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REVIEW ARTICLE

The Effect of Aromatherapy with Lavender on Pain of Needle Insertion and Severity of Restless Legs Syndrome in Hemodialysis Patients; a Systematic Review and Meta-analysis

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Abstract: **Introduction:** Pain experienced during the insertion of a catheter into the arteriovenous fistula (AVF) and restless legs syndrome (RLS) are prevalent issues among Hemodialysis (HD) patients. The primary objective of this systematic review and meta-analysis was to consolidate the findings from randomized clinical trial (RCT) studies examining the impact of aromatherapy with lavender on the pain associated with AVF catheter insertion and RLS in HD patients. **Methods:** A systematic search was conducted on PubMed, Web of Science, Scopus, Cochrane, Embase, ClinicalTrials.gov, and Google Scholar search engine from inception to August 1, 2022, using keywords extracted from Medical Subject Headings, such as "Aromatherapy", "Lavender", "Arteriovenous fistula", "Pain", "Restless legs syndrome", and "Hemodialysis". **Results:** Finally, eleven articles were included in this systematic review and meta-analysis. The results showed that aromatherapy reduced the average pain of catheter insertion in AVF compared to the control group (Standard Mean Difference: -1.60, 95% Confidence Interval: -2.32 to -0.87, Z=4.32, I2:90.3%, P<0.001). Also, aromatherapy massage reduced the average severity of RLS compared to the control group, which was statistically significant (Weighted Mean Difference: -13.21, 95% Confidence Interval: -17.50 to -8.91, Z=6.03, I2:93.0%, P<0.001). Also, the subgroup analysis showed that lavender in the intervention group significantly decreased the pain intensity compared to the "no intervention" group (P<0.001), yet it was not significant compared to the placebo group (P=0.12). **Conclusion:** In summary, the findings indicate a notable reduction in catheter insertion pain in AVF and relief from RLS among HD patients through the use of lavender essential oil. As a result, future research is encouraged to include a comparison of lavender's effects with those of a placebo group.

Keywords: Aromatherapy; Lavender oil; Pain; Arteriovenous Fistula; Restless Legs Syndrome; Massage

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1. Introduction

Chronic kidney disease (CKD) poses a worldwide public health challenge, resulting in substantial economic burdens on healthcare systems, and is recognized as an autonomous risk factor for cardiovascular diseases (1). Affecting approximately 11-13% of the global population, this condition is characterized by signs of kidney impairment, including an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m² and typically the presence of proteinuria, often assessed through the albumin-to-creatinine ratio (2). Hemodialysis (HD) is the prevailing treatment employed in adults (3). A crucial requirement for initiating HD treatment is to establish sufficient vascular access, with the arteriovenous fistula (AVF) being the most frequently utilized method (4). Typically, patients receive HD treatment about ten times per month by inserting a catheter into the AVF, and this regimen continues either indefinitely or until a successful kidney transplant is achieved (5). The patients experience considerable pain due to the frequent insertion of AVF catheters, which has been attributed to the size and length of the catheter used (6). More than 20% of patients find the pain caused by repeated AVF catheter insertions to be unbearable. This recurrent pain can contribute to depression and a diminished quality of life (7). A 2008 study revealed that catheter insertion pain was a prevalent issue among HD patients and played a role in discouraging individuals over the age of 65 from undergoing HD (8). Restless leg syndrome (RLS) is another complication faced by HD patients. RLS is a common sensory-motor disorder characterized by an irresistible urge to move the legs (9). Reports indicate that 30 to 50% of CKD patients, particularly those undergoing HD, experience RLS (10). This sensory-motor disorder can significantly impact patients' quality of life by affecting their psychological and physiological well-being and daily activities. More than two-thirds of RLS patients also suffer from sleep disturbances (11). To enhance comfort during HD and promote patient compliance with treatment over an extended period, interventions to alleviate pain and RLS, both pharmacological and non-pharmacological, are essential (12, 13). Aromatherapy is a non-pharmacological approach and falls under the umbrella of phytotherapy, which involves using plant-based treatments. Aromatherapy entails the inhalation or massage application of herbal essences to alleviate symptoms (14). Approximately 150 different types of essential oils are employed in aromatherapy, with lavender essen-

tial oil being a noteworthy and extensively used option due to its perceived suitability for managing various mental and physical complications while posing minimal toxicity risks (15, 16). Lavender essential oil, containing components like linalyl acetate and linalool, is recognized for its pain management (17, 18). Aromatherapy, as a non-pharmacological and alternative method, is cost-effective and carries fewer side effects compared to conventional medicine (19). Aromatherapy-massage also stimulates the amygdala and hippocampus within the limbic system of the brain, leading to improvements in physical, emotional, and mental well-being (20). Oils like lavender are applied through skin massage to induce relaxation, alleviate muscle tension, provide anti-anxiety and anti-depressant effects, offer neuroprotection, and reduce inflammation (21-24).

To the best of our knowledge, there has been no previous meta-analysis investigating the impact of lavender on the pain associated with catheter insertion in AVF for HD patients. Likewise, there is no existing research dedicated solely to examining the effects of lavender aromatherapy on RLS. In a prior meta-analysis, the effects of massage were assessed, with three of the included studies specifically examining aromatherapy massage involving lavender (25). Based on the cases discussed, it appears that lavender aromatherapy demonstrates positive outcomes in alleviating various forms of pain. This study aimed to fill these gaps by not only summarizing findings from various studies into a single comprehensive report, but also by quantifying the effect size and significance of lavender essential oil on the mentioned outcomes.

2. Methods

2.1. Study design

This systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (26) and followed the procedures outlined in the Cochrane Handbook for Systematic Reviews of Interventions. The research protocol for this systematic review and meta-analysis Was approved by and registered on PROSPERO (CRD42022355242). Additionally, the study obtained ethical approval from the ethics committee at Esfarayen University of Medical Sciences.

Given the significance of the topic and the conflicting results in existing research regarding the effects of lavender aromatherapy on catheter insertion pain in AVF and RLS in HD patients, this systematic review and meta-analysis sought to consolidate the evidence from randomized controlled trials (RCTs) about the impact of lavender aromatherapy on catheter insertion pain in AVF and RLS among HD patients.

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2.2. PICO framework

To clarify the purpose of the study, the PICO framework was used. Accordingly; population (P): human studies conducted on adult CKD patients undergoing hemodialysis, intervention (I): use of lavender essential oil, comparison (C): control or placebo group to compare with the intervention group, and finally Outcome (O): the RLS and pain related to the insertion of the catheter in the AVF.

2.3. Search strategy

A systematic search was conducted on PubMed, Web of Science, Scopus, Cochrane, ClinicalTrials.gov, and Google Scholar search engine from inception to August 1, 2022, using keywords extracted from Medical Subject Headings, such as "Aromatherapy", "Lavender", "Pain", "Arteriovenous fistula", "Restless legs syndrome", and "Hemodialysis". For example, the search strategy in the PubMed/MEDLINE database was ("Aromatherapy" OR "Lavender" OR "Lavender oil") AND ("Pain" OR "Ache") AND ("Arteriovenous fistula" OR "Arteriovenous aneurysm") AND ("Restless legs syndrome") AND ("Hemodialysis" OR "Renal dialysis"). The studies included in this review exclusively utilized the English language. Two separate authors independently conducted the searches. The exploration of gray literature, encompassing conference presentations, expert opinions, dissertations, research and committee reports, and ongoing research, was not exhaustive in this systematic review. This decision was made due to the potential for incomplete representation of results and the risk that unpublished findings could significantly impact the overall conclusions. It is important to note that "gray literature" pertains to written materials produced in both print and digital formats but falls outside the domain of for-profit publishers' control (27).

2.4. Inclusion and exclusion criteria

The inclusion criteria encompassed articles involving patients aged 18 and above, which examined the use of lavender aromatherapy or aromatherapy massage as interventions to mitigate pain and RLS. These studies were required to have a comparison group (control or placebo), be written in English, and report at least one outcome related to pain or RLS. On the other hand, articles that did not pertain to the topic, those for which the full text was unavailable, as well as reviews, letters to the editor, and quasi-experimental articles were excluded. Also, studies that were not in English were excluded from this systematic review and meta-analysis.

2.5. Study selection

EndNote 8X was employed to organize and manage the references of this systematic review. The selection of studies based on the predefined inclusion and exclusion criteria was conducted independently by two researchers. Initially, duplicate articles were identified through a thorough review of titles, abstracts, and full-text content. Subsequently, to ensure no data loss, this process underwent a manual cross-check. In instances where discrepancies arose between the two researchers during the study selection, the involvement of a third researcher facilitated resolution. The final step involved a meticulous examination of references to safeguard against any inadvertent data omission.

2.6. Data extraction

Using a structured form, we extracted the following details from the eligible studies: first author's name, year of publication, country, sample size, male/female ratio, age, duration and dose of intervention, number of aromatherapy sessions, pain severity, RLS severity, and key findings of the study. The data extraction process was conducted by two researchers, independently, and disagreements were resolved by consultation with the third reviewer.

The scales used to examine pain in HD patients in the studies included in this systematic review and meta-analysis were the visual analog scale (VAS) and numeric Rating Scale (NRS). The Visual Analog Scale (VAS) is frequently employed to gauge subjective sensations like pain in clinical and research environments. It typically comprises a 10-centimeter line, with endpoints symbolizing the utmost extremes of the sensation under investigation. In the context of pain assessment, the left endpoint usually signifies "absence of pain" or "no sensation," while the right endpoint denotes "the most severe imaginable pain" or the highest intensity of the sensation being examined (28). The NRS finds extensive application in clinical and research environments for assessing subjective experiences, primarily pain. This straightforward scale employs a numeric continuum, typically spanning from 0 to 10. Each numeric value corresponds to a specific degree of intensity or severity. Traditionally, 0 signifies the absence of pain or sensation, while 10 signifies the utmost imaginable pain or the highest possible intensity of the sensation under consideration (29).

2.7. Risk of bias

Two authors independently employed the Cochran tool (version 2) for evaluating bias in RCT (Randomized Controlled Trial) studies. This assessment focused on various types of bias, including inadequate outcome data, selective reporting, blinding of participants and personnel, random sequence generation, allocation concealment, and blinding of outcome assessment. The risk of bias was categorized into three levels: high, low, or non-reporting (30).

2.8. Data analysis

We utilized STATA software version 14 for conducting the meta-analysis. To calculate the overall effect size, we extracted sample sizes, mean changes, and standard deviation changes for both the intervention and control groups. For the pain outcome, we reported the Standard Mean Difference (SMD), due to the use of various assessment tools like VAS and NRS. For the RLS outcome, we reported the Weighted Mean Difference (WMD). Our findings were presented using forest plot diagrams, and significance levels were determined based on a 95% confidence interval (CI). Heterogeneity was assessed using the I^2 statistic, which is categorized as follows: 0% to 25% indicating low heterogeneity, 25% to 50% suggesting moderate heterogeneity, 50% to 75% reflecting substantial heterogeneity, and 75% to 100% signifying significant or considerable heterogeneity. To further explore the data, subgroup analyses were conducted based on various factors. For the pain outcome, subgroups were established according to the assessment scale used, type of intervention, lavender concentration, type of control group, and the country of study. For the RLS outcome, subgroup analysis considered the number of sessions and the duration of the intervention.

2.9. Sensitivity analysis

Sensitivity analysis was employed to assess how the exclusion of each study affected the overall effect size outcome.

2.10. Publication bias

Publication bias was evaluated using a Funnel plot, followed by the examination of results from the Egger and Begg's tests. To address potential publication bias, the trim and fill method was utilized for correction.

3. Results

3.1. Study selection

As shown in Figure 1, a thorough search of electronic resources yielded a total of 291 articles. Within this pool of studies, 31 were eliminated due to redundancy, while 205 were removed because they did not align with the study's objectives and lacked an experimental nature. The full texts of 41 studies were then evaluated in the next stage; 24 studies were dropped due to issues with their designs and unsatisfactory findings (Such as not using appropriate statistical tests, not reporting statistical significance, etc.), and one study was dropped for a lack of the required data. Finally, eleven studies were included in this systematic review and meta-analysis.

3.2. Characteristics of included studies

As shown in Table 1, a total of 722 patients undergoing hemodialysis were included in eleven studies (7, 9, 16, 21, 31-

37). The mean age of the patients was 55.89 (SD = 9.82) years. 48.34% of the participants were in the intervention group. Seven studies (7, 9, 21, 31-33, 36) were conducted in Iran and four studies (16, 34, 35, 37) were conducted in Turkey. The type of aromatherapy was massage-inhalation in five studies (9, 21, 31, 32, 36), inhalation in four studies (16, 33, 34, 37), and topical in two studies (7, 35). Also, six studies (7, 16, 33-35)(37) examined pain and five studies (9, 21, 31, 32, 36) examined RLS.

3.3. Risk of bias

Generation of a randomization sequence was high-risk in two studies (32, 37). In two studies, the participants were not blinded (21, 37). Also, in one study, the evaluators were not blinded (9). The results of the study were correctly reported and the tools used to measure them were found to be appropriate. In two studies, the sample size of the intervention and control groups was found to be insufficient, and therefore they were considered to have a high risk of bias (32, 37). In one article, "age group" was heterogeneous between the intervention and control groups before the initiation of the intervention and therefore, the study had a high risk of bias (Figure 2) (16).

3.4. Meta-analysis

3.4.1. Pain severity

The results showed that aromatherapy with lavender reduced the average pain of catheter insertion into AVF compared to the control group, which was statistically significant (SMD: -1.60, 95%CI: -2.32 to -0.87, Z=4.32, I2:90.3%, P<0.001) (Figure 3).

The results of the subgroup analysis according to the scale (VAS, NRS), the type of intervention (inhalation and topical), and the concentration of the essential oil used (pure and diluted) showed that the use of lavender significantly reduced the intensity of pain in the intervention group compared to the control group (Table 2). Also, the subgroup analysis showed that the lavender essential oil significantly decreased the pain intensity compared to no intervention (P<0.001), but it was not significant compared to the placebo group (P=0.12). Comparing the intervention and control groups in the studies conducted in Iran, showed that there was no statistically significant difference between them (P=0.07) (Table 2).

3.4.2. RLS severity

Aromatherapy with lavender reduced the average severity of RLS compared to the control group, which was statistically significant (WMD: -13.21, 95%CI: -17.50 to -8.91, Z=6.03, I2:93.0%, P<0.001) (Figure 4).

The results of the subgroup analysis according to the number of sessions (≥9 vs. <9) and the intervention duration (≥15 min vs. <15 min) showed that the intervention significantly

decreased the severity of RLS in the intervention group compared to the control group (Table 2).

3.5. Sensitivity analysis

Sensitivity analysis showed that the overall effect sizes regarding the effects of lavender on the pain (95%CI: -2.56 to -0.69) and RLS (95%CI: -19.35 to -7.41) did not depend on a single study.

3.6. Publication bias

Based on the visual inspection of the funnel plot, an asymmetry was observed; however, when the Begg (P=0.81) and Egger's regression tests (P=0.33) were performed, no significant publication bias was seen for the effects of lavender on RLS (Figure 5). Also, Egger's regression test indicated possible publication bias for the effect of lavender on pain intensity (P=0.01). Therefore, we did the trim-and-fill method and found that adding missing studies did not change the overall effect size (SMD: -1.60, 95%CI: -2.32 to -0.87).

4. Discussion

This study was conducted to examine the existing evidence regarding the impact of lavender essential oil on the severity of pain during catheter insertion in AVF as well as its effect on RLS in HD patients. Ultimately, the findings demonstrated that the use of lavender resulted in a significant reduction in both pain severity and RLS outcomes. The alleviation of pain in hemodialysis patients through the application of lavender essential oil in aromatherapy may be attributed to its psychological impacts, potential endorphin release, anti-inflammatory properties, and the enhancement of sleep quality (38-40). Also, the alleviation of RLS in HD patients following aromatherapy with lavender essential oil may be attributed to the reduction of stress, enhancement of sleep quality, sensory stimulation, improved blood circulation, and relief from pain (9, 25, 36, 41).

In the majority of the studies examining the effect of lavender on pain, the intervention yielded a notable reduction in pain intensity.

However, there was one study in which after the intervention the pain levels exhibited a statistically significant difference, but when considering the mean change before and after the intervention, no significant difference was observed between the intervention and control groups (33). In this study, participants inhaled lavender at a concentration of 10% and were compared to a control group. Furthermore, the intervention consisted of only three sessions, with three drops administered per session. It's worth noting that the number of sessions, the number of drops, and the concentration of essential oil used in this study were notably lower compared to the majority of studies included in the current meta-analysis.

Subgroup analysis results indicated that the pain intensity did not exhibit a significant reduction in the intervention group when compared to the placebo group. However, notably lower pain was observed in the intervention group compared to those not receiving the intervention. This discrepancy may be attributed to the placebo effect, which can activate distinct brain regions and involve neurotransmitters such as opiates and dopamine (42).

Furthermore, the outcomes of the subgroup analysis revealed that studies conducted in Iran did not demonstrate a significant reduction in pain within the intervention group when compared to the control group, as opposed to studies conducted in Turkey. Several factors, including the limited number of studies conducted in Iran and potential cultural differences, may contribute to this outcome. Notably, among the three studies conducted in Iran, two of them compared the intervention group with a placebo group, while in Turkey, only one out of the four studies made this specific comparison (34).

Regarding the RLS outcome, all five studies incorporated into the analysis demonstrated that the use of lavender led to a reduction in RLS symptoms. Notably, a previous meta-analysis study (25) investigating the impact of massage on RLS in HD patients included three articles out of the five studies that were ultimately included in the final analysis (9, 31, 36). The findings from this earlier study also supported the notion that aromatherapy massage using lavender essential oil significantly reduced RLS symptoms, aligning with the results of the current study.

Subgroup analysis results indicated that the number of sessions (9 sessions or more vs. less than 9) had a significant impact on reducing RLS symptoms. Similarly, the duration of the intervention (15 minutes or more vs. less than 15 minutes) significantly affected pain reduction with the use of lavender oil. However, due to the limited number of studies available, arriving at a conclusive decision was challenging. Future research endeavors may explore the effects of both the number of sessions and the duration of the intervention on the severity of RLS.

In addressing the risk of bias within the included articles, researchers must place a heightened emphasis on key aspects. This includes ensuring the robustness of random allocation generation and concealment, implementing effective blinding procedures for both participants and evaluators, and meticulously considering the utilization of an adequate sample size as well as ensuring homogeneity in demographic information before the commencement of the study.

4.1. Implications for clinical practice and research

In summary, aromatherapy stands as a straightforward, swift, cost-effective, and minimally intrusive approach. Furthermore, it can be independently administered by nurses for nursing interventions. In consideration of these outcomes, aromatherapy may serve as a valuable complement to other therapies for aiding hemodialysis patients dealing with both RLS and the discomfort associated with needle insertion in the AVF.

4.2. Limitations

In our current study, the primary objective was to scrutinize all studies accessible through extensive electronic searches in reputable databases. Nevertheless, we encountered difficulties in obtaining the full text of an article published in Turkey. Although we reached out to the corresponding author via email, unfortunately, we did not receive a response. In total, we analyzed eleven articles, which investigated two primary outcomes, conducted in two distinct countries, namely Turkey and Iran. It is worth noting that this geographical diversity may influence the generalizability of our findings in different cultural contexts. Despite our exhaustive database searches, it is important to acknowledge the potential for reporting bias, as not all relevant studies on this topic may have been uncovered. Lastly, it is essential to recognize that our study exclusively included research reported in English, which may introduce a language bias into our findings.

5. Conclusion

In summary, this systematic review and meta-analysis provided compelling evidence that lavender essential oil effectively reduces the pain experienced during catheter insertion in AVF and alleviates RLS symptoms in HD patients. The subgroup analysis results highlight the potential for future research to explore the comparison between this intervention and a placebo group in greater detail. Furthermore, it is advisable for researchers embarking on future studies to carefully outline their methods for random allocation, concealment of random allocation, blinding procedures, and ensuring an adequate sample size. These considerations can enhance the quality and reliability of future research in this area.

6. Declarations

6.1. Acknowledgments

None.

6.2. Consent for publication

The authors declare that there is no conflict of interest.

6.3. Funding

None.

6.4. Authors' contribution

All authors have agreed on the final version, and those listed as authors are qualified for authorship according to the following criteria: Have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; been involved in drafting the manuscript or revising it critically for important intellectual content; given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

6.5. Availability of data

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

6.6. Ethics approval statement

The protocol of this systematic review and meta-analysis was registered in PROSPERO (CRD42022355242). Also, the present study was approved by the ethics committee of Esfarayen University of Medical Sciences.

6.7. Using artificial intelligent chatbots

None.

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Table 1: The basic characteristics and main results of the studies are included in the systematic review and meta-analysis

First Author/year	Location	Sample size (Control/Placebo /Intervention)	Age • Control group • Intervention group • Total	• Control • Placebo	Type of Intervention	• Administration route • Number of sessions • Dosage • Duration (min)	Tool	Outcome	Main results
Ozen et al., 2022 (37)	Turkey	24 (11/0/13)	• 63.00 (SD=14.79) • 56.77 (SD=13.29) • 59.88 (SD=14.04)	None	Lavender essence was diluted with sweet almond oil at a ratio of 1:10	• Inhalation • 12 • 3 drops • 3	VAS	Pain	Lavender aromatherapy could be a good option for reducing the pain level of HD patients.
Tüzün Özdemir et al., 2021 (35)	Turkey	60 (30/0/30)	N/R	None	100% lavender essential oil	• Topical • 3 • 3 drops • 5	VAS	Pain	After inhaler and topical application of lavender oil, a significant decrease in the severity of pain was recorded for patients at the time of arterial insertion of needles.
Sahin et al., 2021 (34)	Turkey	74 (0/38/36)	• 53.62 (SD=11.03) • 50.75 (SD=18.02) • 52.18 (SD=14.52)	Olive oil	100% lavender essential oil	• Inhalation • 3 • 5 drops • 5	NRS	Pain	Inhalation of lavender aromatherapy was effective in relieving the pain of AVF puncture in patients.
Taşana et al., 2019 (16)	Turkey	60 (30/0/30)	N/R	None	The mixture contains a 1:10 ratio of lavender oil and sweet almond oil	• Inhalation • 3 • 5 drops • 3 to 5	VAS	Pain	Lavender oil inhalation to patients undergoing HD decreased pain level.
Ghods et al., 2015 (7)	Iran	102 (34/34/34)	N/R	• None • 3 puffs of water were sprayed	100% lavender essential oil	• Topical • 3 • 3 puffs (0.3 ml) • 5	NRS	Pain	The topical application of lavender significantly decreases moderate intensities of pain during the insertion of dialysis needles.
Bagheri-Nesami et al., 2014 (33)	Iran	92 (0/46/46)	• 58.06 (SD=1.83) • 60.95 (SD=1.93) • 59.50 (SD=1.88)	Sweet almond oil	lavender essence with a concentration of 10% (diluted 1:10 with sweet almond oil)	• Inhalation • 3 • 3 drops • 5	VAS	Pain	A significant difference was observed between the two groups in terms of the mean score of pain severity
Amrollahi et al., 2022 (32)	Iran	41 (20/0/21)	N/R	Routine care	Not mentioned	• Massage-inhalation • 12 • 10 cc • 30	RLS rating scale	RLS	The use of lavender oil during massage therapy can serve as a complementary treatment along with other care to alleviate the symptoms of RLS
Ghasemi et al., 2021 (21)	Iran	70 (0/35/35)	• N/R • N/R • 50.46 (SD=0.86)	Relaxing techniques	Linalool	• Massage-inhalation • 24 • 10 cc • 15	RLS rating scale	RLS	Aromatherapy massage reduced the RLS severity, but reflexology did not appear to cause any significant reduction in it.
Oshvandi et al., 2021 (36)	Iran	70 (35/0/35)	N/R	Routine care	(27.11%) and linalyl acetate (23.33%) in the ratio of 3:3:2:2 mL in 100 mL of coconut carrier	• Massage-inhalation • 9 • 10 to 15 cc • 18	RLS rating scale	RLS	Aromatherapy prepared with lavender oil and sweet orange may be recommended to reduce the RLS level of HD patients.

Table 1: The basic characteristics and main results of the studies are included in the systematic review and meta-analysis

First Author/year	Location	Sample size (Control/Placebo/Intervention)	Age • Control group • Intervention group • Total	• Control • Placebo	Type of Intervention	• Administration route • Number of sessions • Dosage • Duration (min)	Tool	Outcome	Main results
Mirbagher Ajorpaz et al., 2019 (31)	Iran	59 (30/0/29)	• 56.10 (SD=13.56) • 56.95 (SD=13.50) • 56.52 (SD=13.53)	Routine care	Oil	• Massage-inhalation • 12 • 10 to 15 cc • 45	RLS rating scale	RLS	The differences between the control and lavender oil groups, as well as the control and glycerin oil groups, were significant.
Hashemi et al., 2015 (9)	Iran	70 (35/0/35)	• 56.10 (SD=13.56) • 57.50 (SD=14.60) • 56.80 (SD=14.08)	Routine care	Essential oil 1.5%	• Massage-inhalation • 6 • 10 to 15 cc • 10	RLS rating scale	RLS	The lavender oil massage was effective in improving RLS in HD patients.

HD: hemodialysis; VAS: visual analog scale; NRS: numeric Rating Scale; N/R: not reported ;SD: standard deviation;
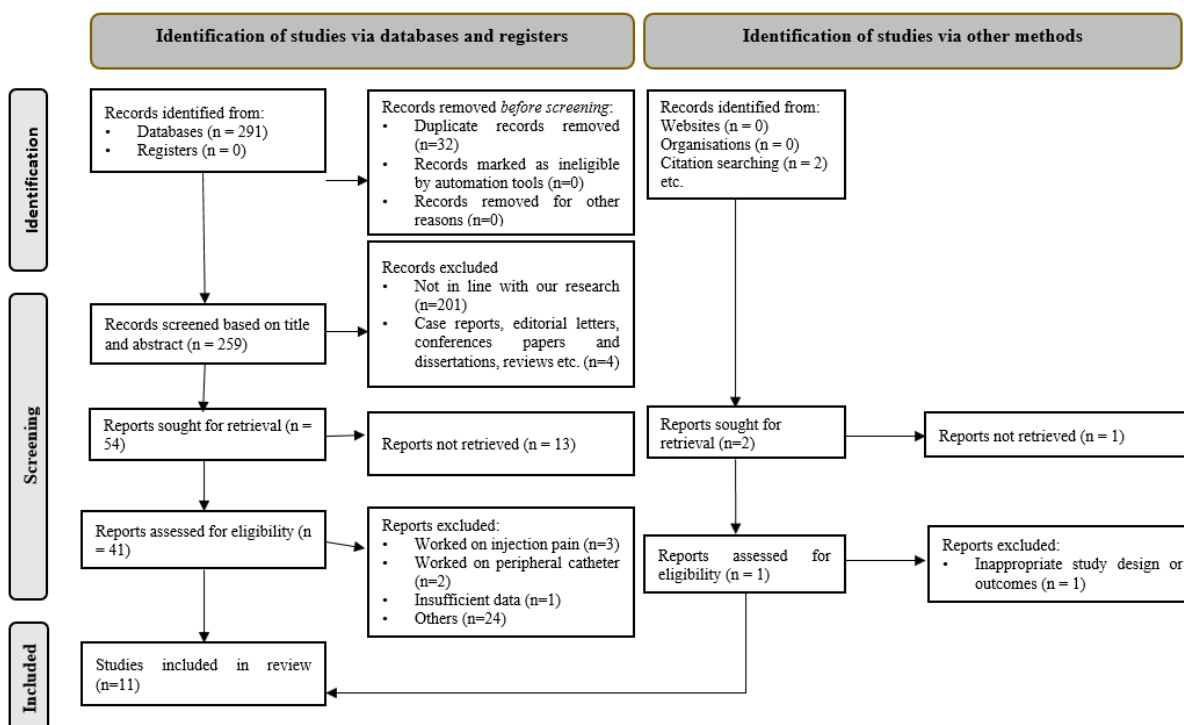RLS: restless legs syndrome; AVF: arteriovenous fistula.

Figure 1: Flow diagram of study selection.

Table 2: Results of subgroup analysis

Outcome	Source	Sub-categories	Number of studies	Effect size (SMD)	95% CI	Z	P	I^2
Pain	**Scale**	VAS	5	-1.89	-3.11 to -0.67	3.04	0.002	93.6%
		NRS	3	-1.19	-1.93 to -0.45	3.15	0.002	79.1%
	Intervention	Inhalation	5	-1.93	-3.11 to -0.75	3.20	0.001	94.0%
		Topical	3	-1.09	-1.65 to -0.53	1.39	<0.001	56.2%
	Lavender concentration	100% lavender essential oil	4	-1.61	-2.88 to -0.34	2.48	0.01	94.4%
		Diluted oil	4	-1.57	-2.44 to -0.70	3.55	<0.001	83.3%
	Control	No intervention	5	-2.03	-2.79 to -1.27	5.25	<0.001	79.7%
		Placebo	3	-0.90	-2.02 to 0.23	1.55	0.12	93.0%
	Country	Turkey	5	-2.18	-2.64 to -1.72	9.37	<0.001	46.4%
		Iran	3	-0.52	-1.09 to 0.05	1.80	0.07	70.3%
RLS	**Session**	< 9 sessions	2	-14.41	-22.40 to -6.42	3.54	<0.001	94.5%
		≥9 session	3	-12.40	-18.14 to -6.67	4.24	<0.001	93.3%
	Duration	<15 min	2	-8.78	-11.45 to -6.12	6.47	<0.001	63.5%
		≥15 min	3	-16.35	-18.70 to -14.01	13.68	<0.001	49.3%

CI: confidence interval; VAS: visual analog scale; NRS: numeric Rating Scale; RLS: restless legs syndrome; SMD: standard mean difference.

Author name	Random sequence generation	Allocation concealment	Blinding of participation and personal	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases
Ozen *et al.*, 2022 (37)	−	+	−	+	+	+	−
Tüzün Özdemir *et al.*, 2021 (35)	+	+	+	+	+	+	+
Sahin *et al.*, 2021 (34)	+	+	+	+	+	+	+
Taşana *et al.*, 2019 (16)	+	+	+	+	+	+	−
Ghods *et al.*, 2015 (7)	+	+	+	+	+	+	−
Bagheri-Nesami *et al.*, 2014 (33)	+	+	+	+	+	+	+
Amrollahi *et al.*, 2022 (32)	−	+	+	+	+	+	−
Ghasemi *et al.*, 2021 (21)	+	+	−	+	+	+	+
Oshvandi *et al.*, 2021 (36)	+	+	+	+	+	+	+
Mirbagher Ajorpaz *et al.*, 2019 (31)	+	+	+	+	+	+	+
Hashemi *et al.*, 2015 (9)	+	+	+	−	+	+	+

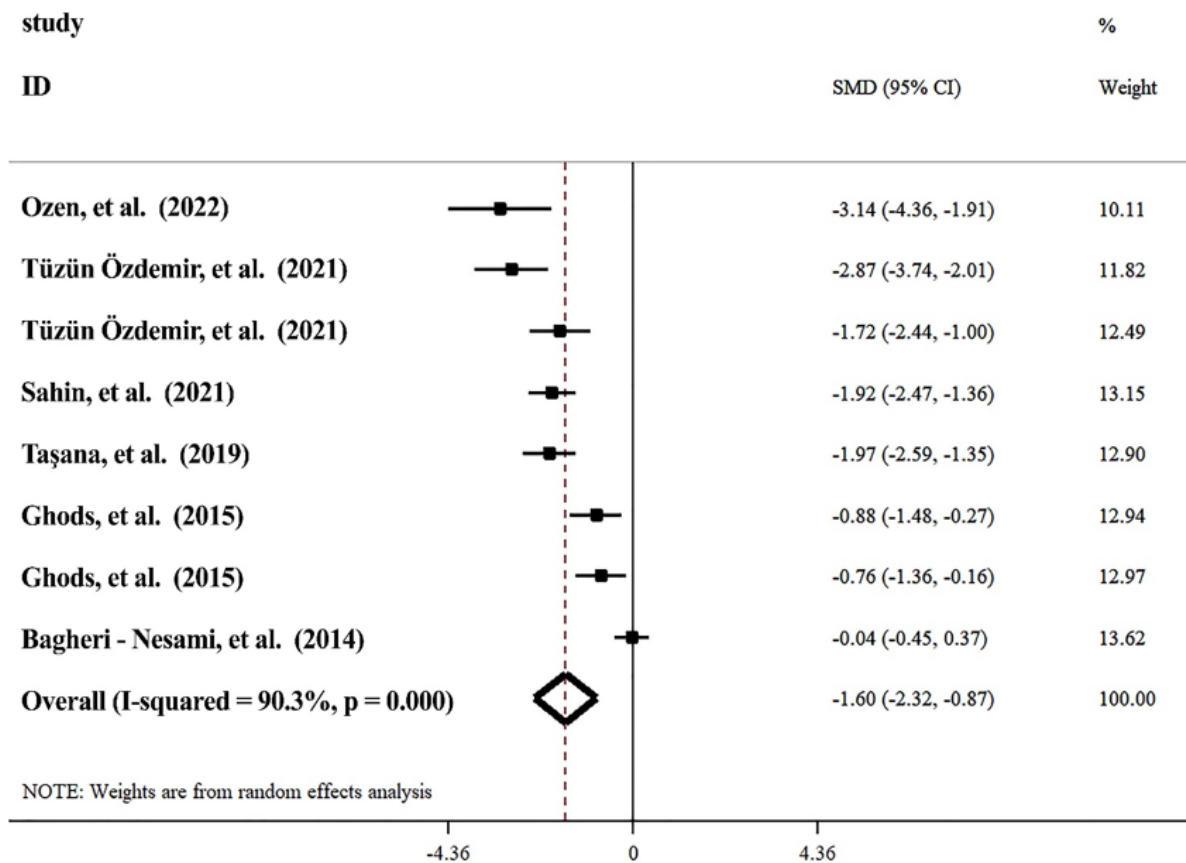**Figure 2:** Risk-of-Bias of included studies based on Rob II.

Figure 3: Effect of aromatherapy with lavender on pain of catheter insertion in arteriovenous fistula. (SMD: standard mean difference).
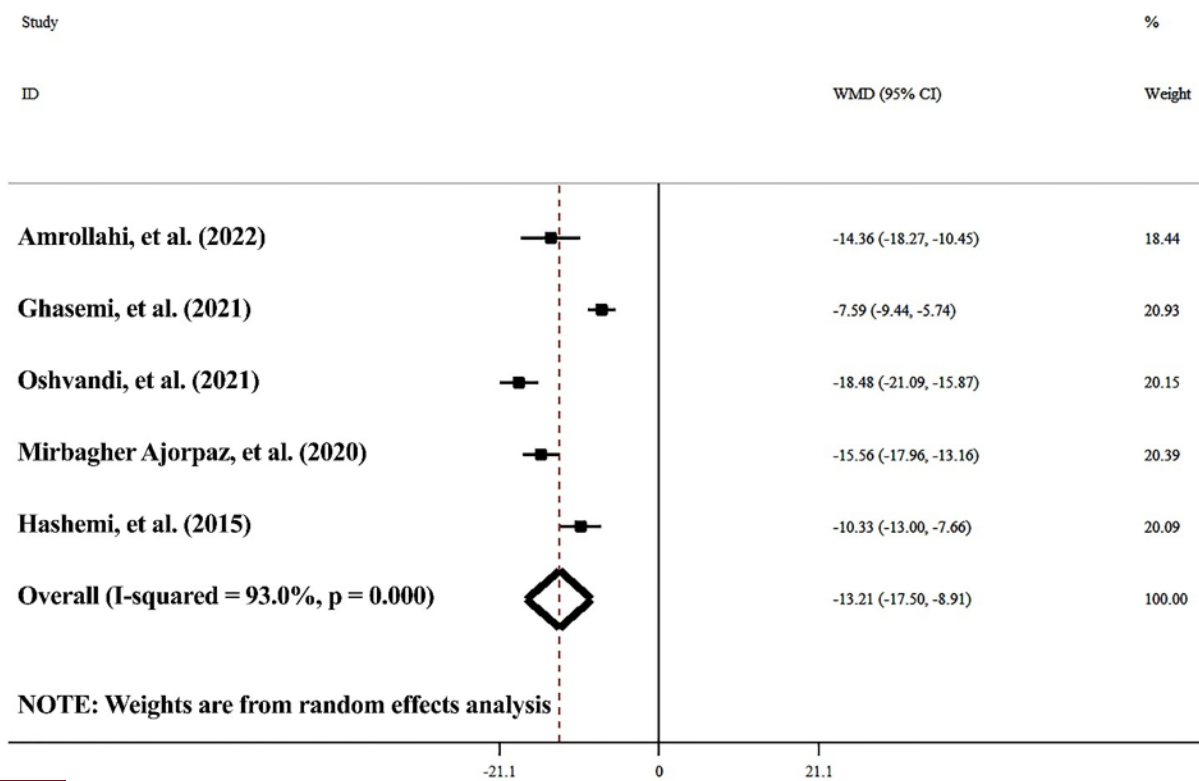
Figure 4: Effect of aromatherapy with lavender on restless legs syndrome. (WMD: weighed mean difference).
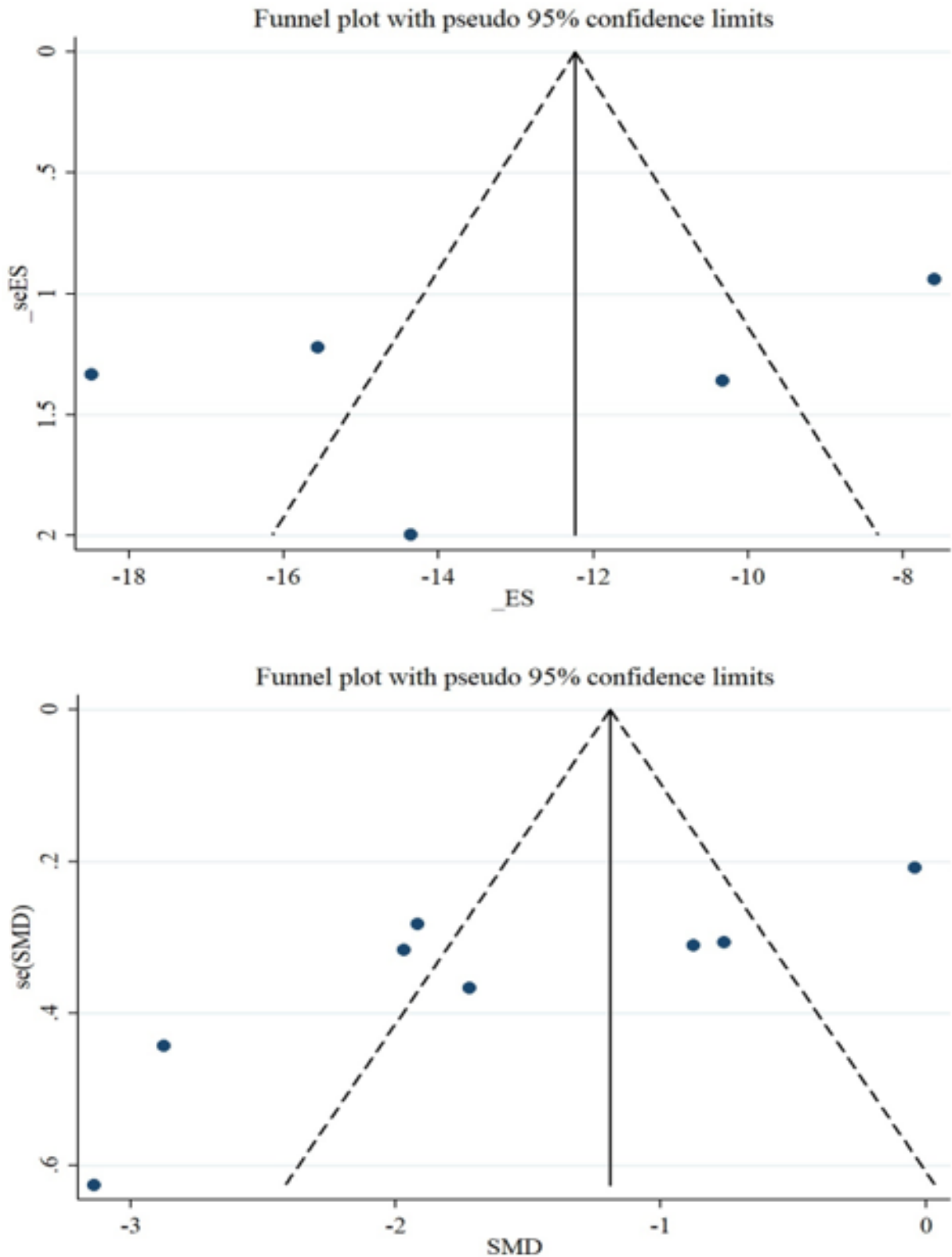
Figure 5: Funnel plot for outcome of restless legs syndrome (high) and pain (low).