



# Effect of Lavender Aromatherapy on Anxiety and Fatigue in Hemodialysis Patients: A Systematic Review and Meta-Analysis

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(Received 16 Jun 2023; accepted 14 Sep 2023)

## Abstract

**Background:** Several studies have evaluated the effects of lavender essential oil on the anxiety of hemodialysis (HD) patients, but most of them did not estimate the pooled effect size. The current systematic review and meta-analysis was conducted to evaluate the effects of lavender on anxiety and fatigue among HD patients.

**Methods:** Eligible studies were selected based on the PRISMA steps and protocol. Literature was retrieved from PubMed, Web of Science, Scopus databases, Cochrane, ClinicalTrials.gov, and Google Scholar Search Engines until Sep 2022. The risk of bias and analysis were evaluated using version 2 of the Cochrane risk-of-bias tool and STATA v.14 software, respectively. Effect sizes were pooled using random effect models.

**Results:** Nine studies were included. Lavender oil significantly reduced the average anxiety of HD patients compared to the control group (SMD: -2.51, 95% CI: [-3.56, -1.45], Z=4.67, P<0.001, I<sup>2</sup>:89.9%). Also, it significantly reduced the average fatigue compared to the control group (SMD: -1.56, 95% CI: [-2.49, -0.63], Z=3.29, P=0.001, I<sup>2</sup>:92.2%). Subgroup analysis indicated controversial results regarding session frequency and drop number of lavender oil.

**Conclusion:** Using Lavender oil significantly reduced fatigue and anxiety in HD patients.

**Keywords:** Lavender; Aromatherapy; Anxiety; Fatigue; Hemodialysis; Meta-analysis

## Introduction

Chronic kidney disease (CKD) refers to kidney damage lasting for more than three months originated from various factors. A significant number of CKD patients eventually progress to end-stage renal disease (ESRD), requiring treatment with renal replacement therapy (RRT) (1). Hemodialy-

sis (HD) is considered the most popular and cost-effective RRT for ESRD patients in most countries. The global population of maintenance HD patients is rapidly increasing (2). However, patients on HD often face severe psychological and social challenges brought about by CKD.



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These occurred due to frequent hospital visits, long waiting times for treatment, feelings of uncertainty about the future, fear of mortality, and diminished self-confidence.

Given the importance of psychological issues, numerous investigations have performed the prevalence of related symptoms in HD patients, both in Iran and other countries. HD patients experience a high prevalence of psychiatric disorders including anxiety, depression, and fatigue (3). Anxiety, in particular, stands out as a significant factor (4). It is characterized by worry and irritability arising from an increased awareness of a real or imaginary threat to the one's existence (5, 6). Anxiety is considered a common problem in HD patients with prevalence rates ranging from 19% to 43% (7). Although survival time has increased due to HD treatment, living with a life-threatening disease can ultimately lead to death anxiety (8). The presence of mental disorders significantly impairs adherence to treatment regimens such as follow-up HD, quality of life, hospitalizations frequency, and overall mortality. Hence, implementing effective interventions to decrease anxiety is crucial (7).

Fatigue is another common complication experienced by HD patients. It is characterized by a persistent feeling of weakness, lack of energy, and motivation (9, 10). Also, it considered prevalent and bothersome problem in adults, especially among cancer and HD patients. Fatigue can manifest at any stage of the disease's progression (9, 11), associated with an increased risk of physical and mental illnesses such as cardiovascular events, anxiety, depression, and sleep disorders (12, 13). Although the exact mechanisms underlying fatigue remain unclear, failure to achieve HD adequacy is related to it.

Pharmacological and non-pharmacological interventions have been proposed for managing anxiety and fatigue to improve comfort during HD and facilitate patients' compliance with treatment over a more extended period (13, 14). Non-pharmacological interventions, such as isometric exercise, massage, and aromatherapy, have indicated effectiveness in managing HD patients' well-being (15, 16). Aromatherapy a form of phy-

totherapy, which utilizes plant-derived essences, has considered a cost-effective intervention with minimal side effects. It involves using herbal essences such as inhalation and massage to reduce disease symptoms (17). All forms of essential oils can be used in aromatherapy. Lavender oil is one of the most popular essential oils that widely used and studied in human treatment to alleviate various mental and physical symptoms and complications (18, 19). Considering a non-pharmacological intervention, lavender aromatherapy has demonstrated cost-effectiveness and a low incidence of side effects (20).

Studies investigating aromatherapy's effects on HD patients have reached conflicting conclusions. While one study evaluated the effect of lavender oil (administered three times a week for one month) on the fatigue of HD patients and found no statistically significant difference between control and intervention groups (21), others have suggested that aromatherapy could significantly reduce fatigue and anxiety in this population (22, 23).

There was no meta-analysis study to investigate the effect of lavender on the anxiety of HD patients. However, fatigue has been studied in systematic reviews, and the results were reported qualitatively (24). A meta-analysis study in Chinese was done on fatigue among adult patients, and HD patients were not separated in the results (13). Moreover, another study measured the effect of different essential oils among HD patients (25). Thus, no specific study has investigated the effect of lavender essential oil on fatigue among HD patients.

We aimed to investigate lavender essential oil's effects on adult HD patients' anxiety and fatigue.

## **Methods**

This systematic review followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and the Cochrane Handbook for Systematic Reviews of Interventions (26). The present systematic review and me-

ta-analysis protocol was approved in PROSPERO (CRD42022355242).

**Search strategies**

The search strategy was combined using the PICO framework. Studies that evaluated the effect of lavender on fatigue and anxiety severity in adult HD patients were included in the study. A systematic search was conducted on PubMed,

Web of Science, Scopus databases, Cochrane, ClinicalTrials.gov, and Google Scholar Search Engines using keywords extracted from Medical Subject Headings (Mesh), such as “Aromatherapy”, “Lavender”, “fatigue”, “anxiety”, and “Hemodialysis”, from the inception to Sep 2022. We provided details of search in each database in Table 1. English was the only language used in the studies.

**Table 1:** Details of search conducted in the databases

Databases	Search strategy	Preliminary searches	Piloting of the study selection process
PubMed	((("Hemodialysis"[Mesh] OR "Hemodialysis" [tiab] OR "Hemodialysis"[Title/Abstract] OR "Renal Dialysis"[Mesh] OR "Renal Dialysis" [tiab] OR "Renal Dialysis"[Title/Abstract] AN))) AND ((("Hemodialysis"[Mesh] OR "Hemodialysis" [tiab] OR "Hemodialysis" [Title/Abstract] OR "Renal Dialysis"[Mesh] OR "Renal Dialysis" [tiab] OR "Renal Dialysis" [Title/Abstract])) AND (("Fatigue"[Mesh] OR "Fatigue"[tiab] OR "Fatigue"[Title/Abstract] OR ("Anxiety"[Mesh] OR "Anxiety"[tiab] OR "Anxiety"[Title/Abstract]))))	A total of 1,731 articles were found by combining keywords with Boolean operators (AND, OR). The search strategy comprised the selection of Mesh fields as well as the title/abstract to refine the query in the search box.	Irrelevant articles and non-RCT designs (review, letter, case reports and, etc.) were excluded (n=1750). Abstracts and full text of remaining articles were checked and 7 studies were identified as suitable for data extraction. Also, references and citations within each eligible article were assessed, resulting in the analysis of 2 additional studies.
Scopus	TITLE-ABS-KEY (“Aromatherapy” OR “Lavender” OR “Lavender oil”) AND TITLE-ABS-KEY (“fatigue” OR “anxiety”) AND TITLE-ABS-KEY (“Hemodialysis” OR “Renal dialysis”)	After utilizing the advanced search option and narrowing down the selection to the title, abstract, and keywords, a total of 29 studies were discovered.	12 articles were in line of our purpose. Finally, 5 studies were eligible to assess the full-texts that were similar to the studies found in PubMed databases.
Google Scholar	("Aromatherapy" OR "Lavender" OR "Lavender oil") AND ("fatigue" OR "anxiety") AND ("Hemodialysis" OR "Renal dialysis")	2800 articles were eligible based on search strategy.	Out of the total 1,778 articles, none of them aligned with the study aims. However, out of the 26 full-texts that were examined, only 7 articles were found suitable for data extraction.
Cochrane	Title Abstract Keyword ("Aromatherapy" OR "Lavender" OR "Lavender oil") AND Title Abstract Keyword ("fatigue" OR "anxiety") AND Title Abstract Keyword ("Hemodialysis" OR "Renal dialysis")	We gathered 39 research papers through an extensive search. Our search strategy included considering the title, abstract, and keywords.	12 studies were identified as suitable to assessed the full-texts. Finally, 7 articles were considered to extract their data.
Web of sciences	((TS=("Aromatherapy" OR "Lavender" OR "Lavender oil" )) AND TS=("fatigue" OR "anxiety" )) AND TS=("Hemodialysis" OR "Renal dialysis")	After using advanced search and combining keywords with search operators, a total of 26 articles were discovered.	14 articles were evaluated, and 5 full-texts were included in the final analysis.
clinicaltrials.gov	Condition or disease :("Hemodialysis" OR "Renal dialysis") AND Intervention/Treatment: ("Aromatherapy" OR "Lavender" OR "Lavender oil") AND Other terms: ("fatigue" OR "anxiety")	Three study protocols have been registered.	One study was related to the inclusion criteria.

Two authors conducted the database searches independently (MF, GRM). Discrepancy between

of authors resolve with scientific discussion and opinion of third author (LJ). The grey literature,

which includes conference presentations, expert opinions, dissertations, research and committee reports, and ongoing research, was not thoroughly searched and, therefore, not included in the review and meta-analysis. The term "grey literature" refers to written works created in print and digital form but not peer-reviewed or under the control of for-profit publishers (27).

#### ***Inclusion and exclusion criteria***

The inclusion criteria were articles in which hemodialysis patient, age over 18 years, use of aromatherapy with lavender oil, comparison with a control or placebo group, English article language, and outcomes of anxiety or fatigue were investigated. Also, Exclusion criteria included lack of access to the full text of articles and qualitative, letters to the editor, quasi-experimental and review studies.

#### ***Study selection***

The systematic review's data were managed with EndNote 8X. Based on the inclusion and exclusion criteria, the studies for this review were chosen separately by the two researchers (MF, GRM). Any disagreements between the first two researchers were resolved during a third researcher's selection of the studies (LJ). Duplicate articles were initially weeded out by looking at the titles, abstracts, and full texts of article. References were finally carefully examined to prevent data loss.

#### ***Data extraction***

Data extraction was carried out independently by two investigators (MF, KY). Using a structured form, the following details were extracted from the eligible studies: first author name, year of publication, country, sample size, duration and dose of lavender aromatherapy intervention, frequency of aromatherapy sessions, scales to measure outcomes, fatigue and anxiety severity score, and key findings of studies. Required data for meta-analysis were entered into an Excel file.

#### ***Risk of bias***

Using the Cochran tool (version 2) for clinical trial research, two authors independently assessed the risk of bias in RCT studies (MF, GRM). The biases in this tool include insufficient outcome data, selective reporting, blinding of participation and individual, random sequence generation, allocation concealment, and blinding of outcome evaluation. High, low, and non-reporting were the three classifications for bias risk (28).

#### ***Statistical analysis***

Quantitative analysis was performed in STATA software version 14. The degree of heterogeneity was checked with the I<sup>2</sup> statistic. Due to the heterogeneity of over 50%, the random effects model was used to estimate the standard mean difference (SMD) as the pooled effect size. The forest plot was used to report the effect sizes. Also, Sub-group analysis was applied to check the source of heterogeneity. Publication bias was determined by visual inspection of the funnel plot. Egger and Begg's tests were used to evaluate the publication bias quantitatively. The trim and fill method was done to correct the publication bias (29, 30). Sensitivity analysis evaluated each study's effect on the pooled effect size. We considered a 95% confidence interval to determine the significance level.

## **Results**

#### ***Search results***

Finally, nine studies related to anxiety (22, 31-34) and fatigue were included in the final analysis (21-23, 35, 36) (Fig. 1). The characteristics of the included RCTs are outlined in Table 2. One study reported both outcomes (22). In all studies, lavender was administered through inhalation. In two studies The State-Trait Anxiety Inventory (STAI) (31, 32) was used in measuring anxiety, while the other three studies (22, 33, 34) employed different tools. Three studies measured the outcome of fatigue with the Fatigue Severity Scale (21-23), while others used various other tools (35, 36) (Table 2).

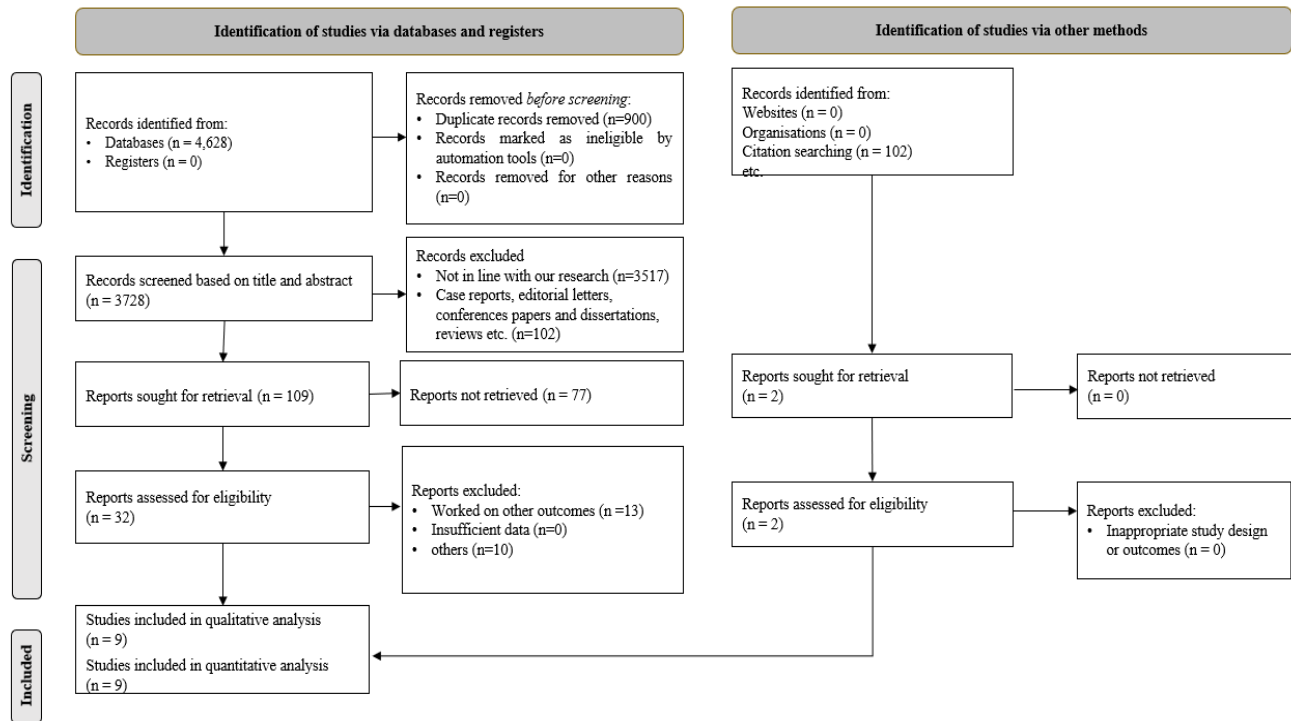


Fig. 1: Flow diagram of study selection

Table 2: Basic characteristics and main results of the studies included in the systematic review and meta-analysis

<i>First Author/year</i>	<i>Sample size (Control/Placebo/Intervention)</i>	<i>Control</i> <i>• Placebo</i>	<i>Type of Intervention</i>	<i>Aromatic type</i> <i>• Number of aromatherapy sessions</i> <i>• Dosage</i> <i>• Duration (min)</i>	<i>Tool</i>	<i>Outcome</i>	<i>Main results</i>
Ozen, et al., 2022 (31)	24(11/0/13)	-R/C -None	Lavender essence was diluted with sweet almond oil at a ratio of 1:10	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• 12</li> <li>• 3 drops</li> <li>• 3</li> </ul>	STAI	Anxiety	Lavender aromatherapy could be a good option for reducing the pain, anxiety, and discomfort level of HD patients.
Sahin et al., 2021 (32)	74(0/38/36)	-none - Olive oil	100% lavender essential oil	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• three times a week</li> <li>• Five drops Oil 5%</li> <li>• 5</li> </ul>	State-Trait Anxiety Inventory (STAI)	Anxiety	halation of lavender aromatherapy was effective in relieving pain of AVF puncture and anxiety in patients

Table 2: Continued...

Karadag, et al., 2019 (37)	60(30/0/30)	-R/C -None	2-mL lavender +98-mL water (2%)	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• 30 days (2 or 3 times a week)</li> <li>• 2</li> <li>• 20</li> </ul>	AI) - Beck Anxiety Inventory were - Fatigue Severity Scale	- Anxiety - Fatigue	Mean scores of fatigue and anxiety decreased significantly following aromatherapy and also fatigue and anxiety levels declined
Senturk, et al., 2018 (45)	34(17/0/17)	-R/C -None	Lavender oil was supplied to the intervention group in 15-mL lightproof blue bottles that were tightly closed with a metal lid to prevent volatility	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• 1 week</li> <li>• 2</li> <li>• 30</li> </ul>	- Hamilton Anxiety Assessment Scale	- Anxiety	The mean score of total and subdimensions of Hamilton Anxiety Assessment Scale of intervention group and control group was significantly different
Kiani, et al., 2016 (34)	70(35/0/35)	-R/C -None	5% lavender essence combined with sweet almond oil	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• This method was done daily two times during four weeks in hemodialysis ward and home</li> <li>• 2</li> <li>• 15-20</li> </ul>	Spielberg anxiety scale	- Anxiety	there is a significant difference between state and trait anxiety marks in examined groups according to one sided variance analysis
Rahimi, et al., 2022 (35)	62(0/31/31)	-R/C -sweet almond oil 100%	lavender essence with a concentration of 7% (diluted 1:10 with sweet almond	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• 3 times a week</li> <li>• for 4 weeks</li> <li>• 2</li> </ul>	Piper Fatigue Scale	- Fatigue	aromatherapy with lavender essential oil can significantly reduce the severity, total, and subdimension scores of fatigue

Table 2: Continued...

			oil)				
Ahmady, et al., 2019 (23)	60(0/30/30)	-R/C - distilled water	100% pure	<ul style="list-style-type: none"> <li>• half hour of each HD session</li> <li>• Inhalation</li> <li>• 14 days: six interventions at the hospital and eight interventions at home were performed.</li> <li>• 5</li> <li>• 30</li> </ul>	Fa-tigue Se-veri-ty Scale	Fa-tigue	aromatherapy with lavender essential oil and orange essential oil was an effective way to reduce the fatigue, significantly
Hassanzadeh, et al., 2018 (36)	70(35/0/35)	-R/C -None	5% lavender essential oil	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• This method was followed in the dialysis ward and at home twice a day for four weeks</li> <li>• 2</li> <li>• 15-20</li> </ul>	brief fa-tigue in-ven-tory (BFI )	Fa-tigue	Aromatherapy with lavender essential oil can decrease the level of fatigue in the patients undergoing hemodialysis compared to Benson relaxation techniques
Bagheri-Nesami et al., 2016 (21)	59(30/0/29)	-R/C -None	lavender essence 5%	<ul style="list-style-type: none"> <li>• Inhalation</li> <li>• consecutive three times a week for 4 weeks</li> <li>• 3</li> <li>• 10</li> </ul>	Fa-tigue Se-veri-ty Scale	Fa-tigue	No statistically significant differences were observed between the two groups in terms of the fatigue scores

**Risk of bias evaluation**

Randomization sequence generation was high risk in three studies (31, 34, 35); the remaining three did not imply it (22, 32, 33 ). One article had high bias (33), another showed low bias (36), and the other did not mention the concealment of random allocation. Blinding of the participants

was not done in three studies (23, 31, 33) while the rest did not indicate this issue. The evaluation was not blinded in one study (33), but in three other studies, the evaluator was blinded (21, 31, 35), while the rest did not mention it. The loss of samples in the included studies did not affect the results. In two studies, we found that the sample

sizes in the intervention and control groups were insufficient and considered a high risk of bias (31, 33) (Table 3).

**Table 3:** Risk-of-Bias of included studies based on Rob II.

Tools name	Rob II						
	Random sequence generation	Allocation concealment	Blinding of participation and personal	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases
Items							
Author name							
Ozen, et al., 2022	-	?	-	+	+	+	-
Sahin et al., 2021	?	?	?	?	+	+	+
Rahimi, et al., 2022	-	?	?	+	+	+	+
Karadag, et al.,2019	?	?	?	?	+	+	+
Ahmady, et al., 2019	+	?	-	?	+	+	+
Hassanzadeh, et al., 2018	-	+	?	?	+	+	+
Bagheri- Nesami et al., 2016	+	?	?	+	+	+	+
Senturk, et al., 2018	?	-	-	-	+	+	-
Kiani, et al., 2016	-	?	?	?	+	+	+

?: Unclear/ +: Low risk/ -: High risk/

**Clinical efficacy**

The results showed that aromatherapy reduced the average anxiety of HD patients compared to the control group, which was statistically significant (SMD: -2.51, 95% CI: [-3.56, -1.45], Z=4.67,

$P<0/001$ , I2:89.9%, Fig. 2). Also, aromatherapy decreased the average intensity of fatigue compared to the control group, which was also statistically significant (SMD: -1.56, 95% CI: [- 2.49, - 0.63], Z=3.29,  $P=0.001$ , I2:92.2%, Fig. 3).



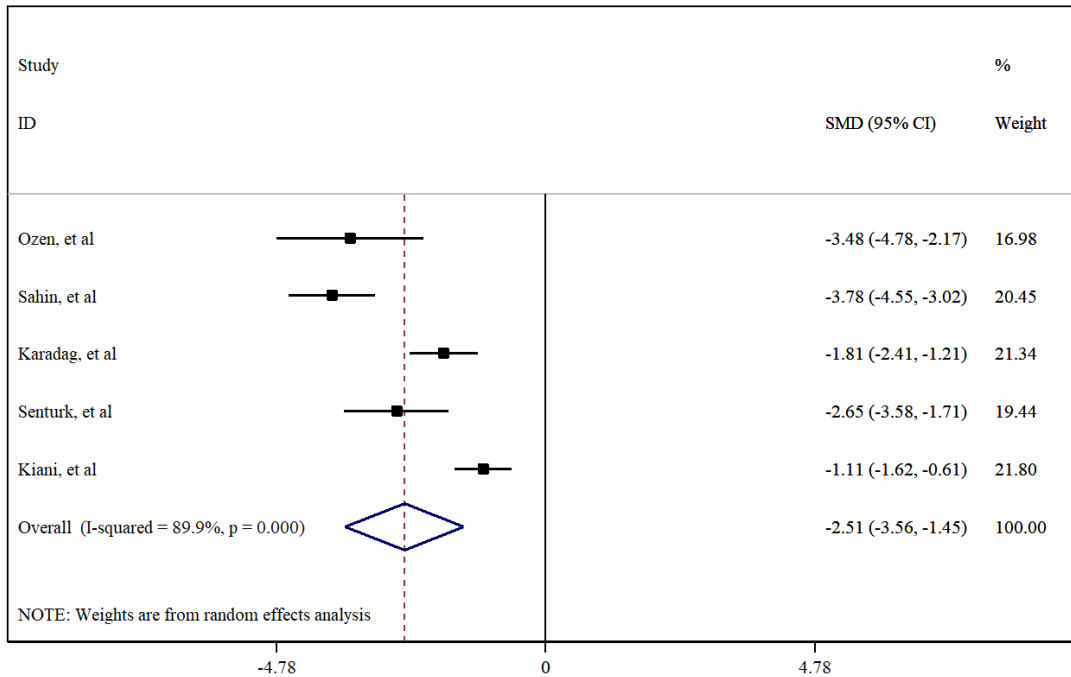


Fig. 2: Effects of aromatherapy with lavender on anxiety

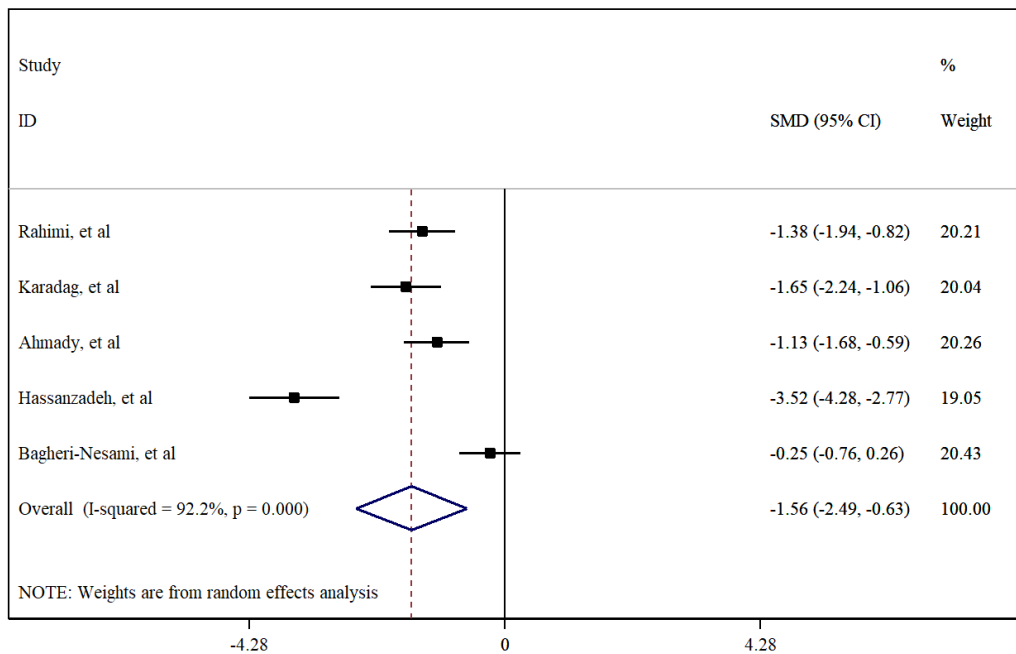


Fig. 3: Effects of aromatherapy with lavender on fatigue

### Sub-group analysis

The results of the sub-group analysis according to the duration of the intervention in each session ( $\leq 15$  min,  $> 15$  min), the number of drops in each intervention session ( $\leq 2$  drops,  $> 2$  drops),

and the concentration of the essence used (pure and diluted) indicated that the use of lavender significantly reduced the intensity of anxiety in the intervention group compared to the control group (Table 4).

**Table 4:** Results of sub-group analysis

	Source	Sub-categories	Number of studies	Effect size (SMD)	Lower CI	Upper CI	Z	P	I <sup>2</sup> (%)	
Fatigue	Scale	Fatigue Severity Scale	3	-1.00	-1.81	-0.19	2.42	0.016	84.8	
		Other	2	-1.19	-1.93	-0.45	2.27	0.023	95.0	
		Sessions number	≤ 12 sessions	3	-1.08	-1.95	-0.22	2.46	0.001	86.5
		>12 sessions	2	-2.31	-4.66	0.03	1.94	0.053	96.0	
	Drops per Session	Number	≤2 drops	3	-1.61	-3.35	-0.98	3.55	<0.001	90.8
			>2 drops	2	-0.69	-1.55	0.18	1.55	0.12	81.4
	Control	No intervention	Placebo	3	-1.79	-1.64	-0.86	1.98	0.048	96.0
			Placebo	2	-1.25	-2.44	-0.70	6.31	<0.001	0.0
	Duration		≤15 min	2	-3.70	-4.37	-3.04	10.97	<0.001	0.0
			>15 min	3	-1.78	-2.58	-0.98	4.36	<0.001	77.5
Anxiety	Drops per Session	Number	≤2 drops	3	-1.78	-2.58	-0.98	10.97	<0.001	77.5
			>2 drops	2	-3.70	-4.37	-3.04	10.97	<0.001	0.0
	Lavender concentration	concentration	100% lavender essential oil	2	-3.25	-4.36	-2.14	5.72	<0.001	70.6
			Diluted oil	3	-1.96	-2.98	-0.94	3.77	<0.001	83.3

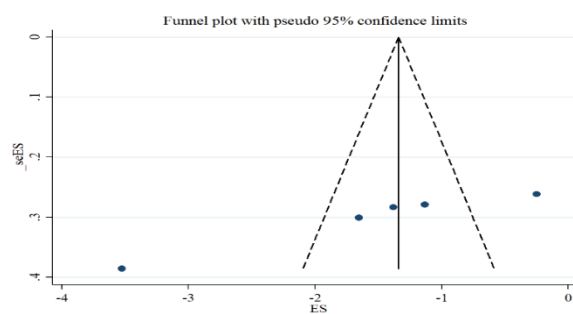
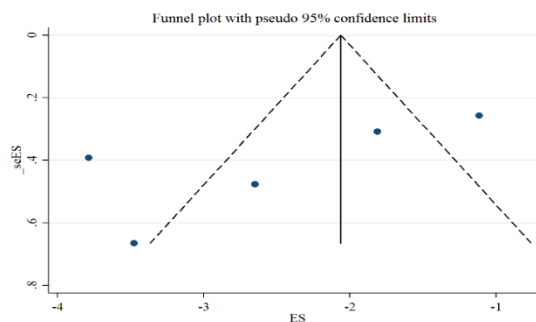
The results of the sub-group analysis in each of the subgroups according to the scale (other, Fatigue Severity Scale) and the type of control group (placebo and routine care) found that lavender significantly reduced the severity of fatigue in the intervention group, the control group (Table 4). Lavender intervention in the groups that applied less than 12 sessions reduced the intensity of fatigue in the intervention group compared to the control group ( $P=0.001$ ). However, this reduction was borderline significant in the group with more than 12 sessions ( $P=0.05$ ). Comparison of the intervention and control groups in studies that the number of drops was more than two drops found no statistically significant difference between the intervention and control groups ( $P=0.18$ ) (Table 4).

**Sensitivity analysis**

Sensitivity analysis showed that the overall effect sizes regarding the effects of lavender oil on anxiety (CI range: -4.17, -1.16) and fatigue (CI range: -2.90, -0.36) did not depend on a single study.

**Publication of bias**

Based on the visual inspection of the funnel plot, we found an asymmetry; however, when we did the Begg ( $P=0.22$ ) and Egger's regression tests ( $P=0.13$ ), no significant publication bias was seen for the effects of lavender on anxiety (Fig. 4). Also, Egger's regression test indicated possible publication bias for the effects of lavender on fatigue intensity ( $P= 0.006$ ). Therefore, we did the trim-and-fill method and found that adding missing studies did not change the overall effect size (SMD: -1.56, 95% CI: -2.49, -0.63).



**Fig. 4:** Funnel plot for outcome of anxiety (left) and fatigue (right)

## Discussion

We aimed to investigate the effect of lavender on the anxiety and fatigue in HD patients. Using lavender oil significantly reduced fatigue and anxiety among the target group.

A meta-analysis study examining the effects of different essential oils on the fatigue of HD patients reported a significant effect of lavender, decreasing fatigue by 1.14 in the intervention group compared to the control group (38). This research included six articles with a RCT design, using essential oils such as lavender and orange. The reduction in fatigue observed in the mentioned study was lower than in the present meta-analysis, which can be attributed to the use of different essential oils. In our study, we specifically focused on the effects of lavender. Another meta-analysis evaluated the effect of aromatherapy on the fatigue in adult patients, with seven of the final studies were related to the effect of lavender on fatigue. It was found that lavender significantly reduced the fatigue in various patients, such as cancer, hemodialysis, and experiencing postpartum fatigue (13). The effect size of lavender essence on fatigue in that study was reported 0.72, whereas in our study, it was 1.56. This difference in effect size can be attributed to the patients included in the study, as well as the dose and duration of lavender aromatherapy. The current study was focused on HD patients, so it specifically addressed the effect of lavender on patients' fatigue. The literature review highlighted that most of the meta-analysis studies on the fatigue in HD patients are concentrated to the effects of intradialytic exercise. Using the results of fifteen parallel RCT studies, this intervention showed a significant reduction in fatigue of 0.81 in the intervention group compared to the control group, which was a smaller reduction compared to the lavender intervention (39). One of the strengths of this study is the higher number of included studies with RCT design.

One study did not show a statistically significant effect of lavender on the fatigue of HD patients,

while the other four studies reported essential oil significantly reduced this outcome. The study that did not find a significant effect administered three drops of 5% essential oil for 12 sessions. We did not find a convincing reason for this non-significant result compared to the other four studies; however, the small sample size in this study could be an influential factor (21). Also, aromatherapy insignificantly decreased patients' fatigue in studies that administered more than two drops of lavender and had more than 12 sessions. Considering the small number of studies in subgroup analysis, further research is required to further explore this phenomenon.

The use of lavender essential oil significantly reduced the anxiety of HD patients. So far, no meta-analytic study has investigated aromatherapy on the anxiety of HD patients, although its effect has been investigated in other diseases. A meta-analysis aimed to evaluate the effect of lavender on the anxiety of different patients, and the results suggested a significant effect size of 0.72 (40). This finding was in line with the results of the present study, which had an effect size of 2.51.

The present study evaluated the effect of lavender essence on the anxiety of HD patients. This difference in effect size can be related to the various effects of lavender essence on different patients, which is necessary to pay attention to in future studies. Also, most of the meta-analyses on anxiety in HD patients are related to investigating the effects of music therapy. The result of music therapy on the anxiety of HD patients based on five RCT articles showed a reduction of 0.52 in the intervention group compared to the control group, while the use of lavender reduced anxiety by 2.51. Future studies can compare these two interventions.

We specifically considered articles published in English language. The inclusion or exclusion of studies reported in the local language poses a significant challenge when conducting a systematic review to published results in language English journals. Some researchers argued that authors are more likely to publish their significant find-

ings in English journals, while they are report the non-significant research findings in the local journals. Additionally, result from a review study demonstrated no evidence of a systematic bias resulting from the use of language restrictions in systematic review-based meta-analyses (41, 42). Usually, children with CKD undergo peritoneal dialysis and therefore experience different conditions compared to those undergoing HD. Moreover, age group is an effective factor on the intensity of anxiety and fatigue (43). Although, no study was excluded from the current review due to different age group. Also, we only included RCT design studies in final analysis. Quasi-RCT studies have a high risk of bias due to the lack of randomization and occupy a lower position in the pyramid of evidence (44). As a solution, it is possible to separately analyze the results of each study design and then draw general conclusion.

## Limitations

The small number of studies can be one of the limitations of the present study, which affects the results of the sub-group analysis; however, this study can trigger researchers to pay more attention to this issue. Using different tools to measure both outcomes can be another limitation, although SMD was used in the analysis to estimate the effect size. We included articles written in English, but future studies could focus on articles published in local databases. Although RCTs and non-RCTs studies had different position in the evidence pyramid, upcoming research can separately analyze and compare their results. This approach can assist to use of broader range of evidences and enhance decision-making.

## Conclusion

Using Lavender significantly reduced fatigue and anxiety in HD patients. The sub-group analysis results found that more studies are needed to evaluate the effects of session frequency and the number of drops on fatigue and anxiety outcomes.

## Journalism Ethics considerations

Ethical issues such as plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc. have been completely observed by research team.

## Acknowledgements

The authors would like to express their gratitude to Golestan University of Medical Sciences for the support to conduct this project.

## Conflict of Interest

Non-declared.

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