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REVIEW

Exosomes and Hair Regeneration: A Systematic Review of Clinical Evidence Across Alopecia Types and Exosome Sources

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Abstract: Mesenchymal stem cell (MSC)-derived exosomes are recognized a promising cell-free therapy for alopecia. These nano-vesicles facilitate intercellular communication and contain a variety of bioactive molecules that can potentially stimulate hair follicle regeneration. However, the safety and efficacy of exosome therapy for alopecia remains to be determined. This systematic analysis aimed to determine the clinical safety and effectiveness of exosome therapy for hair growth, particularly androgenetic alopecia (AGA) and other forms of hair loss. Systematic searches were conducted on PubMed, Scopus, and Embase databases to find clinical studies published from inception until 10th May 2025 that explored exosome-based interventions for hair loss. Eleven studies included: two RCTs, three retrospective studies, three prospective single-arm studies, one case series, and two case reports. Extracted data included method of preparation, outcomes of hair regrowth (density, thickness, patient satisfaction), and side effects. Quality of evidence was assessed using the Oxford Centre for Evidence-Based Medicine (OCEBM) levels and risk of bias tools (RoB 2 and ROBINS-I). All the studies included demonstrated improvements in at least one hair parameter, with MSC-derived exosomes from adipose tissue, placenta, hair follicles, bone marrow, foreskin, and umbilical cord having substantial increases in hair density (9.5 to 35 hairs/cm²) and hair thickness (up to 13.01 μm). Patient satisfaction was generally high (3–10 point scales), and no serious adverse events were noted. The greatest level of evidence came from RCTs with adipose- and plant extract–derived exosome formulation. However, heterogeneity in design and outcome limited direct comparisons. Exosome therapy, particularly with MSC-derived sources, appears to be a new and safe treatment modality for hair restoration in AGA and other alopecias. The current evidence is, however, limited by heterogeneity in studies, small sample sizes, and varying follow-up durations. More well-standardized, high-quality RCTs are required to confirm these findings and establish standardized treatment protocols.

Keywords: exosomes, hair regeneration, androgenetic alopecia, hair density, hair thickness

Introduction

Alopecia, or hair loss, is a global clinical condition of significant psychological and social impact. Among the numerous forms of alopecia, the most prevalent, affecting both women and men all over the globe, is androgenetic alopecia (AGA).[1] Additional forms of alopecia, such as chemotherapy-induced alopecia and trichorrhexis nodosa, present equally formidable challenges to therapy.[2] Despite the availability of pharmacologic treatments like minoxidil and finasteride, and procedural modalities like hair transplantation, the effectiveness of these treatments is often limited by variable response rates, side effects, and the progressive nature of hair loss. Thus, a growing interest exists in newer regenerative therapies with improved efficacy and safety profiles.[1]

Mesenchymal stem cell (MSC)-derived exosomes are a type of small extracellular vesicle that carries proteins, lipids, mRNA, and microRNA reflecting the regenerative and immunomodulatory properties of their parent cells. These

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molecules can influence the behavior of recipient cells by modulating signaling pathways and gene expression. They represent a novel cell-free regenerative therapeutic approach.[3]

Androgenetic alopecia is primarily caused by the miniaturization of hair follicles due to dihydrotestosterone, altered dermal papilla cell signaling, inflammation around the hair follicle, and a shorter anagen phase. The ability of exosomes to control vital biological mechanisms, such as dermal papilla cell growth, neovascularization, and the regulation of inflammatory pathways, has been demonstrated. These mechanisms are essential for the hair regrowth cycle.[4]

Preclinical studies have suggested that exosomes derived from different cell sources, such as adipose tissue, bone marrow mesenchymal stem cells, umbilical cord, placenta, hair follicles, and foreskin, can induce hair growth by enhancing anagen entrance and suppressing apoptosis of follicular cells.[5] Some exosome formulations have also been combined with adjunct therapies, such as plant extracts, with the potential goal of modulating therapeutic efficacy. The mechanism of action is believed to be mediated via signaling molecules such as Wnt/β-catenin, VEGF, and TGF-β, among others.[6] However, despite the promising results in vitro and in animal models, clinical efficacy and safety of exosome-based therapies on human hair growth remain to be clearly established.

To date, there have been several clinical studies, ranging from randomized controlled trials (RCTs) to retrospective analyses to case reports, which have investigated the treatment of alopecia disorders with exosomes. Most have explored AGA,[7] but new cases have been reported in other alopecias, such as chemotherapy-induced alopecia and structural alopecia diseases such as trichorrhexis nodosa.[8] These studies vary considerably by source of exosomes, dosing, route of delivery, outcome measure (eg, hair thickness, hair density), and follow-up time, leading to a progressive evidence base.

Although some narrative reviews have examined the potential of exosomes for treating hair loss, none have yet systematically evaluated clinical outcomes across different exosome sources and types of alopecia. This review aims to address this critical gap. Given the increasing clinical application of exosome-based therapy and the heterogeneity of data that are presently available, a global overview of literature is required. In this systematic review, the clinical evidence favoring the application of exosomes in hair regeneration has been evaluated, with special emphasis on exosome source, efficacy of treatment (eg, hair density, quality), type of alopecia treated, and safety or side effects experienced. By organizing and analyzing the current data, the review seeks to inform clinicians and researchers about the current status and future directions of exosome-based interventions in the management of alopecia.

Materials and Methods

Methodology and Registration

The protocol of this meta-analysis was registered at the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD420251058477) on 22 May 2025.

The conduction and reporting of this meta-analysis followed the principles of the Cochrane Handbook for Systematic Reviews of Interventions, version 6 and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9]

Research Question

What is the current clinical evidence for the efficacy and safety of exosome-based therapy for hair growth in patients with androgenetic alopecia and other forms of alopecia?

Research Aim and Objectives

This study aimed to systematically review and summarize clinical studies establishing the impact of exosomes from various biological sources to stimulate hair growth, focusing on the outcome of the therapy as well as safety among alopecia of different nature.

- To systematically search and briefly summarize clinical studies investigating the use of exosomes in hair regrowth in various types of alopecia.

- To categorize exosome therapies based on their biological source (eg, adipose tissue, umbilical cord, placenta, hair follicle, foreskin, bone marrow).
- To evaluate the treatment outcomes in terms of variation in hair density and hair thickness in patients receiving exosome therapy.
- To assess the use of exosomes in non-androgenetic forms of alopecia, for example, chemotherapy-induced alopecia and trichorrhexis nodosa.
- To explore the safety profile and adverse effects of exosome-based hair restoration therapy.

Eligibility Criteria for the Included Studies

Types of Studies

This systematic review included clinical trials evaluating the use of exosomes in hair growth published from inception to 10th May 2025. The following study designs were included:

- Randomized Controlled Trials (RCTs)
- Non-randomized prospective studies (eg, single-arm trials)
- Retrospective cohort or case series studies
- Case reports.

Participants

Eligible studies enrolled patients with any form of alopecia but not limited to androgenetic alopecia (AGA), chemotherapy-induced alopecia or trichorrhexis nodosa. There were no restrictions on age, sex, or ethnicity for participants. Nevertheless, studies must have reported clinical results related to hair regeneration in human subjects.

Interventions

Included studies assessed the use of exosome-based treatments, either as monotherapy, or combined with adjunctive agents (eg, plant extracts). Exosomes can be isolated from any biological source including adipose tissue, placenta, bone marrow, hair follicles, umbilical cord, or foreskin. Delivery methods (eg, injection, topical) were not restricted provided that the exosomes formed the core of the intervention.

Exclusion Criteria for the Studies

Studies were excluded if they met one of the below criteria:

- Preclinical (animal or in vitro) studies
- Review articles, comments, or letters without accompanying original data
- Conference posters or abstracts without available full text
- Studies where cell-based treatments (eg, stem cells) had been used without applying exosomes for the isolation
- Studies that did not report any clinical hair regrowth findings
- Non-English publications

Search Strategy

Electronic Searches

The following electronic databases were searched for eligible studies: MEDLINE/PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, ProQuest, and Scopus. The search was set for all articles published in English from inception till the 10th of May 2025. The following search terms were used: ("Exosomes" OR "Extracellular Vesicles" OR Vesicle*Extracellular OR Exovesicle* OR "Exosomal Membrane Proteins" OR "Mesenchymal Stem Cell-Derived Exosomes" OR "Exosomes Secreted by Human Circulating Fibrocytes" OR "Plant-derived Exosome-like Nanoparticles" OR "Exosomes of Adipose Stem Cells" AND ("alopecia" OR "hair follicle" OR "dermal papilla cell" OR "root sheath" OR "Wnt pathway").

Other Resources

The first reviewer searched within the reference lists of obtained articles for other potentially relevant studies that were not retrieved by electronic search.

Selection of Studies

The first reviewer screened the retrieved reports for eligibility through title and abstract and full-text screening. The second reviewer checked the retrieved studies and discrepancies were solved through discussion with a third reviewer.

Data Extraction

The first reviewer carried out data extraction from the included studies using a standardized data sheet which included: (a) the study's characteristics (the author, year, the country, study design); (b) participants' characteristics (sample size, hair condition, treatment received); (c) treatment details (source of exosomes, preparation, injection technique, follow-up duration), and (e) the outcomes; hair density, patient satisfaction, hair thickness, and adverse events. The second reviewer checked the collected data for consistency and clarity. Any disagreements were settled by refereeing the third reviewer.

Measured Outcomes

- Hair density: The number of hairs per unit area of the scalp, typically expressed as hairs/cm² (mean and SD).
- Patient Satisfaction: The subjective perception of treatment benefit reported by patients. It was assessed using numerical rating scales ranging from 3-point, 5-point, or 10-point formats.
- Hair thickness: The diameter or caliber of individual hair shafts.
- Adverse events: Any undesirable effects or complications experienced during or after the intervention.

Assessment of the Risk of Bias in Included Studies

The risk of bias (ROB) in the included studies was assessed using the National Institute for Health and Care Excellence (NICE) checklists for randomized controlled clinical trials.[10]

Data Synthesis

Initially, 2178 records were retrieved from electronic database searches. After removing duplicates and excluded studies, 33 studies were finally eligible, of which 11 clinical studies[11–21] (298 patients), two randomized clinical trials (RCT),[11,15] 3 retrospective studies,[14,16,17] 4 single arm prospective studies,[12,13,18] one case series,[19] and 2 case reports[20,21] were included (Table 1), while the 22 excluded studies from the SR were either irrelevant (n=9) or duplicate (n=3) or animal study (n=6) or preclinical study (n=3) or not accessible (n=1), these studies are mentioned in Figure 1.[22]

Results

Study Characteristics and Classification of Evidence

This review included 11 clinical studies[11–21] published between 2022 and 2025, encompassing randomized controlled trials (RCTs), prospective and retrospective observational studies, case series, and case reports. Sample sizes ranged from 1 to 85 participants, predominantly adults with AGA, but also including other alopecias such as chemotherapy-induced alopecia and acquired hair shaft disorders. Follow-up durations varied from 6 weeks to 12 months (Table 1).

The overall quality of evidence was assessed using a modified Oxford Centre for Evidence-Based Medicine (OCEBM) scale:[23]

- Level I (High-quality RCTs): 2 studies (Amini et al[11] pilot RCT; Nadeem et al[15] RCT).
- Level II (Prospective cohort studies): 4 studies (Wan et al,[18] Ersan et al,[13] Lueangarun et al,[20] Norooznezhad et al[21] case report with prospective follow-up).
- Level III (Retrospective observational studies): 2 studies (Gentile et al[14] and Park et al[16]).
- Level IV (Case series and reports): 3 studies (Chen et al,[19] Sasaki et al,[17] and Norooznezhad et al[21]).

Table 1 Summary of the Included Studies

Author	Year	Country	Study Design	Sample Size	Hair Condition	Treatment Received	Source of Exosomes	Preparation	Injection Techniques	Follow-Up Duration	Outcomes	Key Results
Amini et al[11]	2025	Malaysia	Pilot RCT	20 (10/group)	Male androgenetic alopecia (Norwood 2–3)	ECPE (plant extracts + exosomes) vs placebo	Ecklonia cava and Thuja orientalis plant extracts	Prepared by DASAN C& Tech CO. LTD. (10 billion exosomes per vial)	Intradermal injections (0.05–0.1 mL/site) bi-weekly for 4 sessions	12 weeks	Hair count, self-assessment	ECPE group: Significant increase in hair count (median +9.5 hairs) vs placebo (+1.5 hairs)
Dehghani et al[12]	2024	Iran	Phase I/II single-arm clinical trial	12 patients analyzed (initially 75 assessed, 40 excluded, 35 allocated)	Androgenetic alopecia (AGA): Ludwig grade I–II (women), Norwood-Hamilton III–IV (men)	Placental-derived mesenchymal stem cell (P-MSC) exosome injections	Placenta-derived mesenchymal stem cells (P-MSCs)	Exosomes isolated from placental MSCs via Thery protocol; quality control included electron microscopy, DLS, flow cytometry, infection screening.	Intradermal injections (24-gauge insulin syringe, nappage technique), 0.1 mL per point, 1 cm spacing, every 14 days for 2 months (4 sessions).	Baseline, 3 weeks, and 6 weeks post-intervention.	Hair density (hairs/cm²), hair diameter (mm), hair loss count.	Hair density: Increased from 96.5 to 163.5 hairs/cm² ($p<0.0001$), Hair diameter: Increased from 0.049 mm to 0.059 mm ($p<0.0001$), Hair loss: Reduced from 200 to 80 hairs ($p<0.0001$).
Ersan et al[13]	2024	Turkey	Prospective single-arm study	30 male patients	Androgenetic alopecia (Norwood-Hamilton scale III–VI)	Exosome injection	Foreskin-derived mesenchymal stromal cells	Isolation via ATPS (PEG/dextran), NTA, flow cytometry for characterization	Nappage technique (3 mL total: 2 mL frontal, 1 mL vertex)	12 weeks (assessments at 4 and 12 weeks)	Hair density (Trichoscan), patient satisfaction (survey)	Significant increase in hair density ($p < 0.05$) and patient satisfaction.
Gentile et al[14]	2025	Multicentric (Italy, India, Turkey)	Multicentric, retrospective, observational, evaluator-blinded study (EBM Level III)	60 patients (40 males with MPHL, 20 females with FPHL)	Androgenetic alopecia (AGA): MPHL (Norwood-Hamilton I–III vertex) and FPHL (Ludwig I–II)	Autologous micrografts (MCGs) containing HF-MSCs and exosomes	Human follicle mesenchymal stem cells (HF-MSCs) from craniofacial biopsies	Mechanical disaggregation using Rigeneracons® device, centrifugation, filtration, and NTA for EV characterization	Interfollicular infusions (0.1 mL/cm²) with 30-gauge needles	12 months (assessments at baseline, 4 weeks, 3, 6, and 12 months)	Hair density (Trichoscan), patient/physician satisfaction, in vitro EV analysis	Significant HD increase (FPHL: +28 ± 4 hairs/cm²; MPHL: +30 ± 5 hairs/cm² at 12 months; $p < 0.05$). EVs confirmed via TEM and fluorescence microscopy.
Nadeem et al[15]	2024	Pakistan	RCT	85 patients	Androgenic Alopecia (AGA; Norwood-Hamilton II–V for men, Ludwig I–II for women)	MSC-derived exosomes (intradermal injections + microneedling)	Human adipose-derived MSCs	10^11 exosomes/mL (quantified via NTA)	Intradermal micro-needling (3 sessions, 4-week intervals)	12 weeks	Hair density, thickness, patient satisfaction, adverse events	35 hairs/cm² increase in density ($p=0.001$), 13.01 µm increase in thickness ($p=0.001$)
Park et al[16]	2022	South Korea	Retrospective study	39 patients	AGA (Hamilton-Norwood IIIa–V for men, Ludwig I–II for women)	ASC-exosomes (microneedle roller application)	Adipose-derived stem cells (ASCs)	6×10^10 particles/vial (AAPE® v2.0)	Microneedle roller (weekly for 12 weeks)	12 weeks	Hair density, thickness, adverse events	24.9 hairs/cm² increase in density ($p<0.001$), 8.8 µm increase in thickness ($p<0.001$)

(*Continued*)

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Table 1 (Continued).

Author	Year	Country	Study Design	Sample Size	Hair Condition	Treatment Received	Source of Exosomes	Preparation	Injection Techniques	Follow-Up Duration	Outcomes	Key Results
Sasaki et al[17]	2022	USA	Retrospective open-label, nonblinded, nonrandomized institutional review board (IRB) study	31 patients (22 females, 9 males)	Male and female pattern hair loss (MPHL: Norwood-Hamilton III–IV; FPHL: Ludwig I-3 to III); early stages or in remission from previous treatments.	Single intradermal injection of extracellular vesicles (XoFlo, Direct Biologics, LLC).	Human bone marrow mesenchymal stem cell-derived EVs (XoFlo).	Thawed frozen XoFlo, diluted with bacteriostatic 0.9% normal saline (ratios: 1:2 to 1:10). Undiluted volumes (2–8 mL) preferred for higher EV concentration.	Intradermal injections (32-gauge needle); microneedling (2.5 mm depth) and LLLT (678-nm laser helmet) used adjunctively in some patients.	6 MONTHS	Hair density, follicle diameter, terminal/velus ratio (trichoscan); global photography; Patient/ Investigator Global Aesthetic Improvement Scale (PGAIS/ IGAIS).	Growth response: 54.5% females, 88.9% males, Better outcomes in older females (50–70 years) and younger males (20–50 years), Larger undiluted XoFlo volumes correlated with improved results.
Wan et al[18]	2025	South Korea	Prospective Open-Label Study	16 males	Mild to Moderate AGA (Norwood-Hamilton III–V for men)	Exosome therapy (ADMSC-derived) + microneedling	Adipose-derived mesenchymal stem cells (ADMSCs)	10 billion particles/ vial (ZISHEL XOMAGE)	Microneedling (1.5-mm dermatoller) + topical exosome application	12 months	Hair density, patient satisfaction, adverse events	35 hairs/cm² increase in density (SD=6.5), 80% reported noticeable improvement
Chen et al[19]	2025	China	Case series	3	Acquired trichorrhexis nodosa (ATN)	MSC exosomes	Human mesenchymal stem cells (MSCs)	Centrifugation and filtration (0.22 μm), resuspended in saline (1×10^{10}/mL)	Subcutaneous (0.1 mL/ site, 0.5–1 cm intervals) monthly for 4–6 sessions	1 year	SEM, dermoscopy, clinical photos	Hair cuticle restoration, increased density/length, reduced breakage
Lueangarun et al[20]	2022	Thailand	Case report	1 male patients	Androgenetic Alopecia (AGA)	Scalp injection of exosome-rich conditioned medium	Human umbilical cord mesenchymal stem cells (hUC-MSCs)	Conditioned medium containing exosomes; specific isolation technique not described	1 mL of exosome-rich solution injected at 0.2–0.3 cm intervals using 30-gauge needle	6 months	Hair density and thickness measured by trichoscopy; global photography; patient satisfaction questionnaire	Significant improvement in hair density and thickness in all patients
Norooznezhad et al[21]	2023	Iran	Case report	1	Persistent chemotherapy-induced alopecia (PCIA)	MSC-derived EVs	Human placental MSCs	EVs isolated via ultracentrifugation (140–160 μg/ session)	Subcutaneous (12 sites/ scalp) every 4 weeks for 3 sessions	10 months	Clinical photos, patient report	Complete terminal hair regrowth

Abbreviations: ECPE, Exosome Combined with Plant Extracts; MSC, Mesenchymal Stem Cell; HD, hair density; AGA, androgenetic alopecia; ASC, adipose-derived stem cells; EVs, extracellular vesicles.

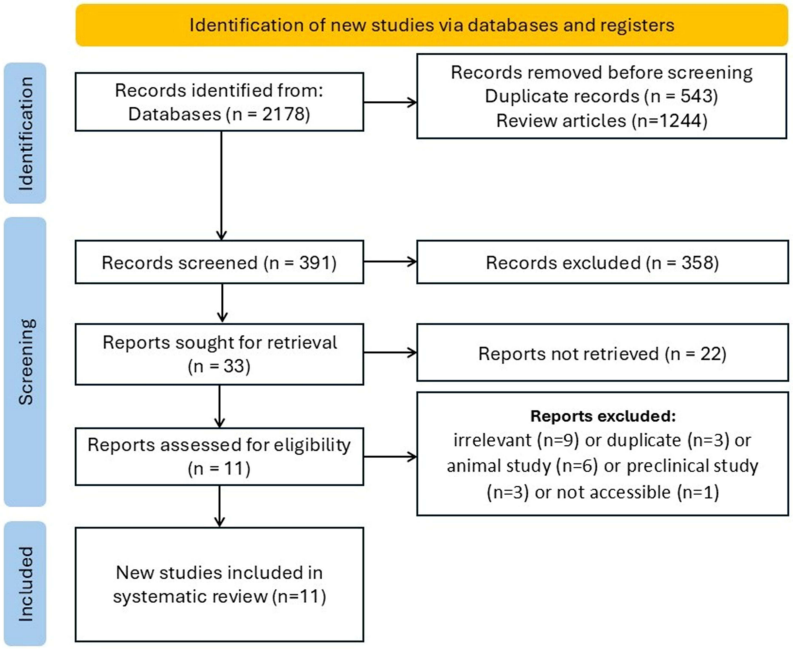

Figure 1 PRISMA flow chart.
Notes: PRISMA figure adapted from Liberati A, Altman DG, Tetzlaff J et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100. Creative Commons.[9]

The evidence levels reflected the heterogeneity of study designs and sample sizes, with RCTs providing the strongest evidence for efficacy.

Exosome Source and Preparation

Exosomes were derived primarily from MSCs obtained from various tissues: placenta, adipose tissue, hair follicles, bone marrow, foreskin, and umbilical cord. One study used exosomes combined with plant extracts (Ecklonia cava and Thuja orientalis). Preparation methods varied, including ultracentrifugation, filtration, mechanical disaggregation, and proprietary commercial kits. Quantification was generally performed by nanoparticle tracking analysis (NTA), confirming typical exosome size distributions (~100–150 nm).

Hair Regeneration Outcomes

Mesenchymal Stem Cell-Derived Exosomes

Placenta-Derived MSC Exosomes

Placenta-derived mesenchymal stem cell (P-MSC) exosomes have shown promising results in hair regeneration, particularly for AGA. In a Phase I/II single-arm clinical trial by Dehghani et al[12] (Level II), 12 patients with AGA received intradermal injections of P-MSC exosomes every two weeks for two months. The results demonstrated a significant increase in hair density, from 96.5 to 163.5 hairs/cm² ($p<0.0001$), and an increase in hair diameter from 0.049 mm to 0.059 mm ($p<0.0001$) at six weeks post-treatment. Hair loss counts also dropped markedly, from 200 to 80 hairs ($p<0.0001$). Notably, no adverse events were reported, and patient satisfaction was high. Additionally, a case report by Norooznezhad et al[21] (Level IV) described complete terminal hair regrowth in a patient with persistent chemotherapy-induced alopecia after three sessions of subcutaneous P-MSC exosome injections, further supporting the regenerative potential of placental exosomes in various hair loss conditions.

Foreskin-Derived MSC Exosomes

Foreskin-derived mesenchymal stromal cell exosomes have also been evaluated for AGA. In a prospective single-arm study by Ersan et al[13] (Level II), 30 male patients with AGA received intradermal exosome injections using the nappage technique over 12 weeks. The study reported a significant increase in hair density at both four- and twelve-weeks post-

treatment ($p<0.05$), with mean hair density rising from 149.7 to 157 hairs/cm². Patient satisfaction was notably high, and no adverse events were observed, highlighting both the efficacy and safety of this exosome source.

Adipose-Derived MSC Exosomes

Adipose-derived mesenchymal stem cell (ADMSC) exosomes have been the focus of several high-quality studies. In a randomized controlled trial by Nadeem et al[15] (Level I), 85 patients with AGA received intradermal ADMSC exosome injections combined with microneedling over 12 weeks. The treatment group experienced a significant increase in hair density (by 35 hairs/cm², $p=0.001$) and hair thickness (by 13.01 µm, $p=0.001$), with high patient satisfaction (8.5/10) and only mild, transient redness reported in 20% of cases. Similarly, Wan et al[18] (Level II) conducted a prospective open-label study in 16 males with mild to moderate AGA, using microneedling plus topical ADMSC exosome application. After 12 months, hair density increased by 35 hairs/cm² (SD=6.5), and 80% of patients reported noticeable improvement, with only minor scalp irritation that resolved quickly. Park et al[16] (Level III) retrospectively studied 39 patients, finding a 24.9 hairs/cm² increase in density ($p<0.001$) and an 8.8 µm increase in thickness ($p<0.001$) after 12 weeks of weekly microneedle roller application of ASC-exosomes, with no adverse events reported.

Hair Follicle-Derived MSC Exosomes

Exosomes derived from human hair follicle mesenchymal stem cells (HF-MSCs) have also demonstrated efficacy in AGA. In a multicentric, retrospective, evaluator-blinded study by Gentile et al[14] (Level III), 60 patients (both male and female) received autologous micrografts containing HF-MSCs and exosomes. After 12 months, hair density increased significantly-by +28 ± 4 hairs/cm² in female pattern hair loss (FPHL) and +30 ± 5 hairs/cm² in male pattern hair loss (MPHL) ($p<0.05$). Patient satisfaction was high, with 80% of participants indicating a good level of satisfaction regarding scalp coverage. Minor adverse events, such as itching, redness, numbness, and headaches, were reported but were not severe.

Bone Marrow-Derived MSC Exosomes

Bone marrow-derived MSC exosomes have been evaluated in a retrospective open-label study by Sasaki et al[17] (Level IV), where 31 patients with male and female pattern hair loss received a single intradermal injection of bone marrow MSC-derived extracellular vesicles (EVs), sometimes combined with microneedling and low-level laser therapy. Responders experienced an 11.1–24.2% increase in hair density over six months, with high levels of satisfaction reported by both males (88.9% satisfied to extremely satisfied) and females (54.5% very satisfied). No severe adverse events were observed, with only transient swelling or pain attributed to microneedling.

Umbilical Cord-Derived MSC Exosomes

Finally, umbilical cord-derived MSC (hUC-MSC) exosomes have shown positive outcomes in a prospective interventional study by Lueangarun et al[20] (Level II). A single male patient with AGA received scalp injections of exosome-rich conditioned medium, resulting in significant improvements in both hair density and thickness at six months, with no serious adverse reactions reported.

Plant Extract-Derived Exosomes

Amini et al[11] (Level I) evaluated an exosome formulation containing Ecklonia cava and Thuja orientalis extracts in a pilot RCT of 20 males with AGA. The treated group experienced a median increase of 9.5 hairs compared to 1.5 in placebo ($p=0.006$), with significantly higher self-perceived satisfaction (4.2/5 vs 2.9/5, $p=0.013$). Mild scalp irritation occurred in 20% of patients treated.

Outcomes in Other Types of Alopecia

Limited evidence suggests exosome therapy may benefit other alopecias. Norooznezhad et al[21] (Level IV) reported complete terminal hair regrowth in a patient with persistent chemotherapy-induced alopecia after placental MSC-derived extracellular vesicle treatment over 10 months. Chen et al[19] (Level IV) documented restoration of hair cuticles, increased density and length, and reduced breakage in acquired trichorrhexis nodosa after MSC exosome treatment.

Safety and Adverse Events

Across all studies, exosome therapy exhibited a favorable safety profile. Adverse events were predominantly mild and transient, including scalp irritation, redness, swelling, itching, and occasional headaches. No serious systemic side effects, infections, or immunogenic reactions were reported.

Risk of Bias Assessment

ROB for the RCTs

The risk of bias was assessed across seven standard domains for the two included randomized studies. In terms of random sequence generation and allocation concealment, both Amini et al[11] and Nadeem et al[15] demonstrated low risk, indicating adequate methods for randomization and participant allocation. For blinding of participants and personnel (performance bias), both studies again showed low risk, suggesting effective masking that minimized potential influence on treatment administration or behavior. Similarly, blinding of outcome assessment (detection bias) was adequately maintained in both trials, reducing the likelihood of biased outcome evaluation. Incomplete outcome data (attrition bias) was well-handled in both studies, with full or appropriately accounted follow-up. Regarding selective reporting (reporting bias), no major concerns were identified in either study, with outcomes appearing consistent with prespecified objectives. Finally, other sources of bias were not identified in either study. However, it is noteworthy that Nadeem et al[15] had an unclear risk for allocation concealment due to insufficient reporting, which slightly reduces the overall confidence in internal validity for that study. Overall, both trials exhibited a low risk of bias across most domains, with Amini et al[11] demonstrating consistently low risk throughout, and Nadeem et al[15] showing low risk except for a single unclear domain (Figures 2 and 3).

ROB for the Non-Randomized Studies

The overall risk of bias using ROBIN II tool across the included studies remains predominantly serious, largely due to inherent limitations in study design, such as lack of control groups, retrospective data collection, and subjective outcome assessments. Case-based reports and small case series, such as those by Chen et al,[19] Lueangarun et al,[20] Norooznezhad,[21] Gentile,[14] and Ersan,[13] exhibited high risk of bias due to serious confounding, unclear selection processes, and selective outcome reporting. Sasaki,[17] though detailed, remains at serious risk due to its retrospective, non-randomized nature and unblinded outcome assessments. In contrast, Wan et al[18] demonstrated the lowest overall risk of bias, benefiting from a prospective design, standardized assessments, and blinded outcome evaluation, although it lacked a control group. Park et al[16] and Dehghani[12] showed potential for lower bias; Dehghani was reassessed to low RoB due to clearly defined outcomes and participant selection, while Park's rating was reduced to moderate with improved clarity on methods. These findings emphasize the need for future well-controlled, prospective, and ideally randomized studies with blinded assessments to ensure more robust evidence in the evaluation of exosome therapies for hair loss (Table 2).

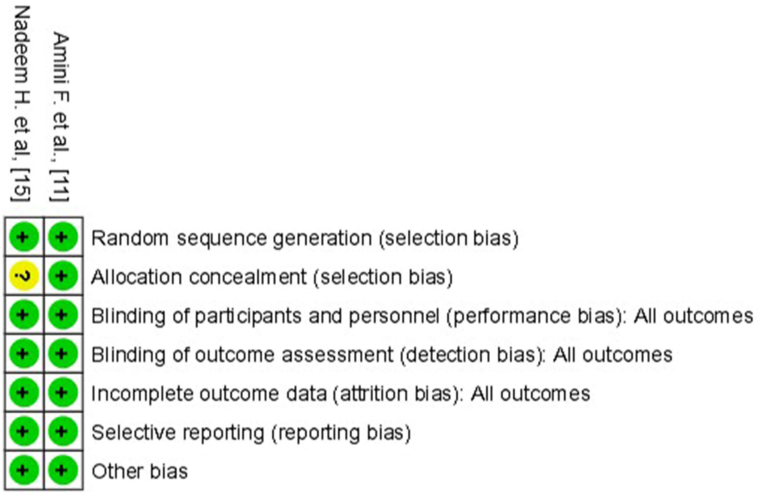

Figure 2 Risk of bias graph.

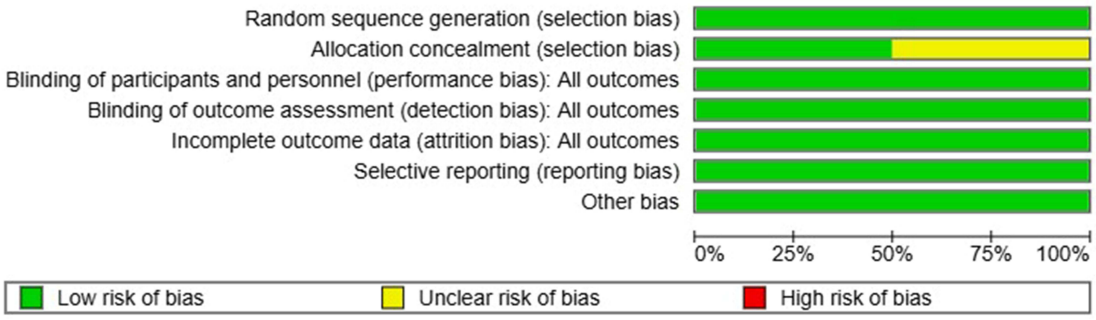

Figure 3 Risk of bias summary.

Discussion

Hair loss disorders such as androgenetic alopecia (AGA) and other non-scarring alopecias are a significant cosmetic and psychologic issue in men and women. While present therapies such as minoxidil, finasteride, and hair transplantation yield some benefit, their limitations have generated interest in regenerative therapies. In the last few years, MSC-derived exosomes have emerged as cell-free therapeutics due to their ability to deliver bioactive molecules that modulate inflammation, promote angiogenesis, and activate hair follicle regeneration.[24] This systematic review integrated 11 clinical trials examining various sources of exosomes and their efficacy and safety as therapeutic agents for the management of AGA and other types of hair disorders.

Exosomes from placental MSC have shown strong regenerative activity. In a prospective single-arm trial, Dehghani et al[12] showed evidence of increased hair density (from 96.5 to 163.5 hairs/cm²) and diameter (from 0.049 to 0.059 mm) after intradermal injections in AGA patients with no side effects. These findings were confirmed by Norooznezhad et al,[21] who reported complete terminal hair regrowth in chemotherapy-induced alopecia by the same exosome source. The resulting effects are in accordance with the immunomodulatory and pro-angiogenic actions attributed to placental MSC-derived extracellular vesicles.

Adipose-derived exosomes were evaluated in three studies. Nadeem et al[15] conducted a remarkable RCT with statistically significant improvement in hair thickness and density, with extremely high satisfaction and zero side effects. Wan et al[18] confirmed these findings in a prospective study with topical application after microneedling. Similarly, Park

Table 2 Risk of Bias Assessment Using the RoBINS-I Tool Across Included Studies Evaluating Exosome Therapy for Hair Loss

Domain	Chen et al[19]	Dehghani et al[12]	Ersan et al[13]	Gentile et al[14]	Lueangarun et al[20]	Norooznezhad et al[21]	Park et al[16]	Sasaki et al[17]	Wan et al[18]
1. Bias due to confounding	Serious	Moderate	Serious	Serious	Serious	Serious	Moderate	Serious	Moderate
2. Bias in selection of participants into the study	Moderate	Low	Moderate	Moderate	Serious	Moderate	Low	Serious	Low
3. Bias in classification of interventions	Low	Low	Low	Low	Low	Low	Low	Moderate	Low
4. Bias due to deviations from intended interventions	Low	Low	Low	Low	Low	Moderate	Low	Moderate	Low
5. Bias due to missing data	Low	Low	Moderate	Moderate	Low	Low	Low	Low	Low
6. Bias in measurement of outcomes	Moderate	Moderate	Low	Low	Serious	Serious	Low	Moderate	Low
7. Bias in selection of the reported result	Moderate	Low	Moderate	Serious	Serious	Moderate	Low	Low	Low
Overall Risk of Bias	Serious	Low	Serious	Serious	Serious to Critical	Serious	Moderate	Serious	Low

et al[16] retrospectively showed significant improvement by weekly microneedle-assisted delivery. These studies support the efficacy and safety of adipose tissue-derived exosomes, which are particularly attractive due to the ease of harvesting adipose tissue and abundant exosome yield.

Gentile et al[14] evaluated autologous hair follicle MSC-derived exosomes in 60 patients. There was significant improvement in hair density in male and female pattern hair loss, with mild side effects of itching and numbness. This source of exosomes has the potential advantage of follicle-specific signaling, but logistical and technical limitations remain.

Ersan et al[13] reported positive outcomes of 30 male AGA patients treated with foreskin-derived MSC exosomes. Hair density was noticeably improved at week 12, and patient satisfaction was ranked high. These results support the hypothesis that neonatal MSCs, including foreskin-derived ones, are especially vigorous in their regenerative capacity owing to their young cellular profile.

Sasaki et al[17] assessed bone marrow-derived exosomes in 31 patients. Hair density improvement was observed in both genders, with high patient satisfaction and no adverse effects. The retrospective nature and correlation with microneedling and laser treatment may confound the results.

Lueangarun et al[20] reported significant improvement in hair parameters in one male AGA patient treated with umbilical cord-derived exosomes. Although encouraging, this is a single case and must be validated in larger cohorts.

Amini et al[11] conducted a pilot RCT on a novel combination product of exosomes with Ecklonia cava and Thuja orientalis. Greater improvement in hair density and self-assessed satisfaction was seen in the exosome group compared to placebo. These findings suggest there may be synergistic activity of botanicals and exosomes that could be explored further.

While the majority of studies focused on AGA, two case reports suggest broader therapeutic possibilities. Norooznezhad et al[21] described complete hair regrowth in chemotherapy-induced alopecia, and Chen et al[19] demonstrated improvement of trichorrhexis nodosa, a disease of the hair shaft, following treatment with exosomes. These findings open avenues to the application of exosome therapy to other types of alopecia and acquired hair shaft defects.

Patient satisfaction, graded on 3-, 5-, or 10-point scales across studies, was consistently high in exosome-treated cohorts. This concords with observed improvements in objective assessments and the lack of invasiveness and side-effect profile of exosome treatment. Addition of patient-reported outcomes makes findings more clinically relevant, but subjective measures remain prone to placebo response and reporting bias.

Safety was a consistent strength across the studies. Mild, transient adverse effects such as redness, itching, and pain at the injection site were the most common events. There were no reports of severe systemic reactions, infections, or immune responses, supporting the clinical safety of exosome therapy, even with off-label or non-standardized regimens.

This review is limited by the heterogeneity of the included studies in terms of design, sample size, exosome source, preparation methods, and delivery protocols, which complicated direct comparisons and meta-analysis. Many of the studies were non-randomized, single-arm, or retrospective in nature, with a high risk of bias due to confounding and lack of blinding. Only two randomized controlled trials were identified, and these had relatively small sample sizes, reducing the strength of the evidence base. Furthermore, outcome measures varied across studies, with several relying on subjective patient assessments or non-blinded evaluators. The short follow-up periods in some studies may have failed to capture long-term efficacy or delayed adverse events. Additionally, the lack of standardized dosing, frequency, and administration methods for exosome therapy presents challenges for clinical reproducibility and generalizability. These limitations underscore the need for larger, well-controlled, and methodologically rigorous trials to validate the promising results observed and to establish optimal treatment protocols.

Conclusion

This systematic review highlights the emerging potential of exosome therapy as a promising intervention for various forms of hair loss, particularly androgenetic alopecia (AGA). Across 11 clinical studies, exosomes derived from diverse sources, most notably mesenchymal stem cells (MSCs) from adipose tissue, placenta, foreskin, hair follicles, bone marrow, and umbilical cord—demonstrated consistent improvements in hair density, hair thickness, and overall scalp coverage. The highest-quality evidence came from two randomized controlled trials, which supported the efficacy and tolerability of MSC-derived exosome formulations. Notably, studies involving microneedling or other mechanical delivery methods appeared to enhance treatment outcomes. Regardless of exosome origin or delivery protocol, patient

satisfaction was consistently high and reported outcomes support exosome-based approaches as effective non-surgical alternatives for hair regeneration. While the magnitude of effect varied depending on study design and follow-up duration, the results collectively reinforce the regenerative potential of exosome therapy in clinical trichology.

Exosome therapy was generally safe and well-tolerated across all included studies. Reported adverse events were predominantly mild and transient, such as local scalp irritation, redness, swelling, and itching. These effects were resolved spontaneously and did not necessitate treatment discontinuation. Importantly, no serious systemic complications, allergic reactions, or long-term adverse effects were observed. The absence of significant immunogenicity or infection across multiple formulations, including those derived from allogenic sources like placenta, umbilical cord, or bone marrow, underscores the favorable safety profile of exosome therapies when prepared and administered under appropriate clinical protocols.

Disclosure

The authors report no conflicts of interest in this work.

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