesterol and triglycerides covariates for the association between wet cupping therapy and lipid profile levels, prompting the utilization of a random-effects model for evaluation. However, due to the absence of heterogeneity, a fixed-effects model was utilized for the LDL covariate. The evidence of heterogeneity for blood pressure and lipid profile levels following wet cupping therapy is detailed in Table 3.

Potential publication bias

The evaluation of publication bias across articles was conducted utilizing Egger's test. Our analysis did not reveal any indications of publication bias for either blood pressure or lipid profile levels. Detailed findings regarding publication bias are presented in Table 3.

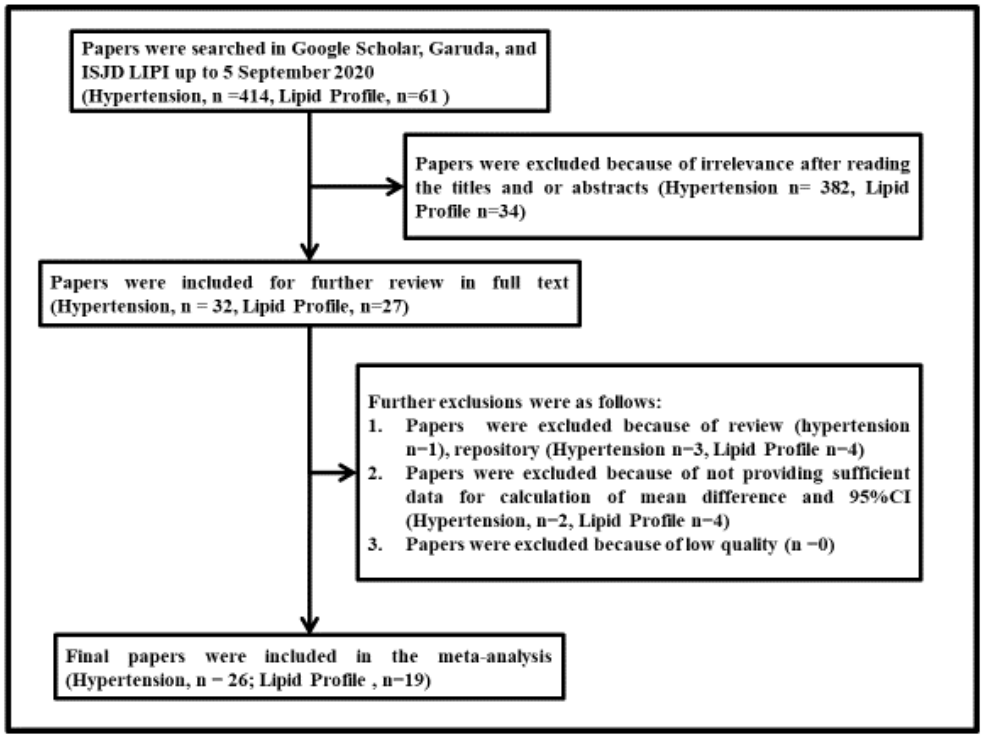

Figure 1. A flowchart of the article selection in our study.

Table 1. Baseline characteristics of articles regarding the efficacy of Al-Hijamah (wet cupping) for treating hypertension included in our study.

Author & year	Region	Sample size		Case setting	Age (year)	Frequency	NOS
		Pre	Post				
Akbar 2013	Semarang	40	40	Primary hypertension	59.9±7.2	Twice	8
Alfiayansah 2018	Garut	22	22	Primary hypertension	NA	Three times	8
Amaliyah et al 2018	Jakarta	38	38	Primary hypertension	40-49	Twice	8
Astuti et al 2018	Yogyakarta	15	15	Primary hypertension	31-40	Twice	8
Burasyid et al 2019	Kediri	15	15	Primary hypertension	NA	Twice	7
Ekanto et al 2012	Semarang	30	30	Primary hypertension	NA	Twice	8
Eliyana et al. 2019	Malang	17	17	Hypertension in pregnancy	33.2±6.3	Twice	8
Fatonah et al 2015	Bandar lampung	30	30	Primary hypertension	49.0±11.7	Twice	8
Fauziah et al 2020	Jakarta	17	17	Primary hypertension	46.8-49.7	Three times	8
G Sangkur et al 2017	Denpasar	27	27	Primary hypertension	NA	Twice	8
Irawan et al 2012	Kediri	14	14	Primary hypertension	45-54	Twice	7
Kusyati et al 2014	Semarang	10	10	Primary hypertension	NA	Twice	8
Lestari et al 2017	Mojokerto	14	14	Primary hypertension	40.0 ±5.9	Twice	8
Muflih et al 2019	Klaten	40	40	Primary hypertension	40.6±11.9	Twice	8
Mulyati et al 2013	Bengkulu	30	30	Primary hypertension	53	Twice	8
Pratama et al 2018	Jember	11	11	Primary hypertension	73.2 ±7.1	Twice	7
Priyanto et al 2020	Bangkalan	16	16	Primary hypertension	36-45	Twice	8
Putri et al 2014	Semarang	10	10	Primary hypertension	NA	Once	8
Rohatami 2015	Surakarta	30	30	Primary hypertension.	46-55	Once	8
Safrianda 2015	Pontianak	16	16	Primary hypertension	36-55	Once	8
Santi et al 2014	Tarakan	10	10	Primary hypertension	36-45	Once	8
Saputra et al 2017	Siak, Kampar	10	10	Primary hypertension	40-55	Three-time	7
Sardaniah et al 2020	Bengkulu	98	98	Primary hypertension	NA	Once	7
Sormin 2018	Bandar Lampung	40	40	Primary hypertension	≥ 35	Once	8
Surayanda et 2017	Prabumulih	47	47	Primary hypertension	≥ 30	Twice	8
Susanah et al 2017	Malang	23	23	Primary hypertension	46-55	Once	8

Notes; Data were presented as mean ± SD or minimum-maximum; NOS, Newcastle-Ottawa Scale; NA, not available.

Table 2. Baseline characteristics of articles regarding the levels of lipid profile after treatment with Al-Hijamah (wet cupping) included in our study.

Author & year	Region	Sample size		Lipid profile	Age (year)	Frequency	NOS
		Pre	Post				
Akbar 2013	semarang	40	40	TC	59.9 ±7.2	Twice	8
Burasyid et al 2019	Kediri	15	15	TC	NA	Twice	8
Fahmy et al 2008	Yogyakarta	30	30	LDL	20-24	Once	8
Faizal et al 2020	Bangka Belitung	17	17	TC	43.7±10.3	Once	8
Fikri et al 2010	Gresik	18	18	TC	45-60	Once	8
Helma et al 2018	Padang	11	11	TC	40-65	Once	8
Hidayat et al 2018	Makassar	45	45	TC	20-45	Once	8
Isnaniar et al 2020	Pekanbaru	53	53	TC	25-45	Once	8
Meinisasti et al 2019	Bengkulu	17	17	TC	NA	Three times	8
Rini et al 2014	Pekanbaru	36	36	TC	41-45	Once	8
Saryono 2010	Purwokerto	30	30	TC	46-65	Once	8
Seto et al 2016	Bandar Lampung	30	30	TC	NA	Once	8
Sinaga et al 2019	Bengkulu	32	32	LDL	NA	Once	8
Sistiyono et al 2016	Yogyakarta	9	9	TC	40-70	Once	8
Sungkawa et 2019	Pontianak	32	32	TC & TG	40-60	Once	8
Surianti et al 2016	Pontianak	30	30	TC	35-60	Once	8
Widodo et al 2014	Semarang	12	12	TC	49-54	Three times	8
Suryanta et al 2016	Yogyakarta	11	11	LDL	40-75	Once	8
Windasari et al 2019	Pontianak	14	14	TC, LDL, &TG	47.3±3.2	Once	8

Notes; Data were presented as mean ± SD or minimum-maximum; NOS, Newcastle-Ottawa Scale; NA, Not available; TC, total cholesterol; LDL, low-density lipoprotein; TG, triglycerides.

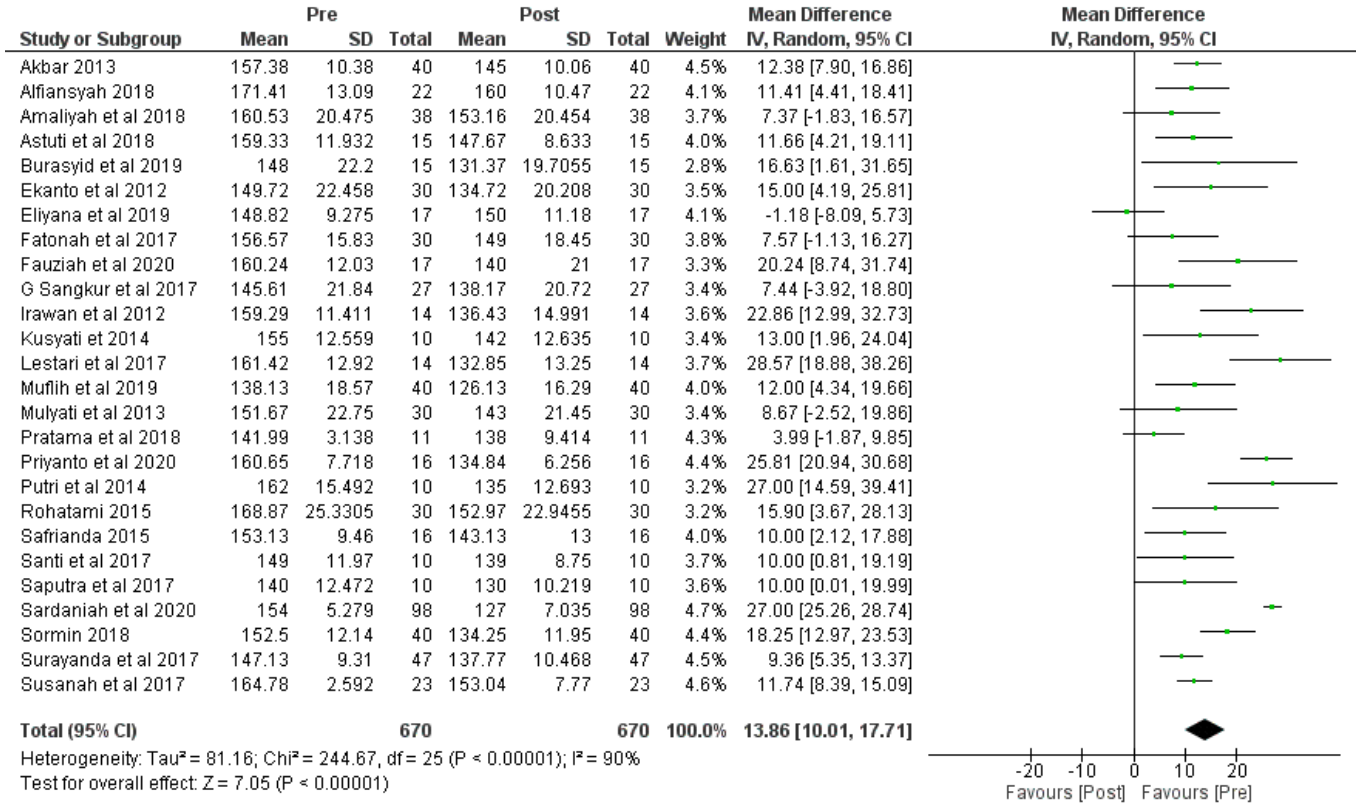

Figure 2. Forest plot of the association between wet cupping and systolic blood pressure.

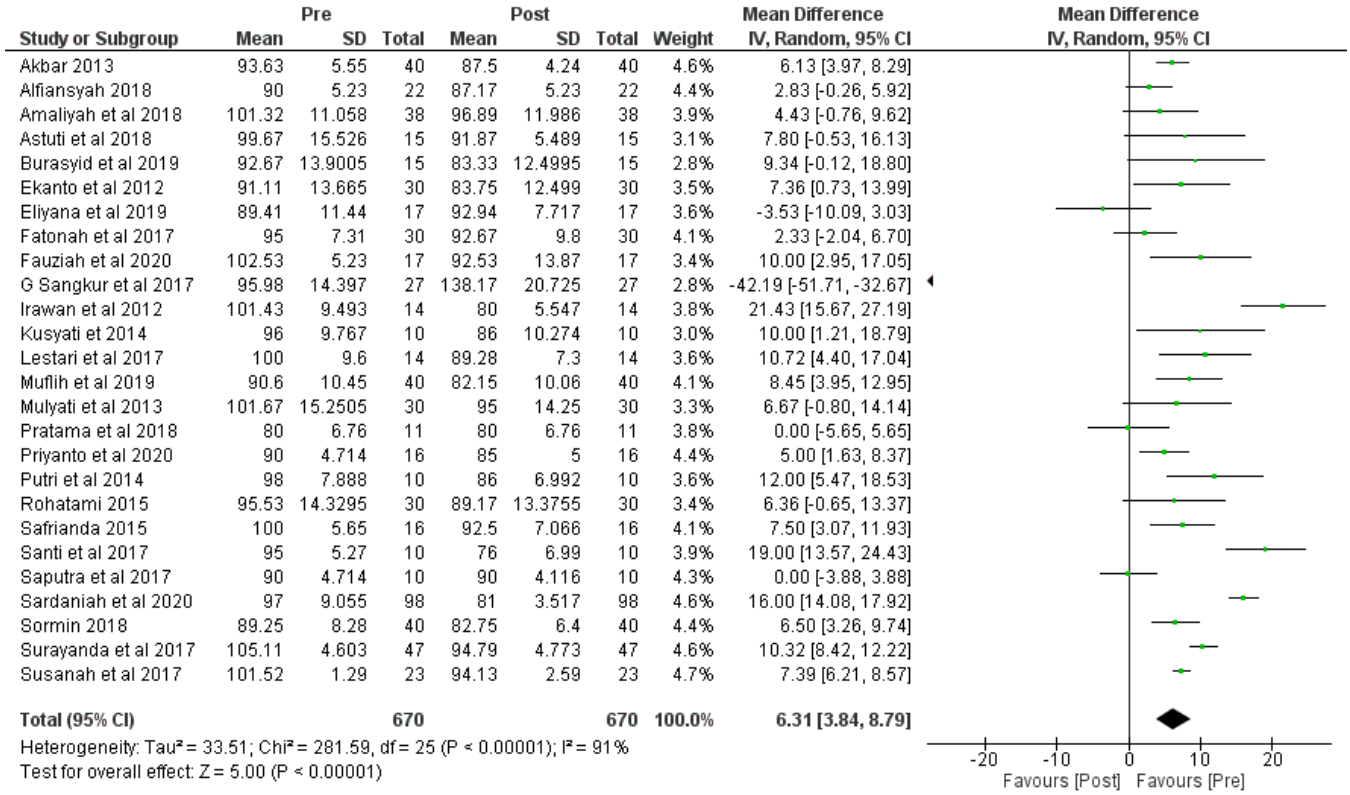

Figure 3. Forest plot of the association between wet cupping and diastolic blood pressure.

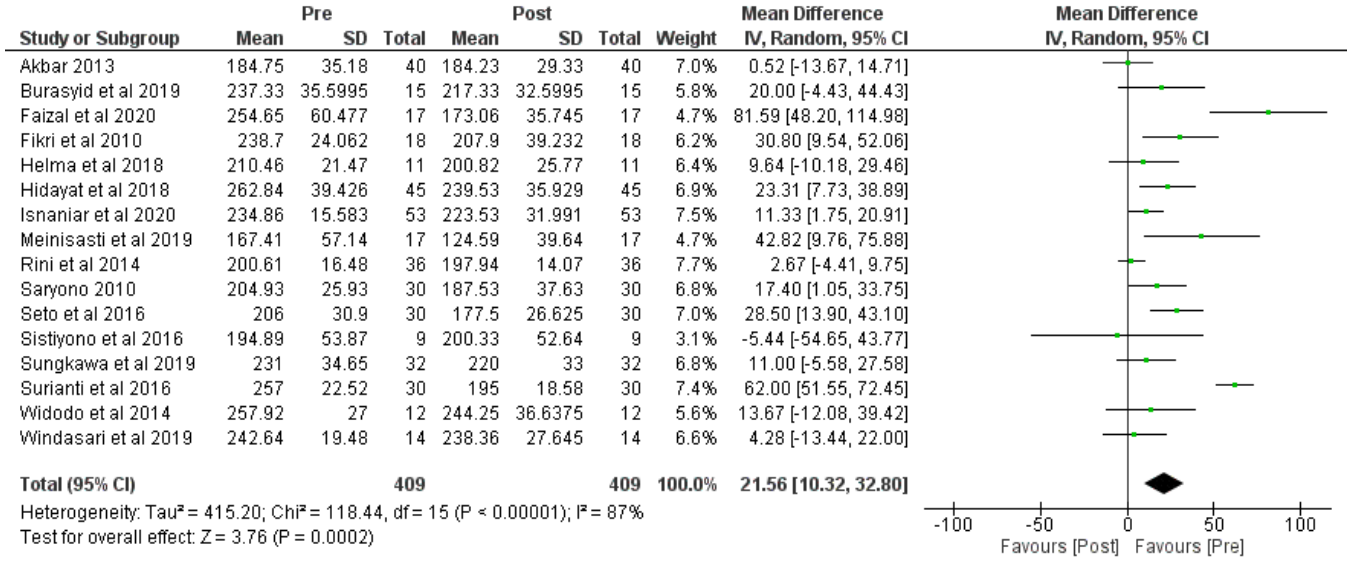

Figure 4. Forest plot of the association between wet cupping and total cholesterol levels.

Table 3. Summary of blood pressure and lipid profile after treatment with Al-Hijamah (wet cupping).

Parameter	NS	Model	Outcome Measure		Mean Diff	95%CI	pE	pHet	p
			Pre	Post					
SBP (mmHg)	26	Random	154.5 ± 13.6	140.6 ± 13.8	13.86	10.01 – 17.71	9.008	<0.0001	<0.0001
DBP (mmHg)	26	Random	95.5 ± 8.9	89.6 ± 8.4	6.31	3.84 – 8.79	5.788	<0.0001	<0.0001
TC (gr/dL)	16	Random	224.1 ± 32.5	201.9 ± 32.3	21.56	10.32 – 32.80	20.376	<0.0001	0.0002
LDL (gr/dL)	3	Fixed	116.3 ± 35.3	129.9 ± 40.4	-4.38	-11.32 – 2.56	1.135	0.5200	0.2200
TG (gr/dL)	3	Random	177.1 ± 55.7	177.9 ± 57.6	8.68	-19.83 – 37.20	19.360	0.0800	0.5500

Notes; Data were presented as mean ± SD; NS, number of studies; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; TC, total cholesterol; LDL, low-density lipoprotein; TG, triglycerides; CI, confidence interval; pE, p-value for Egger test; pHet, p-value for Heterogeneity test.

4. Discussions

Our meta-analysis encompassed 26 studies that investigated the relationship between wet cupping therapy and blood pressure.[16-41] Among these, seven papers on systolic blood pressure [18,22,23,25,30,31,37] and ten papers on diastolic blood pressure [17-20,22,23,30,31,34,37] indicated that wet cupping therapy was not significantly associated with blood pressure levels in primary hypertensive patients. However, an association was found in 19 papers on systolic blood pressure [16,17,19-21,24,26-29,32-36,38-41] and 16 papers on diastolic blood pressure.[16,21,24-29,32,33,35,36,38-41] Our combined analysis demonstrated a decrease in both systolic and diastolic blood pressure subsequent to wet cupping therapy in comparison to baseline measurements. While our current findings contrast with those of a meta-analysis eight years ago,[8] our study aligns with a prior study that shares similar characteristics,[9] which found wet cupping to have promising prospects for treating adults with hypertension.

Theoretically, wet cupping therapy is proposed to compress blood vessels, enhancing blood flow to the skin. This mechanism could lead to the release of vasodilators, such as nitric oxide, thereby reducing peripheral resistance pressure and subsequently lowering blood pressure. Additionally, wet cupping therapy may facilitate the drainage of interstitial fluids, filtering intravascular fluids containing metabolic toxins, and promoting the production of endogenous nitric oxide, which could potentially aid in the management of hypertension. Moreover, wet cupping therapy is associated with regulating the bioavailability and dispersal of microparticles (erythrocyte microparticles or danger-associated molecular patterns),[42] clearing these microparticles known to initiate inflammatory signals and immune cell responses, platelet aggregation, coagulation cascades, and thrombosis formation. Furthermore, microparticles play a role in triggering endothelial dysfunction by inhibiting endothelial nitric oxide synthase (eNOS). These pathological mechanisms play a significant role in governing the pathophysiology of hypertension. Consequently, the clearance effect of wet cupping therapy may modulate protective effects in the microvasculature, ultimately leading to a reduction in blood pressure.[7] This potential mechanism could elucidate the effectiveness of wet cupping therapy in managing hypertension, as demonstrated in our current investigation.

Our search resulted in the identification of 16 studies that examined the relationship between wet cupping therapy and lipid profiles. Of these, eight papers showed that wet cupping was not significantly associated with total cholesterol levels,[16,20,45,49,52,53,55,56] while eight others demonstrated an association.[43,44,46-48,50,51,54] However, we failed to clarify the impact of wet cupping therapy on low-density lipoprotein[56-58] and triglyceride levels.[53,56,59] Our pooled analysis showed a statistically notable decrease in total cholesterol levels post-treatment compared to baseline following wet cupping therapy (Figure 4). Previous meta-analyses conducted on this subject have reported findings consistent with our results.

One plausible theory explaining the mechanism of wet cupping therapy in dyslipidemia is the blood detoxification hypothesis. This hypothesis posits that cupping therapy may extract toxins and causative pathological substances (CPSs) from the body. The negative pressure generated by cupping could aid in extracting these substances from various bodily fluids, including purulent fluid, exudate, interstitial fluid, histolytic enzymes, and metabolites. Additionally, lipids exhibit hydrophobic characteristics, making them challenging to eliminate directly through the renal system but potentially feasible through the skin. Therefore, the utilization of wet cupping therapy on the skin might be conceptualized as an augmented filtration process, akin to "Glomeruli plus."[44] This mechanism offers insight into the outcomes observed in our study, where wet cupping therapy resulted in decreased total cholesterol levels.

Our current study constitutes the inaugural meta-analysis examining the impacts of wet cupping therapy on blood pressure and lipid profiles within the Indonesian population. We observed significant reductions in both blood pressure and total cholesterol levels subsequent to wet cupping therapy. Our investigation encompassed data from 25 provinces across Indonesia, comprising 26 studies on blood pressure and 16 studies on lipid profiles. Despite being practiced by Indonesian healthcare professionals for an extended period, wet cupping therapy has lacked sufficient clinical evidence to support its application. Through our meta-analysis, we provide compelling evidence supporting its efficacy in lowering blood pressure and total cholesterol levels. Nonetheless, further investigations are warranted to elucidate the precise mechanisms underlying wet cupping therapy's effects, particularly on a molecular and genetic level. Moreover, the establishment of a regulatory body may be necessary to standardize wet cupping therapy protocols among practitioners.

Several limitations were identified in our current meta-analysis. Firstly, potential confounding factors such as prior drug usage, family history of hypertension and dyslipidemia, and other medical conditions were not accounted for, potentially impacting our study's outcomes. Secondly, our study lacked detailed descriptions regarding the duration, location, and number of wet cupping therapy sessions administered. Thirdly, Our findings warrant cautious interpretation due to the relatively small sample sizes within each study, despite the inclusion of a substantial number of studies. Fourthly, the majority of studies in our database employed quasi-experimental designs, such as one-group pre-test and post-test designs. To achieve a higher level of evidence, future meta-analyses should incorporate improved study designs. This may involve larger sample sizes, adherence to formal power calculations, and adherence to appropriate treatment dosages (including treatment periods and frequencies) based on clinical guidelines.

5. Conclusions

Our present investigation demonstrates a decrease in both systolic and diastolic blood pressure following wet cupping therapy compared to pre-treatment levels. Furthermore, our results substantiate the association between wet cupping therapy and decreased total cholesterol levels. This study enhances our comprehension of wet cupping therapy's effectiveness in mitigating hypertension and dyslipidemia.

6. Declaration

6.1 Ethics Approval and Consent to participate
Not applicable.

6.2. Consent for publication
Not applicable.

6.3 Availibility of data and materials
Data used in our study were presented in the main text.

6.4 Competing interests
Not applicable.

6.5 Funding Source
There is no funding in our study

6.6 Authors contributions
JUA & ARM conceived and designed the study, conducted research, provided research materials, and collected and organized data. FF, FR, NS, JKF analyzed and interpreted data. JUA wrote initial and final draft of article, and provided logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

6.7 Acknowledgements
None.

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