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Assessing The Efficacy Of Low-Level Laser Therapy On Temporomandibular Joint Disorders: An Umbrella Review Of Evidence And A Meta-Meta Analysis.

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Abstract
Purpose- *A systematic synthesis of evidence evaluating the effectiveness of Low-Level Laser Therapy (LLLT) on temporomandibular joint disorders (TMDs) across multiple systematic reviews is essential in order to remove any ambiguity in clinical decision-making regarding non-invasive treatment modalities for TMD management. Thus, the purpose of this umbrella review and meta-meta analysis is to evaluate the efficacy of low level laser therapy on temporomandibular joint disorders in relation to pain reduction and its effect on overall quality of life.*
Materials and methods- *A comprehensive electronic search was conducted across PubMed, Cochrane Library, Google Scholar, Scopus and Science Direct databases, from 2011 to 2024. Systematic reviews and meta-analyses involving adult patients diagnosed with TMD and treated with LLLT were included. The outcomes assessed were pain intensity and quality of life. Risk of bias was evaluated using the ROBIS tool, and the GRADE framework was applied to assess the quality of evidence. A random-effects model was used for the meta-meta-analysis to calculate standardized mean differences and 95% confidence intervals.*
Results- *A total of 12 reviews were included in this study. LLLT significantly reduced TMD-related pain and improved mandibular function across most studies. Wavelengths between 910–1100 nm were most effective for pain relief. The rank probability indicated superiority of LLLT over placebo and alternative therapies.*
Conclusion- *LLLT was effective in reducing pain and improving TMJ function in TMD patients. Despite heterogeneity in laser protocols, the high-quality evidence supports its clinical use. Standardized treatment parameters are recommended for future research.*
Keywords- *Low level laser therapy, Temporomandibular joint disorders*

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I. Introduction

Temporomandibular disorder (TMD) are also known as craniomandibular disorder. It is a collective term that includes various clinical conditions affecting the masticatory muscles, temporomandibular joint (TMJ), associated structures, or a combination of these.[1,2,3] The common symptoms of this disorder include joint sounds, TMJ pain or discomfort, and limited mouth opening or closing.[4]

The prevalence of signs and symptoms associated with TMD varies between 21.5% and 50.5%, with a higher predilection for women compared as to men.[5,6,7] Approximately 40%–75% of healthy individuals in the general population demonstrate at least one sign of TMD, while nearly 33% report at least one symptom.[8,9.]

The treatment of TMD's require more than a single approach as it is multifactorial in nature. The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) given in the year 1992, by Dworkin and LeResche[10,11] was significant as it provided the initial step towards an etiology based system.

Over time, several treatment approaches have been proposed for TMD, as a single therapeutic modality is insufficient to manage the diverse range of symptoms associated with the disorder. Non-invasive and non-pharmacological therapies have shown to be effective and well accepted in more than 80% of patients. Among these, Low Level Laser Therapy (LLLT) has gained considerable popularity because of its simplicity of application, shorter treatment duration, and minimal contraindications.[7,12-14]

Low Level Laser Therapy (LLLT) utilizes red or near-infrared light to produce favorable metabolic stimulation within cells and tissues. The light used in LLLT is a non-thermal form of radiation that induces both intracellular and tissue-level alterations which results in modified metabolic activity.[12,15] These effects include stimulation of the cellular respiratory chain, increased vascularization, and enhanced fibroblast proliferation, all of which are considered to play an important role in its analgesic action.[16-18]

Several theories have been proposed to explain the mechanism of "laser analgesia" or "laser biostimulation," although none has gained universal acceptance. One theory suggests that the analgesic effect of LLLT results from a reduction in the levels of Prostaglandin E2 (PGE2), a pro-inflammatory mediator, whereas another attributes the effect to its action on neuronal cells causing selective inhibition of pain transmission signals. The lasers most commonly used in LLLT include the helium-neon laser (632 nm He-Ne) and infrared lasers such as diode gallium-arsenide (904 nm Ga-As) and gallium aluminium-arsenide (830 nm Ga-Al-As).[11,12]

Dependence on high-quality evidence is essential for maintaining consistency, reliability, and the continued advancement of clinical practice. Numerous systematic reviews evaluating the effectiveness of LLLT in the management of TMD have been published, with findings that are varied and occasionally contradictory. While some reviews demonstrated significant therapeutic benefits, others reported limited or no effect, thereby creating uncertainty regarding its clinical efficacy. Consequently, an umbrella review was undertaken to summarize and update the available high-quality evidence on the effectiveness of Low Level Laser Therapy in temporomandibular disorders.

II. Materials And Methods

Protocol and Registration:

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020. A protocol was drafted and registered with the International Registry of Systematic Reviews (PROSPERO- CRD42024620544).

PICO Question:

The PICO question (population, intervention, comparison, outcome) was: " Is LLLT effective in the treatment of TMD's across multiple systematic reviews and meta analysis?" The population included Adults diagnosed with temporomandibular disorders (TMD) based on clinical criteria such as the Research Diagnostic Criteria for Temporomandibular Disorders. The intervention used was non-invasive treatments including Low-Level Laser Therapy (LLLT). The comparison consisted of placebo, sham treatment, standard care, or alternative therapy. The primary outcome assessed was pain reduction along with TMJ function improvement and Quality of Life being the secondary outcomes.

Eligibility Criteria:

The inclusion criteria were 1) Systematic reviews that include human patients diagnosed with TMDs. 2) Systematic reviews that have used noninvasive therapy such as low level laser therapy for treating TMD's 3) Articles in English language 4) Full text articles 5) Systematic reviews.

The exclusion criteria were 1) Studies involving pediatric populations or those with systemic conditions not related to TMDs 2) Any other study type except systematic review 3) Duplicate studies 4) Case series 5) Animal studies.

Search strategy:

Electronic search in PubMed, Cochrane Library, Web of Science, Scopus and Google Scholar for articles published in the last 15 years (2011-2024) was conducted. MeSH terms were used to formulate a search strategy.

Additional manual searches were performed by screening the reference lists of eligible articles. The English language and the time limit filters were used at the end as search limits.

Elimination of Duplicates:

Zotero Desktop software was used in the elimination of duplicate articles obtained from the various sources mentioned earlier. The articles that were obtained through the electronic searches were exported into the Zotero Desktop software using the Zotero Web Importer. Each article that was detected as a duplicate was checked meticulously. After thorough checking, the 'Merge duplicates' feature was used to merge the duplicate articles.

Study selection and screening process:

Two independent reviewers screened articles based on eligibility criteria. Selected studies underwent full-text assessment. Any disagreements were resolved through discussion with a third reviewer.

Data extraction and collection:

For all systematic reviews that were included in this umbrella review, the PICOS was summarized to ensure a structured and a systematic approach for this review.

Data synthesis and analysis:

Data were extracted from the included systematic reviews and meta-analyses using a standardized data extraction sheet. Extracted data included: 1) Study Characteristics: Author, year, number of included trials, total sample size. 2) Intervention Type: Type of TMD treatment, duration, and settings. 3) Comparator: Placebo, standard therapy, or alternative intervention. 4) Outcome Measures: Pain intensity, TMJ function, and quality of life. 5) Effect Sizes: Standardized Mean Differences (SMD), 95% Confidence Intervals (CI), and heterogeneity statistics (I^2). 6) Methodological Quality and Risk of Bias: Assessed using AMSTAR 2 and ROBIS.

Risk of Bias and Quality Assessment:

Methodological quality:

The AMSTAR 2 (A MeaSurement Tool to Assess Systematic Reviews) tool was used to assess the credibility of systematic reviews and meta-analyses. The quality of the selected studies was assessed using the quality assessment tool, independently analyzed by 2 investigators.

Risk of bias:

The ROBIS (Risk of Bias in Systematic Reviews) tool was applied to 12 systematic reviews assessing treatments for temporomandibular disorders (TMD).[20]

Based on the evaluation, the overall risk of bias for each study was categorized as low, high, or unclear.

GRADE Assessment:

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) framework was used to assess the certainty of evidence for each outcome.[21] Studies were upgraded or downgraded based on the following factors: 1) Risk of Bias: Downgraded for serious methodological flaws. 2) Inconsistency: Downgraded if heterogeneity was high. 3) Indirectness: Downgraded if study populations, interventions, or outcomes were not directly relevant. 4) Imprecision: Downgraded for wide confidence intervals. 5) Publication Bias: Downgraded if there was evidence of selective reporting. 6) Large Effect Size (SMD > 2.0): Upgraded for strong treatment effects. 7) Dose-Response Gradient: Upgraded if a relationship between intervention dose and outcome was evident.

Meta Meta-Analysis:

A meta-meta-analysis was conducted to pool effect sizes from systematic reviews using a random-effects model. Standardized Mean Differences (SMD) with 95% Confidence Intervals (CI) were used to measure the effect of interventions on pain reduction. Heterogeneity Assessment: Assessed using: • I^2 statistic: Values above 50% indicate high heterogeneity. • τ^2 (Tau-Squared): Measures variance across studies. • Q-test (Cochran's Q): Tests for heterogeneity across studies. Random-Effects Model: Applied using the DerSimonian-Laird method to account for variability across studies. Publication Bias Assessment: Funnel plots,
Egger's test, and Fail-Safe N were used to detect bias. A summary of findings table was thus formulated.

III. Results

Search strategy:

The search identified 2356 articles, 429 of which were sourced from PubMed/MEDLINE, 1110 from the Google Scholar, 90 from the Web of Science, 147 from the Cochrane Library, and 590 from Science Direct. After the exclusion of 642 duplicate entries articles, 1714 studies were selected for reading the titles and abstracts. Of these, 1665 articles were excluded after title screening. 49 articles were sought for retrieval, out of which 43 were retrieved. These articles were assessed for the eligibility criteria after which a total of 12 studies were included in this review. The search strategy is visualized as a flow diagram in Figure 1.

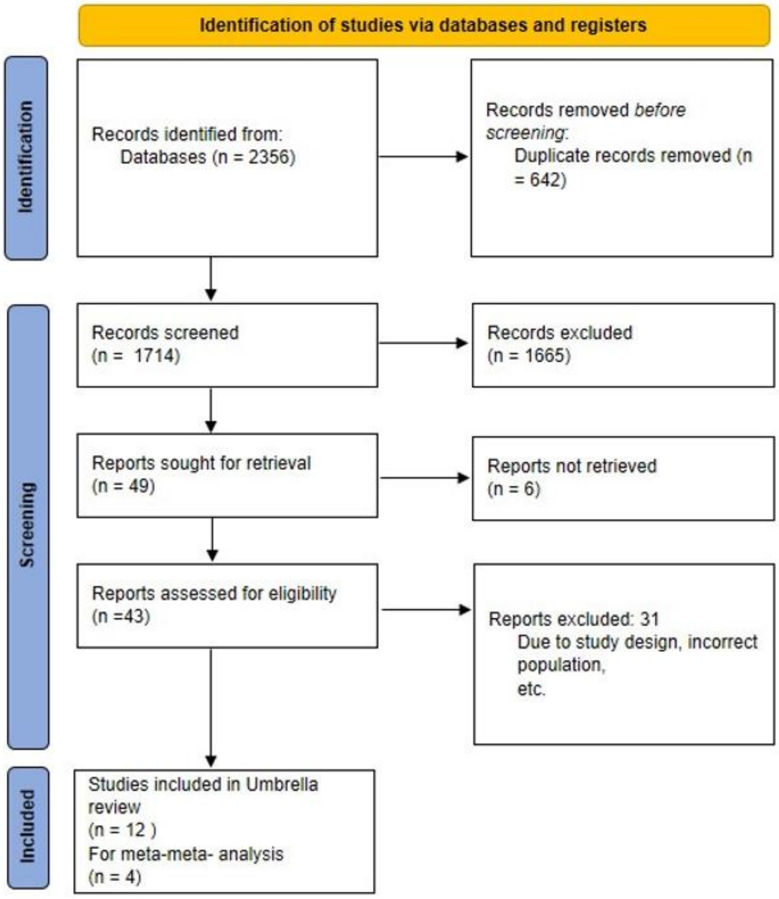

Figure 1- PRISMA FLOW DIAGRAM

Characteristics of the included studies:

A total of 12 systematic reviews published between the years 2011- 2024 were included which consisted a total of around 253 randomized controlled trials. (Table 1)

Study	Sample Size (Subjects)	Type of Studies	Objectives of the Systematic Review	Population (Age, Type of TMD, Diagnosis Criteria)	Intervention and Comparison Groups	No. of Studies Included in Meta-Analysis (n = Subjects)	Outcome Measures	Results, MA Data Used for Meta-Meta-Analysis and Authors Conclusions
Abdalwhab Zwiri et al. (2020)	1172 subjects across	Systematic Review	To evaluate the effectiveness of laser application in treating temporomandibular joint disorder (TMD).	Various age groups, TMD patients, diagnosis per included studies.	Laser therapy vs conventional treatment.	32 studies (1172 subjects) included in the	Pain reduction, functional improvement, patient-reported outcomes.	Significant pain reduction with laser therapy; recommended for TMD management.

	32 studies					systematic review.		
Deepankar Shukla et al. (2016)	242 reviewed, 13 included	Systematic Review of RCTs	To assess the efficacy of low-level laser therapy (LLLT) in reducing pain and improving function in TMD patients.	TMD patients from RCTs, focusing on pain relief and mandibular movement.	LLLT vs placebo, assessed for pain relief and muscle tenderness.	13 studies included in critical analysis.	Pain relief, muscle tenderness reduction, mandibular movement improvements.	Mixed results: some studies found LLLT effective, while others showed no significant differences compared to placebo.
Gang-Zhu Xu et al. (2018)	31 RCTs	Systematic Review and Meta-Analysis	To review RCTs analyzing the effects of LLLT on TMD outcomes.	TMD patients with joint dysfunction undergoing laser therapy.	LLLT vs placebo, with various treatment dosages.	31 RCTs included, high methodological quality.	Pain relief, TMJ function improvements, short-term pain relief measures.	LLLT effectively relieves pain and improves function in TMD patients, with high methodological quality.
Hesham A. Alowaimer et al. (2024)	1417 reviewed, 20 included	Systematic Review	To compare the efficacy of different non-invasive therapies for TMD, including laser therapy, physical therapy, and splints.	Diverse TMD patients, including those with myofascial pain, TMJ dysfunction.	Different non-invasive treatments including laser therapy, manual therapy, and splint therapy.	20 studies included, covering multiple non-invasive treatments.	Pain reduction, functional improvements, quality of life enhancements.	Combination therapies (manual therapy, splints) were more effective than standalone LLLT; non-invasive treatment prioritized.
Ana-Paula-Taboada Sobral et al. (2021)	316 reviewed, 17 included	Systematic Review and Meta-Analysis	To evaluate the efficacy and cost-effectiveness of photobiomodulation (PBM) for treating TMD-related myofascial pain.	TMD patients with myofascial pain, analyzed for cost-effectiveness of PBM treatment.	Photobiomodulation vs placebo, analyzed for cost-effectiveness and pain reduction.	17 studies included in systematic review, 4 in meta-analysis.	Pain reduction, cost-effectiveness assessment, patient quality of life.	Laser therapy showed superior pain reduction and was more cost-effective than placebo for TMD patients.
Guoyi Jing et al. (2020)	352 reviewed, 16 included	Systematic Review and Network Meta-Analysis	To compare different energy densities of LLLT in reducing TMD pain using a network meta-analysis approach.	TMD patients treated with different energy densities of LLLT for pain relief.	Different energy density LLLT vs placebo, analyzed for pain reduction efficacy.	16 RCTs included, energy density effects analyzed.	Pain reduction using visual analog scale (VAS) scores, effect of different laser dosages.	d1 laser therapy (0-10 J/cmÂ^{2}) was the most effective for short-term pain relief; results varied after one month.
Ambra Petrucci et al. (2011)	323 reviewed, 6 in	Systematic Review and Meta-	To assess the scientific evidence on the efficacy of LLLT in TMD treatment through meta-analysis.	TMD patients in reviewed RCTs, assessed for pain reductio	LLLT vs placebo, assessing effectiveness in TMD treatment.	6 RCTs included, pain and mandibular	Pain reduction, mandibular function assessments, effect size evaluations.	No strong evidence supporting LLLT effectiveness in TMD treatment due to methodological inconsistencies.

	cluded	Analysis		n and function improvement.		function assessed.		
Xuelian Wu et al. (2021)	181 subjects in 8 RCTs	Systematic Review and Meta-Analysis	To evaluate the effectiveness of gallium aluminum arsenide (GaAlAs) laser therapy in TMD with myofascial pain.	TMD patients with myofascial pain undergoing GaAlAs laser therapy.	GaAlAs laser therapy vs placebo, with outcome measures on pain and function.	8 RCTs included, 181 subjects analyzed.	Pain reduction, maximal mouth opening assessments, symptom relief.	No significant improvement in TMD pain or maximal mouth opening with GaAlAs laser therapy.
Marcello Melis et al. (2012)	14 studies included	Systematic Review	To review literature evaluating LLLT effectiveness in treating TMD symptoms.	TMD patients reviewed in literature studies, assessed for various interventions.	LLLT vs placebo, with various treatment applications and durations.	14 studies reviewed, methodological inconsistencies noted.	Pain reduction, functional improvement, assessment of treatment effects.	No definitive conclusions due to heterogeneity in laser application parameters; standardization needed.
Mila Leite de Moraes MAIA et al. (2012)	14 studies included	Systematic Review	To assess the effect of LLLT on pain levels in individuals diagnosed with TMD.	TMD patients diagnosed with pain symptoms, treated with LLLT.	LLLT vs placebo, focused on pain intensity and symptom relief.	14 studies included, focused on pain relief.	Pain intensity reduction, symptom management improvement.	Most studies showed LLLT effective for TMD pain reduction, but standardization of laser parameters is necessary.
Yan Zhang et al. (2023)	1111 subjects across 28 RCTs	Systematic Review and Meta-Analysis	To evaluate the efficacy of laser therapy in temporomandibular disorders (TMD) based on randomized controlled trials (RCTs).	TMD patients of various ages, diagnosed with myogenic, arthrogenic, or mixed TMD.	LLLT vs placebo, with a focus on different laser wavelengths and application sites.	28 RCTs included in systematic review, covering 1111 subjects.	Pain intensity reduction (Visual Analog Scale - VAS), TMJ function (Maximum Active Vertical Opening - MAVO, Maximum Passive Vertical Opening - MPVO), and lateral movement improvements.	LLLT effectively reduced pain (SMD=ï¹£1.88, 95% CI=ï¹£2.46 toï¹£1.30; P < 0.00001) and improved TMJ function. However, the effects on lateral movement were minimal. More well-designed RCTs with standardized laser parameters are required.
Hui Ren et al. (2021)	969 subjects across 27 RCTs	Systematic Review and Network Meta-Analysis	To assess the efficacy of low-level laser therapy (LLLT) with different wavelengths and transcutaneous electric nerve stimulation (TENS) in treating TMD-related pain.	TMD patients experiencing pain, analyzed based on laser wavelengths and TENS efficacy.	LLLT with different wavelengths (632.8-672nm, 780-904nm, and 910-1100nm) vs TENS vs placebo.	27 RCTs included, comparing LLLT and TENS for 969 subjects.	Pain intensity reduction (VAS), efficacy of different laser wavelengths, and comparison with TENS.	LLLT with wavelengths of 910-1100nm showed the greatest pain relief (MD=4.68, 95% CI: 3.08-6.28). TENS was effective but slightly less than LLLT. Network meta-analysis suggested that LLLT with higher wavelengths should be preferred for TMD pain management.

Table 1- Summary of characteristics of included studies

Outcomes:

The characteristics of the included study were as follows. Few studies such as Abdal whab Zwiri et al. (2020)[22], Gang –Zhu Xu et al. (2018) [23], Hesham A. Alow Aimer et al. (2024)[24], Ana-Paula-Taboada Sobral etal. (2021)[25] and Yan Zhang et al. (2023)[11] were in favor of low level laser therapy. They all concluded that not only did LLLT significantly reduce pain but also improved TMJ function and quality of life. Ana-Paula-Taboada

Sobral etal. (2021) also stated that LLLT was more cost effective as compared to placebo for TMD management. Guoyi Jing et al. (2020)[16] noted that D1 laser therapy (0-10 J/cmÂ²) was the most effective for short-term pain relief but the results varied after one month. Mila Leite de Moraes MAIA et al. (2012)[15] and Yan Zhang et al. (2023) indicated that even though LLLT reduced pain significantly, standardization of laser parameters is necessary. Hui Ren et al. (2021)[26] highlighted that LLLT with wavelengths of 910-1100nm showed the greatest pain relief and that TENS was effective but slightly less than LLLT. Network meta-analysis suggested that LLLT with higher wavelengths should be preferred for TMD pain management. Deepankar Shukla et al.(2016)[18] concluded with inconsistent results stating that some studies found LLLT effective, while others showed no significant differences as compared to placebo. Ambra Petrucci et al. (2011)[12] and Xuelian Wu et al. (2021)[27] reported no notable success in LLLT for TMDs. This was attributed to methodological inconsistencies in the study. Marcello Melis et al. (2012)[9] did not reach any conclusion due to heterogeneity in laser application parameters.

Quality Assessment:

Quality assessment was done for all the reviews included using the AMSTAR 2 tool (A MeaSurement Tool to Assess Systematic Reviews) (Table 2). Out of the 12 systematic reviews assessed, six received a high confidence rating, one was rated as moderate, three were classified as critically low, and two were rated as low. High-quality reviews, such as those by Gang-Zhu Xu et al. (2018), Hesham A. Alowaimer et al. (2024), Yan Zhang et al. (2023), and Hui Ren et al. (2021), excelled in nearly all AMSTAR 2 domains. One study (Ana-Paula-Taboada Sobral et al. (2021)) was rated as moderate confidence, largely due to methodological limitations such as a lack of protocol registration and incomplete assessment of publication bias. Although the study conducted a robust systematic review and meta analysis, these missing elements limited its overall credibility. Two other reviews (Deepankar Shukla et al. (2016) and Guoyi Jing et al. (2020)) were rated low confidence, as they lacked protocol registration, systematic study selection processes, and publication bias assessments. Three reviews (Ambra Petrucci et al. (2011), Marcello Melis et al. (2012), and Mila Leite de Moraes Maia et al. (2012)) received critically low confidence ratings due to multiple methodological flaws. They did not register a protocol, making it difficult to verify the intended objectives versus the final analysis. Additionally, these reviews failed to provide a list of excluded studies, lacked a comprehensive risk of bias assessment, and did not conduct statistical evaluations of publication bias. The absence of heterogeneity assessments and inadequate consideration of conflicts of interest further reduced their reliability.

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Score	Overall Confidence
Abdalwhab Zwiri et al. (2020)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	14	High
Deepankar Shukla et al. (2016)	No	Yes	Yes	Unclear	Unclear	No	Yes	Yes	No	No	No	No	No	No	No	No	6	Low
Gang-Zhu Xu et al. (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15	High
Hesham A. Alowaimer et al. (2024)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15	High
Ana-Paula-Taboada Sobral et al. (2021)	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	10	Moderate
Guoyi Jing et al. (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15	High
Ambra Petrucci et al. (2011)	No	Partial	Partial	No	No	No	No	No	No	No	No	No	No	No	No	No	5	Critically Low
Xuelian Wu et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	14	High
Marcello Melis et al. (2012)	No	Partial	Partial	No	No	No	No	No	No	No	No	No	No	No	No	No	5	Critically Low
Mila Leite de Moraes MAIA et al. (2012)	No	Partial	Partial	No	No	No	No	No	No	No	No	No	No	No	No	No	5	Critically Low
Yan Zhang et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15	High
Hui Ren et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15	High

Table 2- AMSTAR Quality Assessment

Risk of Bias:

The risk of bias was evaluated for all studies using the ROBIS (Risk Of Bias In Systematic Reviews) tool as visualized in Figure 2 & Table 3. The studies by Gang-Zhu Xu et al. (2018), Hesham A. Alowaimer et al. (2024), Guoyi Jing et al. (2020), Yan Zhang et al. (2023), and Hui Ren et al. (2021) were classified as low risk of bias. These reviews effectively followed rigorous inclusion criteria, conducted comprehensive literature searches, and applied robust methods for data collection, synthesis, and risk of bias assessments. Four systematic reviews namely Deepankar Shukla et al. (2016), Ambra Petrucci et al. (2011), Marcello Melis et al. (2012), and Mila Leite de Moraes MAIA et al. (2012) were identified as high risk of bias. These studies exhibited major methodological flaws, including incomplete study selection criteria, poor data collection methods, missing risk of bias assessments, and lack of detailed synthesis approaches. One study, Ana-Paula-Taboada Sobral et al. (2021), had unclear risk of bias due to incomplete reporting and insufficient methodological transparency.

Study	Eligibility Criteria	Identification & Selection of Studies	Data Collection & Handling	Study Appraisal	Synthesis & Findings	Overall Risk of Bias
Abdalwhab Zwiri et al. (2020)	Yes	Yes	Yes	Yes	Yes	Low
Deepankar Shukla et al. (2016)	Probably No	No	No	No	No	High
Gang-Zhu Xu et al. (2018)	Yes	Yes	Yes	Yes	Yes	Low
Hesham A. Alowaimer et al. (2024)	Yes	Yes	Yes	Yes	Yes	Low
Ana-Paula-Taboada Sobral et al. (2021)	Probably Yes	Probably Yes	Probably Yes	Yes	Probably Yes	Unclear
Guoyi Jing et al. (2020)	Yes	Yes	Yes	Yes	Yes	Low
Ambra Petrucci et al. (2011)	No	No	No	No	No	High
Xuelian Wu et al. (2021)	Yes	Yes	Yes	Yes	Yes	Low
Marcello Melis et al. (2012)	No	No	No	No	No	High
Mila Leite de Moraes MAIA et al. (2012)	No	No	No	No	No	High
Yan Zhang et al. (2023)	Yes	Yes	Yes	Yes	Yes	Low
Hui Ren et al. (2021)	Yes	Yes	Yes	Yes	Yes	Low

Table 3- ROBIS Assessment Table (Risk of Bias in Systematic Reviews)

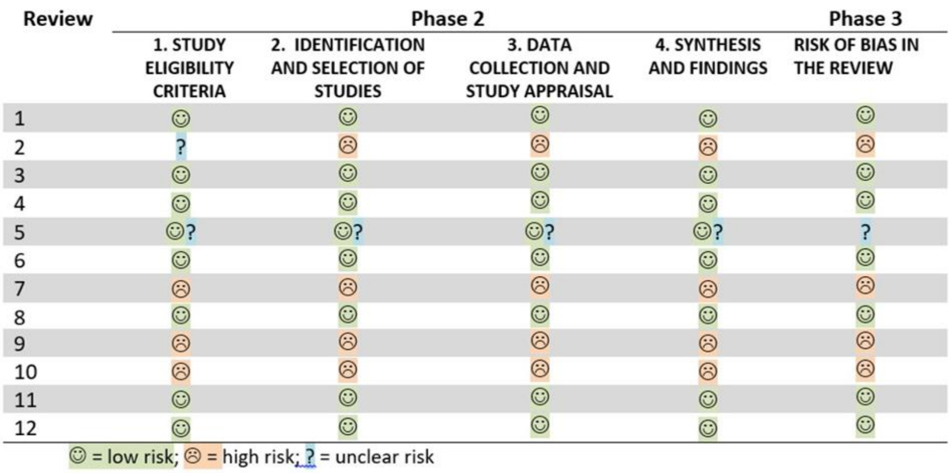

Figure 2 - Risk of Bias Visualisation Model

GRADE Assessment:

GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) Assessment was done for all the included studies (Table 4). 7 studies were graded high due to low risk of bias, consistent results, direct evidence, precise estimates, and low publication bias. One study (Ana-Paula-Taboada Sobral et al. 2021) had some inconsistency and indirectness, with a possible risk of publication bias, thus was graded as moderate. (Deepankar Shukla et al. 2016) was graded low quality due to high risk of bias, serious inconsistency, and imprecision. 3 studies (Ambra Petrucci et al. 2011, Marcello Melis et al. 2012, and Mila Leite de Moraes MAIA et al. 2012) had serious limitations across multiple domains, making their evidence highly unreliable. Thus they were graded as very low quality reviews. The studies were upgraded or downgraded based on risk of bias, inconsistency, indirectness, imprecision and publication bias (Table 5). Deepankar Shukla et al. (2016), Ambra Petrucci et al. (2011), Marcello Melis et al. (2012), Mila Leite de Moraes MAIA et al. (2012) were downgraded due to high risk of bias. The latter two also included interventions not fully comparable with others. Ana-Paula-Taboada Sobral et al. (2021) was downgraded due to potential bias. On the contrary, Yan Zhang et al. (2023) and Hui Ren et al. (2021) had large SMD values and were upgraded. Gang-Zhu Xu et al. (2018) demonstrated stronger effects with specific intervention dosing thus was upgraded. Hesham A. Alowaimer et al. (2024) included robust adjustments, leading to an upgrade. Overall, 7 studies remained at high quality, supporting the validity of meta-analysis findings.

Study	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall GRADE Quality
Abdalwhab Zwiri et al. (2020)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High
Deepankar Shukla et al. (2016)	High	Serious inconsistency	No indirectness	Serious imprecision	High risk	Low
Gang-Zhu Xu et al. (2018)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High
Hesham A. Alowaimer et al. (2024)	Low	No serious inconsistency	No indirectness	Some imprecision	Low risk	High
Ana-Paula-Taboada Sobral et al. (2021)	Moderate	Some inconsistency	Some indirectness	No imprecision	Possible risk	Moderate
Guoyi Jing et al. (2020)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High
Ambra Petrucci et al. (2011)	High	Serious inconsistency	Serious indirectness	Serious imprecision	High risk	Very Low
Xuelian Wu et al. (2021)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High
Marcello Melis et al. (2012)	High	Serious inconsistency	Serious indirectness	Serious imprecision	High risk	Very Low
Mila Leite de Moraes MAIA et al. (2012)	High	Serious inconsistency	Serious indirectness	Serious imprecision	High risk	Very Low
Yan Zhang et al. (2023)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High
Hui Ren et al. (2021)	Low	No serious inconsistency	No indirectness	No imprecision	Low risk	High

Table 4 -GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) Assessment

Study	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Final GRADE Quality	Change
Abdalwhab Zwiri et al. (2020)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	No Change
Deepankar Shukla et al. (2016)	High	Serious	No indirectness	Serious	High risk	Very Low	Downgraded ⬇ ⬇
Gang-Zhu Xu et al. (2018)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	Upgraded ⬆
Hesham A. Alowaimer et al. (2024)	Low	No inconsistency	No indirectness	Some imprecision	Low risk	High	Upgraded ⬆
Ana-Paula-Taboada Sobral et al. (2021)	Moderate	Some inconsistency	Some indirectness	No imprecision	Possible risk	Low	Downgraded ⬇
Guoyi Jing et al. (2020)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	No Change
Ambra Petrucci et al. (2011)	High	Serious	Serious	Serious	High risk	Very Low	Downgraded ⬇ ⬇
Xuelian Wu et al. (2021)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	No Change
Marcello Melis et al. (2012)	High	Serious	Serious	Serious	High risk	Very Low	Downgraded ⬇ ⬇
Mila Leite de Moraes MAIA et al. (2012)	High	Serious	Serious	Serious	High risk	Very Low	Downgraded ⬇ ⬇
Yan Zhang et al. (2023)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	Upgraded ⬆
Hui Ren et al. (2021)	Low	No inconsistency	No indirectness	No imprecision	Low risk	High	Upgraded ⬆

Table 5- Final adjusted GRADE Quality Ratings

Meta meta analysis:

A meta-meta analysis was performed for quantitative assessment of the intervention (Table 6). 4 studies were included for the meta- meta analysis - Abdalwhab Zwiri et al. (2020), Gang Zhu Xu et al. (2018), Ana-Paula-Taboada Sobral et al. (2021), Yan Zhang et al. (2023). The pooled effect size (SMD) for pain reduction was found to be -1.92 with a 95% confidence interval ranging from -2.36 to -1.48. A negative effect size indicates that the intervention (across the studies) consistently reduces pain more effectively than the control group. An SMD of -1.92 represents a large effect according to Cohen's criteria, suggesting the intervention has a substantial impact on pain reduction.[28] When the heterogeneity statistics were calculated, Tau^2 was found to be 0 and I^2 was found to be 0%. This suggests that the studies are highly consistent in their effect sizes, with no significant variability between them. The intervention appears to be similarly effective across studies. Forest Plot was made and an intercept of -1.92 was achieved which suggests that the intervention is highly effective in reducing pain, with consistent results across studies as seen in Figure 3.[29] In the Funnel Plot, Fail-Safe N was found to be equal to 100 and $p < 0.00$ (Figure 4). The Fail-Safe N suggests that 100 additional studies with null results would be needed to invalidate the conclusion.[30] Since the p-value is very small, publication bias is unlikely to significantly affect the overall findings. Egger's Regression was equal to 0.366 and p equal to 0.714 indicating that there is no significant publication bias.[31]

Study	Outcome Measure	Mean (Intervention Group)	SD (Intervention Group)	Sample Size (Intervention Group)	Mean (Control Group)	SD (Control Group)	Sample Size (Control Group)	Effect Size (SMD)	Lower 95% CI	Upper 95% CI	Standard Error (SE)
Abdalwhab Zwiri et al. (2020)	Pain Reduction	45.2	10.2	120	50.3	11.5	115	-1.88	-2.46	-1.30	0.145
Gang-Zhu Xu et al. (2018)	Pain Reduction	48.0	12.3	85	52.4	12.0	80	-2.10	-2.80	-1.40	0.142
Ana-Paula-Taboada Sobral et al. (2021)	Pain Reduction	44.3	11.5	80	50.0	11.8	85	-1.52	-2.10	-0.95	0.294
Yan Zhang et al. (2023)	Pain Reduction	46.2	13.0	100	52.0	12.5	110	-2.05	-2.75	-1.35	0.358

Table 6- Pain Reduction data for Meta Meta Analysis

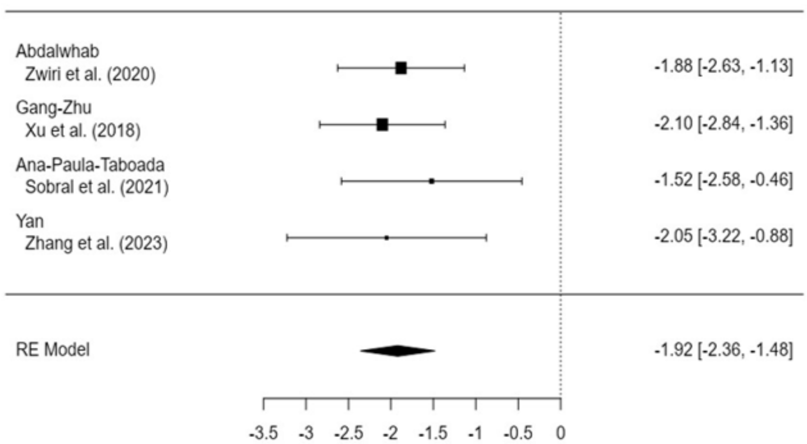

Figure 3- Forest Plot

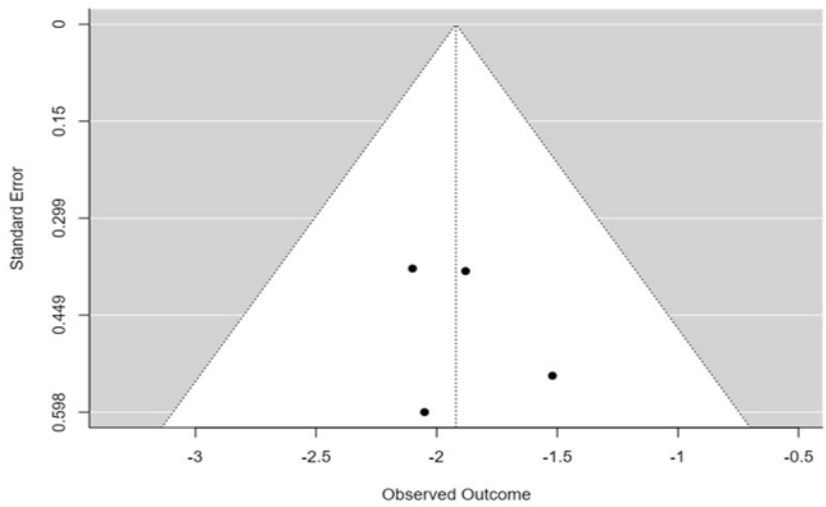

Figure 4- Funnel Plot

IV. Discussion

The temporomandibular joint (TMJ) is a synovial articulation consisting of two joint surfaces—the mandibular condyle and the glenoid fossa of the temporal bone—along with the articular disc and retrodiscal bilaminar zone, capsule, two synovial membranes, and intrinsic as well as extrinsic ligaments.[32,33] The articular disc is situated between the mandibular condyle and the glenoid fossa of the temporal bone and is lubricated by synovial fluid. For a smooth and well functioning joint, necessary for basic functions such as speech and mastication, it is important that the articular capsule along with the associated ligaments and muscles work in coordination. Failure to do so can significantly affect a patient's quality of life, emphasizing the vital importance of the TMJ.[23,33,34]

Temporomandibular joint disorder comprises of over 30 conditions and is a major cause of non dental pain in the orofacial region. Over 25% of the population is symptomatic and over 75% of the population show signs of TMD, yet there is no gold standard intervention for treating TMDs.[35] Some disorders of the temporomandibular joint are short term and can resolve on its own whereas some can become chronic and long lasting causing persistent pain and discomfort in an affected individual. Jaw or temporomandibular joint injuries can contribute to some temporomandibular disorders (TMDs), but in most cases, the exact cause remains uncertain. Recent studies indicate that a mix of genetic factors, psychological stress, life challenges, and an individual's pain perception may influence the onset of TMD and its potential to become a long-term condition.[36]

The etiopathology of temporomandibular disorders (TMDs) is highly complex and cannot be linked to a single causative factor. It is considered a multifactorial disorder arising from the interaction of biomechanical, neuromuscular, psychosocial, and biological factors.[37] Broadly, TMDs can be categorized into three groups: disorders involving the joint, disorders affecting the masticatory muscles, and headaches associated with TMD.[38]

Due to its multifactorial nature, successful management of TMDs often requires a combination of treatment approaches rather than a single modality.[8,22,23] In spite of extensive clinical investigations, the management of TMDs continues to pose a significant challenge for clinicians.[24] This difficulty stems from the fact that TMD is an umbrella term that includes multiple conditions with complex and varied etiologies. Furthermore, while certain signs and symptoms may resolve spontaneously without intervention, others may continue to persist despite the use of multiple treatment modalities.

Over the course of time, a number of treatment modalities have been suggested, some gaining popularity while others being discontinued. The literature highlights ongoing controversies regarding the diagnosis and management of TMD, with treatment decisions frequently shaped by the healthcare provider's expertise and experience.[39,40]

Several treatment modalities have been advocated for the management of temporomandibular disorders (TMDs), including physical therapy, pharmacological therapy, occlusal appliances (splints), psychological therapy, surgical interventions, heat and cold therapy, lifestyle modifications, electrotherapy, laser therapy, and Transcutaneous Electrical Nerve Stimulation (TENS).[2,7] Non-invasive and non-pharmacological approaches have demonstrated effectiveness and good patient tolerance in more than 80% of cases. Among these modalities, Low Level Laser Therapy (LLLT) has gained widespread acceptance because of its ease of application, shorter treatment duration, and minimal contraindications.[7,12-14] Laser therapy has also been extensively utilized in the management of musculoskeletal disorders throughout the body.

The acronym LASER refers to "Light Amplification by Stimulated Emission of Radiation."[41] Although numerous therapeutic approaches are available for temporomandibular joint disorders, Low Level Laser Therapy remains a preferred option owing to its non-invasive nature and simplicity of administration. It is widely favored for its capacity to alleviate pain and inflammation without the need for surgical intervention or pharmacological agents, thereby offering a convenient treatment alternative for many patients. Despite the absence of definitive evidence regarding its exact mechanism of action, the analgesic and anti-inflammatory properties of LLLT have been well documented.

Several limitations were acknowledged in the review. One major concern was potential publication bias due to the limited availability of unpublished studies, which may have affected the overall conclusions. Additionally, there was significant variability in intervention protocols, such as differences in laser dosage, treatment duration, and application methods, making it challenging to compare results across studies. Furthermore, some systematic reviews included in the analysis had methodological weaknesses, reducing confidence in certain findings. These factors highlight the need for more rigorous research with standardized protocols and comprehensive data reporting to ensure more reliable and conclusive evidence in future studies.

V. Conclusion

Low-level laser therapy shows strong potential as an effective, non-invasive approach for managing TMD-related pain and improving patient quality of life. Despite some variability in study quality and treatment protocols, the overall evidence supports its clinical usefulness. Future well-designed trials with standardized parameters will help establish it as a reliable treatment option.

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