

# Clinical features of mesotherapy-associated non-tuberculous mycobacterial infections: A systematic review

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## ABSTRACT

**Background:** Cutaneous infections from non-tuberculous mycobacteria (NTM) are a well-documented but poorly characterized adverse event following mesotherapy injections.

**Objective:** This study aims to consolidate the available literature to characterize demographic and clinical features of mesotherapy-associated NTM infections.

**Methods:** Using PRISMA guidelines, a systematic review of PubMed, Scopus, and Embase databases was undertaken for articles reporting cases of NTM skin infections following mesotherapy. Data were analyzed using Microsoft Excel.

**Results:** Of 1966 search results, 30 articles (N = 423 patients) met inclusion criteria. Studies were largely from South America, and patients were mostly women aged 16-55 with NTM infections arising in the abdomen, buttocks, or thighs. Nearly all patients developed multiple, well-localized lesions without systemic symptoms. Effect summary by meta-analysis revealed most infections resolved after antibiotic therapy, though many patients required multiple antibiotic courses and/or agents to resolve infection. Infections often took weeks to resolve and were complicated by post-treatment scarring.

**Limitations:** The main limitation of this study was the heterogeneity and lack of consistency between case reports.

**Conclusion:** Cutaneous NTM infections associated with mesotherapy generally occur in women of childbearing age, arise from injections contaminated by the environment, and are often complicated by scarring/poor cosmesis and prolonged treatment course.

**Keywords:** cutaneous infection, injections, mesotherapy, non-tuberculous mycobacteria

## Introduction

Minimally invasive cosmetic procedures are increasing in popularity throughout the world. In the United States alone, 16.3 million minimally invasive procedures were performed in 2019: a 237% increase from 2000.<sup>1</sup> Although popular interest is growing, such procedures have been the subject of controversy as they are often made available before rigorous scientific evaluation of their efficacy and methods of safe administration by a licensed professional.<sup>2</sup>

Originally from France, the modern practice of mesotherapy (also called intradermal therapy) has been gaining traction throughout the world including in North and South America. Mesotherapy is an array of microinjection techniques primarily used for body contouring and reduction of subcutaneous fat<sup>2-5</sup>; this was first described by Michel Pistor in 1952.<sup>6</sup> Other applications for treatment with mesotherapy are being investigated, including for skin rejuvenation,<sup>7,8</sup> nasal pore closure,<sup>9</sup> alopecia,<sup>10</sup> lipomatosis,<sup>11</sup> musculoskeletal and neuromuscular pain relief,<sup>12-17</sup> carpal tunnel syndrome,<sup>18</sup> venous insufficiency,<sup>19</sup> and frostbite.<sup>20</sup>

Unlike FDA-approved injection of deoxycholic acid for non-surgical fat reduction,<sup>21</sup> mesotherapy is largely unregulated and may contain various compounds which have not been standardized. Common additives to mesotherapy injections include multivitamins, herbal extracts, hormones, anti-inflammatory agents, vasodilators, muscle relaxants, minerals, and active enzymes.<sup>22,23</sup> Mesotherapy is frequently performed by unlicensed practitioners.<sup>24</sup>

Various adverse events following mesotherapy have been characterized. In a 2012 case study, a 51-year-old woman developed severe acute caffeine poisoning following intradermal caffeine injections.<sup>25</sup> In 2019, a woman presented with “violaceous, painful, suppurative nodules on the buttocks and thighs,” later diagnosed as noninfectious suppurative panniculitis.<sup>26</sup> Broadly, injections are not without consequence; some cutaneous injections have been associated with the development of systemic diseases such as sarcoidosis and multiple sclerosis.<sup>27,28</sup> In other reported cases following mesotherapy, a variety of infectious organisms have been isolated including *Staphylococcus aureus*,<sup>29</sup> *Pseudomonas aeruginosa*,<sup>30</sup> *Sporothrix schenckii*,<sup>31</sup> and *Nocardia brasiliensis*.<sup>32</sup>

Cutaneous infection with mycobacteria is the most well-characterized adverse event following mesotherapy.<sup>33</sup> Such infections often present a clinical dilemma for physicians; the associated abscesses tend to be slow to culture and difficult to treat.<sup>34,35</sup> The mechanism for bacterial infection is not reliably established in all cases. For example, contamination may be found within injected material, dirty needles, or other supplies. Mesotherapy-associated outbreaks are possible if the injected solution is colonized and administered to multiple subjects, or individual patients may theoretically be exposed to pathogens through microtrauma at the injection site.<sup>36,37</sup>

This comprehensive study aims to characterize demographic and clinicopathologic features of mesotherapy-associated cutaneous non-tuberculous mycobacteria (NTM) infections. There

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is 1 systematic review that summarizes NTM species isolated from infected lesions following mesotherapy, compiled from 19 articles.<sup>33</sup> There is currently no existing meta-analysis in the research literature on the topic.

## Methods

### Search strategy and selection criteria

A systematic search of PubMed, SCOPUS, and Embase databases was conducted by 2 independent reviewers to find peer-reviewed articles discussing mesotherapy-associated non-tuberculous mycobacterial infections. Mesotherapy was defined as subcutaneous injections administered for the purpose of aesthetic treatment, lipolysis, or nontraditional pain treatment. Mesotherapy injections administered in all practice settings and by any provider regardless of training or experience were eligible for inclusion in this study. Other practices involving intradermal needle insertion/injection such as acupuncture, tattoo ink, and facial filler were not examined. Injections to any anatomic region were eligible for inclusion. A single lesion was defined as a solitary area of skin involvement or distinguishably independent site of infection as reported by researchers.

All clinical case reports/series and other retrospective study designs with at least 1 diagnosis of cutaneous non-tuberculous mycobacterial infection arising after mesotherapy injections were included. Review articles, conference abstracts, book chapters, and non-scientific publications were excluded. In total, 30 articles were included and 1936 were excluded. The key search terms employed were “mesotherapy,” “intradermal injection,” “subcutaneous injection,” “mycobacterium,” and “infection” separated by standard Boolean operators. Database search parameters were limited to title and abstract. There were no restrictions on the date of publication up to January 2021 when the review was finalized. The articles not published in the English or Spanish language or with no abstract available in the public domain were also excluded. Duplicate articles were removed and any disagreement about relevance was resolved by discussion.

### Data extraction

Demographic and clinical data were extracted from a finalized set of articles. Patient-specific information included age, sex, and race/ethnicity if available. Recorded clinicopathologic features of NTM infection included the intended purpose of the mesotherapy procedure, substance(s) injected, site of injection and anatomic location of consequent lesion, length of time to presentation after injection, lesion type (such as nodule or abscess), additional symptoms (such as fever), histopathologic description, bacterial culture growth results, treatment approach, and result of treatment (such as resolution and/or scarring).

## Statistical analysis

All data were analyzed in Microsoft Excel. Meta-analytic forest plots were generated via the methods outlined by Neyeloff.<sup>38</sup> A weighted effect size was calculated using the weighted variance and standard errors of each study. Cochran's Q test was performed and quantified using the I<sup>2</sup> statistic to evaluate the statistical heterogeneity among the included studies. A random effects model was used to calculate the 95% confidence interval. Studies with zero events were excluded from the final summary statistic. The effect of exclusion was determined to be negligible on the final summary statistic as all confidence intervals were graphically bound by lower and upper limits of 0 and 100.

## Results

### Description of patients and mesotherapy treatments

Patient data were reviewed and collected from 30 articles around the world (Fig. 1).<sup>25,35,39–66</sup> A 43.3% majority of articles (13 of 30) were published from South America. The next 36.7% of articles (11 of 30) were published from Europe. The following 13.3% of articles (4 of 30) were published from North America, and the final 6.7% of articles (2 of 30) were published from other unnamed regions. In total, 423 patients were included in this study. Sex was only available for 338 patients. Of these, 311 identified as female (92.0%) and 27 identified as male (8.0%). Age data were collected for 199 patients, and the average age was 38.7 years old. The youngest age was 16 years and the oldest was 55 years old (standard deviation of 6.2 years).

Of N = 423 patients, 192 reported a reason for undergoing mesotherapy. The most reported reason by 51.0% (98 of 192) of patients was localized fat removal for aesthetic purposes. One-third (33.3%, 64 of 192) of patients reported “generalized aesthetic purposes” which may or may not have also included localized fat reduction. Less commonly, 7.3% and 5.2% of patients reported cosmetology training to administer mesotherapy and breast augmentation, respectively (Fig. 2).

The components of the mesotherapy treatment solution also varied widely. A total of 483 injectable substances were reported. The most injected substance was plant extract (eg, ivy, thuja, artichoke) comprising 21.1% (102 of 483) of the total substances. Plant extracts were followed by algae (eg, fucus), minerals, and salts, which comprised 14.3%, 14.1%, and 14.1%, respectively. Other notable compounds included procaine, phosphatidylcholine, and ampelopsin (Fig. 3).

### Clinical features

The time from mesotherapy injection to clinical manifestation of infection ranged from 1 day to 3 months, with a mean of 32.5 days (n = 135) to presentation. Skin lesions generally arose over the sites of injection. Of 128 patients who reported their number of skin lesions, 97.7% presented with multiple lesions. The number of patients with a singular lesion regardless of size was much

<b>Records identified through database searching:</b> Pubmed: N = 933 Embase: N = 244 Scopus: N = 789	
<b>Records excluded by title and abstract:</b> N = 1922	<b>Records assessed by full text for eligibility:</b> N = 44
<b>Records excluded after in-depth review:</b> N = 14	<b>Records accepted for analysis:</b> N = 30

Fig. 1. PRISMA flow diagram. After a systematic review of 1966 articles, 30 were ultimately selected for inclusion.

### Reason for Mesotherapy Injection

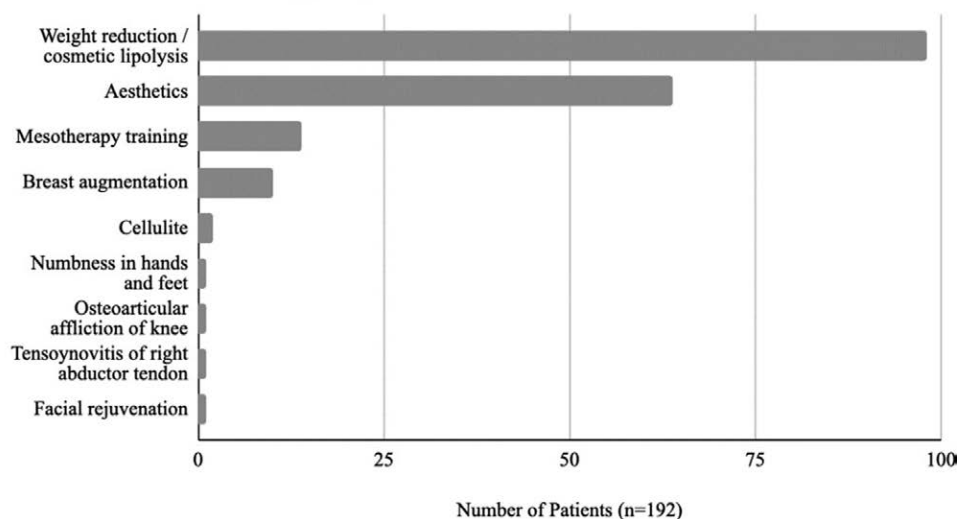


Fig. 2. Reason for mesotherapy injection. The most common reason for mesotherapy injection was for weight reduction/cosmetic lipolysis.

smaller, comprising only 2.3% of the data set. Across all 128 patients, a total of 699 lesions were reported with the most commonly affected sites being the hips and thighs (29.3%), abdomen (26.2%), and gluteus (20.3%) (Fig. 4). Lesion types varied from nontender, subcutaneous nodules to abscesses to suppurative ulcers. In addition to the skin lesions, 8.0% of patients (N = 423) reported systemic symptoms such as fever, malaise, or headache.

### Microbiological features

For the 179 patients for whom definitive microbiological data were available, the specific genus of infection-causing non-tuberculous mycobacteria was identified in 93.3% of patients.

The remaining 6.7% of patients were culture positive, though their unique genus remained unidentified. *Mycobacteroides chelonae* was the most commonly isolated organism, infecting 43.6% of patients. This was followed by *M. abscessus* and *M. fortuitum*, infecting 24.6% and 17.3% of patients, respectively. Less commonly implicated organisms were *M. simiae* and *M. lentiflavum*, each infecting only 0.6% of patients (Fig. 5). Two patients were found to have a co-infection.

### Treatments

Patients were generally treated with at least 1 course of antibiotics and/or surgical drainage/removal. The most commonly

### Compound Injected

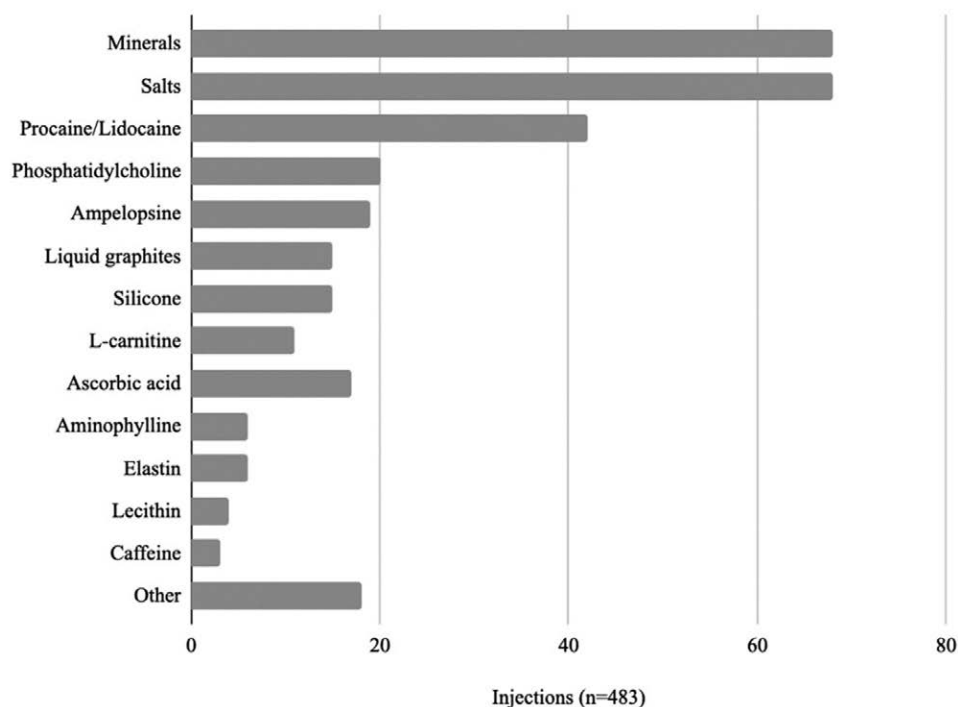


Fig. 3. Mesotherapy component injected. The most injected mesotherapy component was plant extract followed by algae, minerals, and salts.

### Location of Injection

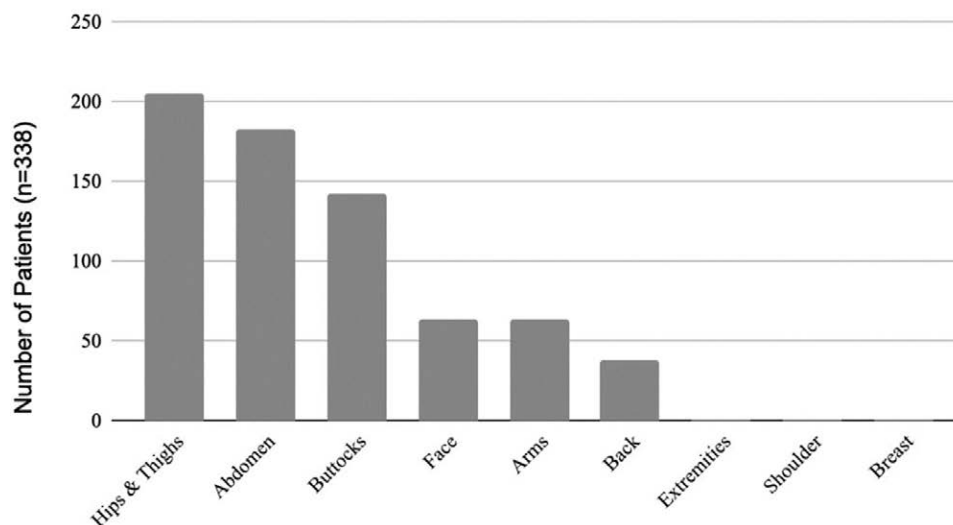


Fig. 4. Location of mesotherapy injection. Mesotherapy injections were most commonly administered to the hips and thighs.

prescribed antibiotic was clarithromycin, making up 41.7% of medications prescribed, followed by fluoroquinolones (specifically ciprofloxacin or levofloxacin), making up 31.6% of medications prescribed. Of the 232 patients who reported their specific antibiotic regimen, 71.1% of patients were simultaneously prescribed more than 1 antibiotic, and the remaining 28.9% of patient infections were resolved with antibiotic monotherapy. Additionally, 47.9% of patients (134 of 280) for which prior or current treatments were detailed required multiple courses of antibiotics to achieve resolution. Some patients failed antibiotics given to them by the mesotherapy provider before presentation. For example, in a 2010 study of mesotherapy-associated cutaneous infections in Colombia, 68.6% of patients (48 of 70) had been treated with a failed course of antibiotics or steroids by their mesotherapy provider before they were treated at a medical institution.<sup>65</sup>

The average minimum treatment time was 19.8 weeks with a standard deviation of 9.0 weeks ( $n = 114$ ). Patients were administered antibiotic therapy for extended periods ranging from 1 to 15 months, with at least 95.0% ( $n = 386$ ) of recorded treatment courses spanning between 3 and 8

months. For <1% of patients (2 of 280) for whom the treatment regimen was recorded, surgical drainage was sufficient to clear the infection without antibiotics. For 23.2% of patients (65 of 280), surgical drainage was performed in addition to antibiotic treatment.

Though many patients were administered multiple courses of treatment, most infections eventually resolved. For a small minority of patients (3.2%, 9 of 280), however, resolution was never recorded even after trialing multiple treatments. For 7 such patients, antibiotics were discontinued prematurely due to adverse medication reactions or patient exhaustion.<sup>35</sup> For the remaining 2 patients, symptoms persisted at least 1 year after treatment.<sup>66</sup>

### Outcomes

Following treatment, 96.9% of patients achieved resolution of their cutaneous infections, defined as the absence of detectable bacteria, newly appearing skin lesions, or systemic symptoms (Fig. 6). The average minimum length of time to resolution based on start of treatment to resolution at follow-up visit was

### Isolated Organism

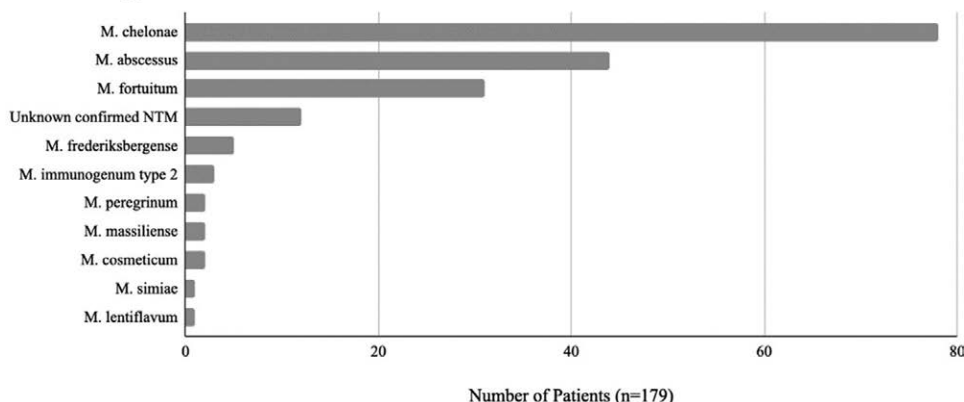


Fig. 5. Causative NTM in cutaneous mesotherapy-associated NTM infections. The most commonly implicated organism in mesotherapy-associated cutaneous NTM infections was *Mycobacteroides chelonae*. NTM, non-tuberculous mycobacteria.



**Fig. 6.** Full resolution after treatment with surgical drainage and/or antibiotics. Following treatment with surgical drainage and/or antibiotics, 96.9%  $\pm$  8.3% of patients achieved resolution.

19.8 weeks, with a standard deviation of 9.0 weeks ( $n = 114$ ). Regardless of resolution, 65.9% of treated patients developed post-treatment complications (Fig. 7). Scarring was the most reported post-treatment complication, affecting 80.3% ( $n = 61$ ) of the patients who reported complications.

## Discussion

Based on these results, the patient population most affected by non-tuberculous mycobacterial skin infections resulting from mesotherapy injections were South American women of childbearing age. Skin lesions present at the sites of mesotherapy injection primarily affected the hips, thighs, abdomen, and buttocks. These tend to be common “problem areas” for women to target, holding cellulite and gynoid fat that can be difficult to eliminate with natural lifestyle modifications.<sup>4</sup> The infected skin lesions, whether nodules or abscesses, tended to occur at multiple sites rather than as isolated or single lesions. This finding supports the theory that such infections are usually caused by contaminated mesotherapy fluid rather than by bacterial entry through a breach in the skin barrier.<sup>37</sup>

Though most patients were cured of their infections with antibiotics, most required multiple antimicrobial agents and more than 1 course of treatment. Infections typically took several months to resolve and were frequently complicated by post-treatment scarring. These findings suggest that mesotherapy-associated NTM infections are difficult to treat and subsequent cutaneous sequelae defeat the originally intended purpose of improving the aesthetic appearance of the skin.

The 2 most commonly responsible pathogens, *M. chelonae* and *M. abscessus*, are often resistant to antibiotics which likely contributes to challenges in treatment.<sup>67,68</sup> Patients considering mesotherapy, therefore, should be informed before the procedure that cutaneous infection arising as a complication of the procedure may have to be treated with multiple antibiotics for several months with probable scarring and

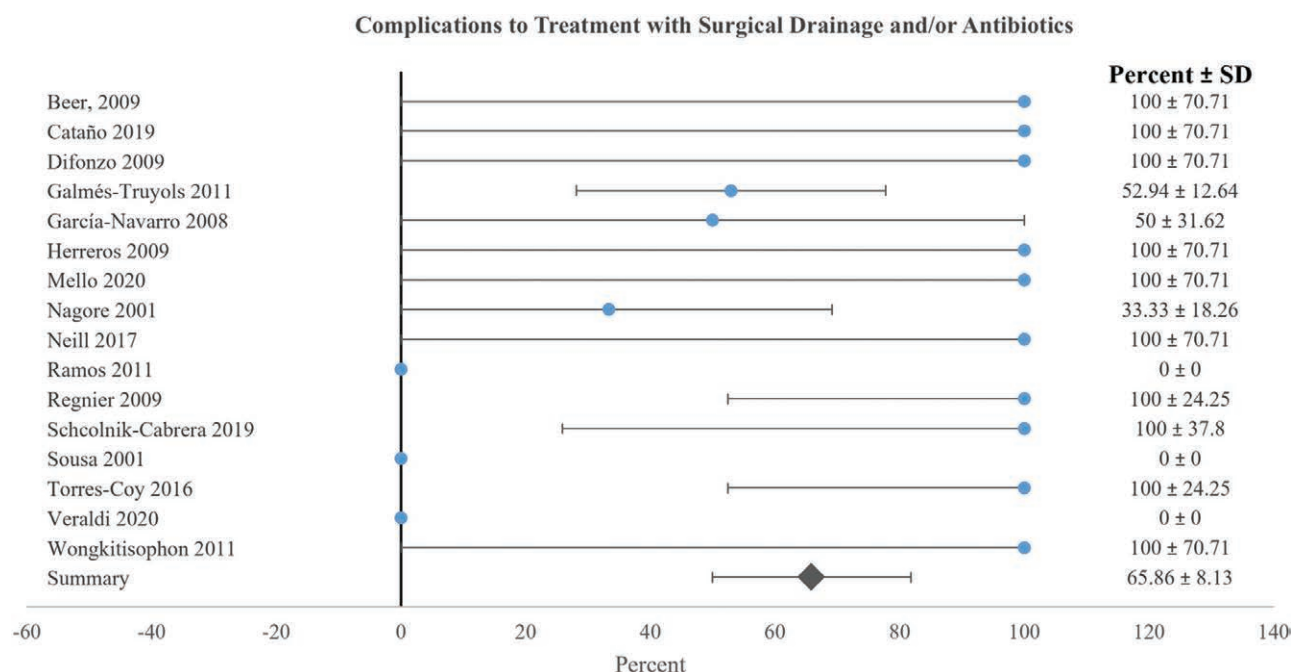
no guarantee of resolution. A common trend throughout the reported cases was that non-medical or otherwise unorthodox treatments were often implicated, leading to the deduction that these settings may be more subject to contamination and subsequent complications. Patients who undergo mesotherapy injections outside of regulated healthcare environments and who are not formally consented will then be subjected to a higher level of risk and simultaneously have less foreknowledge of their risk.

The main limitation of this study was the heterogeneity and lack of consistency between data sets in each included case report. Very few articles reported every sought-after variable, leading to variable sample sizes when examining individual demographic characteristics and clinical features. It was unclear if certain clinical details were purposely omitted due to their absence or simply went unreported. Additionally, time intervals (ie, time to presentation, treatment course length) were difficult to calculate as some papers provided rough estimates which could not enter into a mathematical average.

## Conclusions

Mesotherapy injections are often administered to women of childbearing age by unlicensed providers and are commonly complicated by cutaneous NTM infections. Systematic review and meta-analysis revealed that such infections tend to occur in areas of gynoid fat distribution (hips, thighs, buttocks) and generally present with multiple skin lesions due to environmental contamination of injected fluid. The most isolated organism was *M. chelonae*. Such infections are often marked by a prolonged treatment course and scarring. Future research may focus on interventions related to addressing health literacy and the psychosocial influence of beauty standards on women in affected regions. More importantly, there should be a focus on conducting studies on randomized patients treated by the same, trained health professional according to a





**Fig. 7.** Complications to treatment with surgical drainage and/or antibiotics. Regardless of whether the patient's infection resolved or not, 65.9% ± 8.1% of treated patients developed post-treatment complications.

standardized protocol; the studies included in this review are heterogenous with inconsistent methodology and are therefore of lesser value.

### Conflicts of interest

None.

### Funding

None.

### Study approval

N/A.

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