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ORIGINAL PAPER

Beyond classic vs. crusted: the high-load non-crusted scabies phenotype in a prospective multicenter cohort

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Abstract

In classic scabies, mite burden is typically low, whereas crusted scabies exhibits massive infestation. During recent surges in presentations, we observed immunocompetent patients with non-crusted scabies referred for persistent or relapsing symptoms after standard topical therapy, who appeared to carry higher burdens. We aimed to estimate the frequency of a pragmatic high-load scabies phenotype among patients presenting with apparent topical treatment failure and to summarize its clinical features and outcomes. In a prospective, multicenter cohort across 10 dermatology centers in Türkiye, we enrolled patients with suspected scabies who had persistent or relapsing symptoms despite standard therapy and fulfilled a predefined high-load phenotype (≥50 mite-confirmed burrows on dermoscopy). The primary endpoint was Day-28 dermoscopic clearance, defined as no mites/ova and no new burrows at index sites. At baseline, all burrows were counted under a shared standard operating procedure (SOP). High-load scabies was defined a priori as ≥50 burrows. Of 3,316 patients screened, 76 (2.3%) met the high-load definition. The cohort comprised 42 men (56.1%) and 34 women (43.9%) with a mean age of 30.24 years. Baseline burrow counts ranged 50–400 (mean 86). Age showed a moderate positive association with burrow count (Spearman's $\rho = 0.365$, $p < 0.01$), whereas sex and household high-load history were not associated (both $p > 0.05$). In routine care, combined oral ivermectin plus topical therapy was associated with clinical clearance in 89% ($n = 68/76$) of these high-load cases. This observation reflects outcomes among patients presenting after apparent topical treatment failure and does not establish a causal role of mite burden in treatment failure or transmission. This multicenter cohort defines a pragmatic high-load scabies phenotype (≥50 dermoscopically counted burrows) that lies between classic and crusted disease. Routine dermoscopy allowed pragmatic burden stratification in this cohort; in patients meeting the ≥50-burrow definition, combined oral and topical therapy was associated with high clearance in routine care.

Keywords Sarcoptes scabiei · Scabies · ivermectin · Acaricide · Scabies outbreak · Mite burden

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Introduction

Scabies is an ectoparasitic infestation that causes intense pruritus and recurrent outbreaks. Its clinical burden has risen in recent years in several settings, including Türkiye [1]. In parallel, reports of apparent treatment failure have increased [2]. Although permethrin is frequently implicated, much of the literature emphasizes pseudo-resistance and operational factors rather than proven pharmacologic resistance per se [3]. Cohort studies indicate that most 'treatment failures' cluster around modifiable, non-pharmacologic factors—notably incomplete or single-dose regimens, insufficient laundering/heat treatment of clothing and bedding, and failure to treat close contacts simultaneously—rather than true drug resistance [4]. To date, molecular confirmation of resistance to first-line agents remains inconclusive [2, 3], underscoring the need to examine determinants of non-response beyond drug resistance alone.

Clinically, scabies presents predominantly as classic or crusted disease. Classic scabies typically harbors a low mite burden, often estimated at ~10–20 mites per patient, as first demonstrated in the seminal work of Mellanby [5]; notably, Mellanby himself observed that a small number of patients had unexpectedly high mite counts for which he did not identify a clear explanation, whereas crusted scabies can contain up to 1–2 million mites [6]. Crusted disease is characteristically associated with immunosuppression or major comorbidities and poses substantial therapeutic challenges [7, 8]. Against the backdrop of recent surges in presentations [1], we observed immunocompetent, patients with non-crusted scabies who nonetheless appeared to carry higher-than-expected burdens and frequently presented with persistent symptoms after standard topical therapy.

We therefore designed a prospective, multicenter study to estimate the frequency of this high-load phenotype among patients with apparent topical treatment failure and to summarize its clinical features and routine-care outcomes.

Materials and methods

The study protocol was approved by the Bezmialem University Ethics Committee (Approval No. [2024/30]; [February 2024]) and conducted in accordance with the Declaration of Helsinki. Oversight and harmonization were provided by the Turkish Dermatology Association (TDA) Microscopy Working Group under a prespecified, SOP procedure.

Participants and eligibility

Patients presenting to participating dermatology outpatient clinics with suspected treatment-refractory scabies were assessed. Inclusion criteria were: (1) persistence or relapse of symptoms despite at least one full course of standard antiscabietic therapy; and (2) presence of ≥50 mite–confirmed burrows on dermoscopy.

Definitions: Standard antiscabietic therapy was defined as the adequate application of topical permethrin 5% (typically two applications one week apart) or sulfur-based preparations (typically applied nightly on three consecutive nights, repeated after one week if needed), accompanied by reported household hygiene measures. Persistence was defined as the uninterrupted presence of pruritus and new lesions following treatment; relapse was defined as the recurrence of symptoms after a symptom-free interval.

Exclusion criteria

To isolate a high-load phenotype independent of host immune status and to allow reliable counting, we excluded: (1) Patients with clinically significant immunosuppression (e.g., use of systemic corticosteroids, biologics, cytotoxic chemotherapy, advanced HIV) or major comorbidities traditionally associated with crusted scabies (e.g., sensory neuropathy, Down syndrome); and (2) Pediatric patients (<18 years); (3) individuals whose cooperation was insufficient for reliable whole-body dermoscopic counting; and (4) individuals with crusted scabies, as the study was specifically designed to characterize the non-crusted high-load phenotype.

Dermoscopic assessment and definitions

Dermoscopy was performed at participating clinics. Burrows were identified, marked with a skin marker, and counted after examination. "Mite load" was operationalized as the number of mite-confirmed burrows per patient at baseline. For descriptive purposes, "high-load" refers to a non-crusted scabies presentation with a markedly increased number of dermoscopically identifiable burrows compared with classic scabies. A burrow was counted only when a mite was confirmed within it by visualization of the pathognomonic "delta-wing/jet with contrail" sign, as illustrated in Fig. 1. During real-time dermoscopic examination. During real-time dermoscopic examination, this criterion was applied consistently across all participating centers. While the absolute number of mites may exceed the dermoscopically counted burrows, we used standardized burrow enumeration as a reliable pragmatic proxy for burden in this non-crusted cohort. Mite load was operationalized as the number of burrows per patient at baseline. In representative cases, videos were recorded to document the presence of burrowing mites and characteristic morphological features

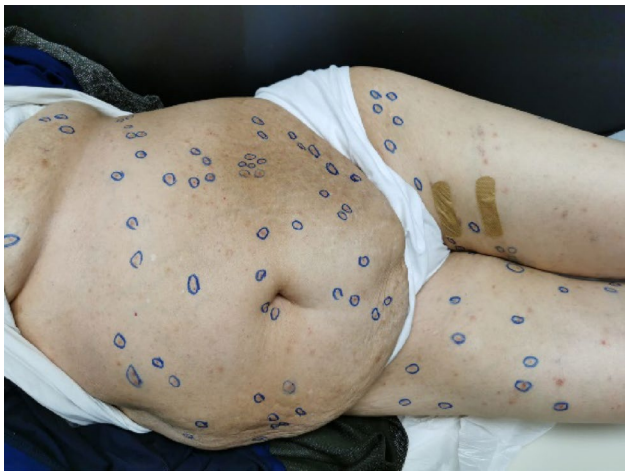

Fig. 1 Dermoscopic assessment of a representative lesion demonstrating the pathognomonic "delta-wing" (jet with contrail) sign. The dark triangular structure at the leading edge corresponds to the head and forelegs of the mite, confirming the presence of a parasite within the burrow

(e.g., delta-wing/jet-with-contrail sign and cheliceral movement) for illustrative and confirmatory purposes, rather than for quantitative behavioral analysis. For operational purposes in this study, a threshold of ≥ 50 burrows was used to identify patients meeting the predefined high-load criterion. We chose this cut-off based on (i) consistent multi-center clinical experience in treatment-refractory cases, (ii) the need to separate heavy but non-crusted disease from both classic and crusted scabies, and (iii) more reliable counting at higher totals.

Data collection

For enrolled participants we recorded: baseline mite load; prior treatments; anatomic distribution; household/family history of infestation; confirmed household high-load infestation; and treatment response. Household history was defined as ≥ 1 cohabitant at the same primary address who was documented with high-load scabies during the study period.

Treatment protocol (inter-center SOP)

Across all centers, the standard of care for high-load scabies was a combination of oral ivermectin plus topical permethrin 5%. Ivermectin was administered at 200 µg/kg on Day 1 and Day 8 (ivermectin was not given to patients < 15 kg or during pregnancy/lactation). Topical permethrin 5% cream was applied from the neck down in a thin layer, left in place for 8–12 h, then washed off, and reapplied on Day 1 and Day 8. However, in patients demonstrating clinical involvement of the face or scalp, the application was extended to include these areas. All household contacts were treated concurrently on the same days with standard topical regimens. Environmental measures were standardized: clothing/bed linens/towels used within the prior 3 days were washed at ≥ 60 °C or sealed in a bag for ≥ 72 h; frequently touched surfaces were cleaned and vacuumed. Symptomatic itch was managed, when needed, with short-course oral antihistamines and emollients; signs of secondary bacterial infection were treated with appropriate antibiotics.

Follow-up and endpoints

The Day 14 visit was planned strictly for clinical management (retreatment decisions) and was not an analytic endpoint. At the Day-14 visit, patients who continued to show dermoscopic evidence of active infestation (presence of the delta-wing sign) received an additional cycle of oral ivermectin (200 µg/kg) plus topical permethrin 5%, using the same protocol as Days 1 and 8. The primary endpoint (clinical clearance) at Day 28 (± 7) required the complete absence of live mites/ova and no new burrows across the entire body surface, including all previously marked sites and any newly symptomatic areas. Dermoscopic resolution was defined as the disappearance of the 'delta-wing/jet with contrail' sign with the presence of disrupted, desquamating empty burrows Fig. 6 .At Day 28, dermoscopic assessment was repeated across the entire body surface to identify whether new burrows had appeared at previously marked sites or at any newly symptomatic areas.

Reporting guideline

This prospective multicenter cohort study is reported in accordance with the STROBE statement for observational studies; a STROBE flow chart and the completed STROBE checklist is provided as Supplementary Fig. 1 and 2.

Statistical analysis

Analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as median [interquartile range, IQR] or mean (standard deviation) as appropriate; categorical variables as n (%). Normality was assessed with the Shapiro–Wilk test. Between-group comparisons of non-normally distributed continuous variables (e.g., mite-load/burrow counts) used the Mann–Whitney U test. Associations between age and mite load were evaluated with Spearman's rank correlation (ρ) with two-sided 95% confidence intervals. Unless otherwise specified, two-sided tests with $\alpha = 0.05$ were used. Missing data were not imputed and denominators are reported where applicable.

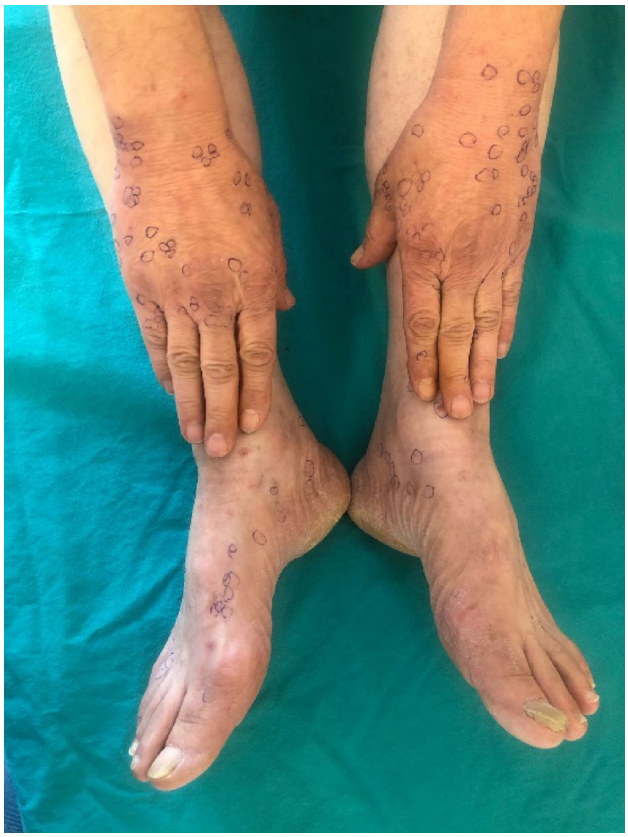

Fig. 2 Truncal distribution in high-load scabies in a 64-year-old female patient (total 267 burrows). Baseline photograph showing dermoscopically identified burrows mapped with a skin marker per SOP. Burrows are scattered over the abdomen, flanks, and proximal thighs with multi-site clustering yet no crusting, consistent with a non-crusted high-load phenotype (≥50 burrows). Each circle denotes one burrow; image is de-identified with written consent. Dense clustering of burrows without crusting is evident, consistent with the non-crusted high-load phenotype

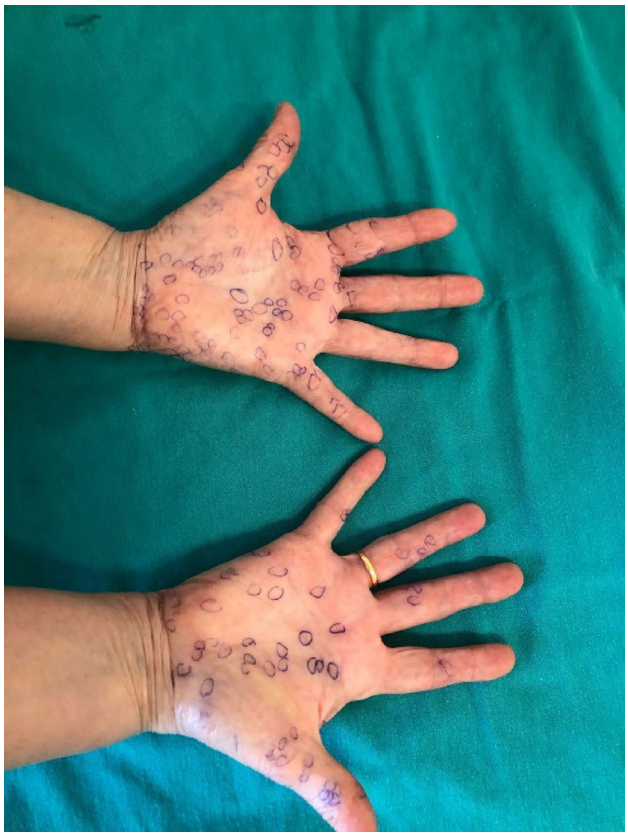

Fig. 3 Acral-dominant distribution—48-year-old man (total 320 burrows). Burrows mapped across dorsal hands, wrists, and lower legs/ankles. Note confluent groupings at the flexural wrists and peri-malleolar areas, consistent with extensive high-load scabies without crusting

Results

Participants and baseline characteristics

Between March-October 2024, across 10 dermatology centers in Türkiye, we screened 3,316 patients with suspected treatmentrefractory scabies (Supplementary Fig. 1).Of these, 76 (2.3%) met the high-load definition and comprised the analytic cohort. The cohort consisted of 42 men (56.1%) and 34 women (43.9%) with a mean age of 30.2 years (standard deviation [SD] ± [11.8]).

Mite load and distribution

Baseline mite load (burrow count) ranged from 50 to 400, with a mean of 86 and a median of 72 (IQR [58]–[110]) (Figs. 2, 3, 4, 5 and 6). There was a moderate positive association between age and mite load (Spearman's $\rho = 0.365$, $p < 0.01$), indicating higher burrow counts at older ages. Mite load did not differ by sex (Mann–Whitney U, $p > 0.05$). Likewise, household history of high-load infestation was not associated with patient burrow counts (Mann–Whitney U, $p > 0.05$). Representative cases were additionally documented with clinical photographs and dermoscopic video recordings (Online Resources 1–3).

Treatment outcomes

Combined oral ivermectin plus topical therapy achieved clinical clearance in 68 of 76 patients (89.5%; 95% confidence interval [CI] 82.6%–96.4%). Note: Detailed analysis of non-responders was not performed due to the high cure rate and limited sample size of failures.)

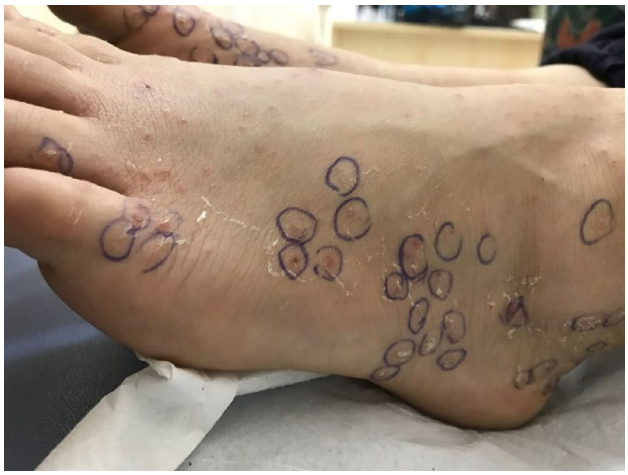

Fig. 4 Palmar burden map—64-year-old woman (total 92 burrows). Baseline clinical photograph showing dermoscopically identified burrows mapped with a skin marker per SOP. Dense clustering along palmar creases and the ulnar/thenar regions illustrates an acral-predominant high-load pattern (≥50 burrows)

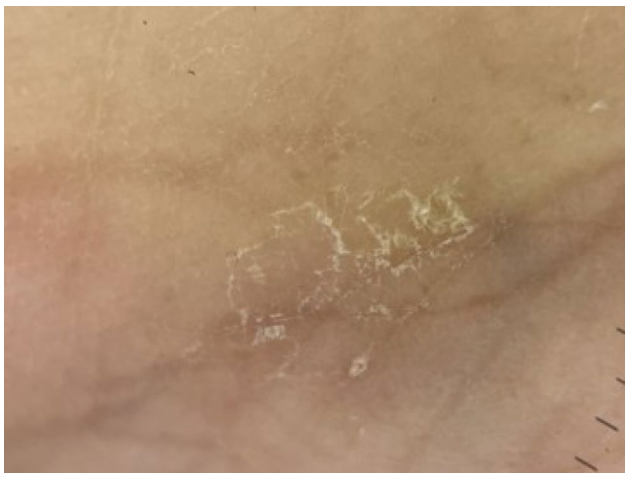

Fig. 5 Clustered burrows at the foot—42-year-old woman (total 293 burrows). Close-up of lateral foot/ankle with dense, coalescent clusters and interdigital involvement. Fine surface scale and excoriations are present. Burrows were enumerated dermoscopically and marked per SOP

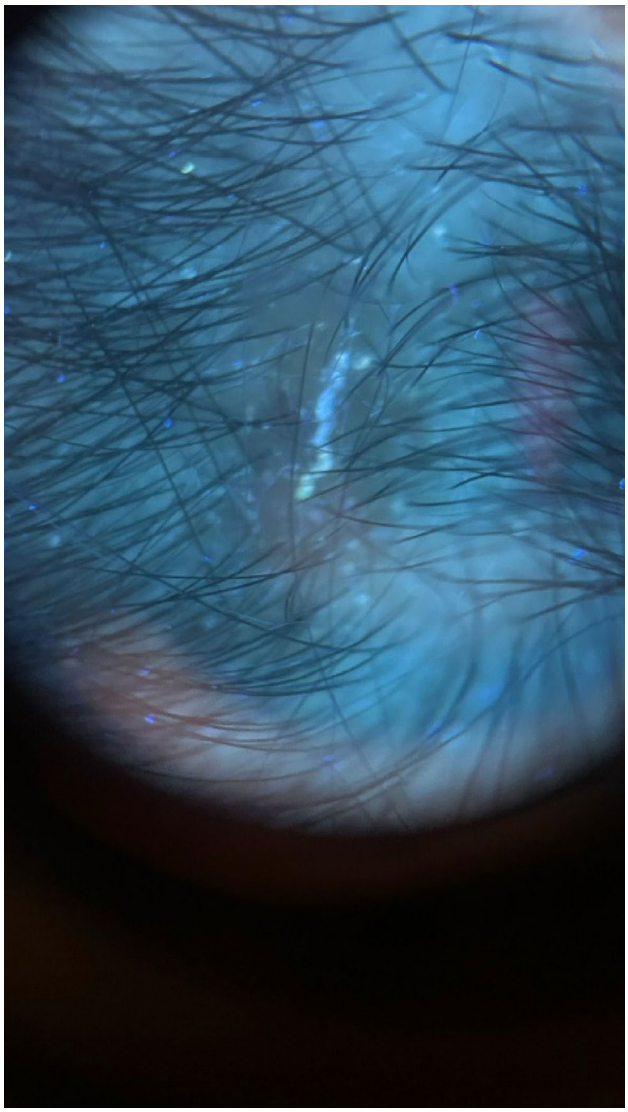

Fig. 6 Post-treatment dermoscopic assessment (Day 28). This image demonstrates the resolution of the infestation. Note the absence of the "delta-wing/jet with contrail" sign (which would indicate a mite). Instead, only the disrupted, white scaling of the empty burrow roof remains, consistent with the desquamation of the stratum corneum following successful treatment

Discussion

Interpretation of key findings

Against the backdrop of rising case numbers and apparent failures of standard topical regimens, this study applies a burden-oriented, physiology-informed perspective to scabies. Our findings suggest that dermoscopy-quantified mite burden may help delineate a clinically relevant subgroup of patients at increased risk of apparent non-response to topical therapy. In this context, high mite burden likely reflects a combination of biological and operational factors that challenge the effectiveness of topical monotherapy and may theoretically increase transmission potential. However, transmission dynamics were not directly assessed in this study.

Phenotypic context and pathophysiologic considerations

Classically, mite burden in immunocompetent hosts is low, maintained by immune control [9–11]. The seminal observations of Mellanby [5] established the expectation of ~10–20 mites per host, although he also noted rare cases of unexpectedly high counts in otherwise healthy individuals.

In our cohort, however, we encountered patients whose clinical appearance resembled classic scabies (non-crusted) yet whose baseline burrow counts (50–400) significantly exceeded the classic range [12]. The absence of immunosuppression and crusting in our exclusion criteria supports the existence of a pragmatic "intermediate" phenotype [13, 14]. We observed a positive correlation between age and mite load, a finding that aligns with recent observations suggesting that older individuals may harbor higher burdens due to factors such as immunosenescence—manifesting as reduced scratching reflexes or diminished cell-mediated immunity. Importantly, age was analyzed as a continuous variable, and the study was not designed or powered to evaluate specific age thresholds or to define an age-based high-risk group for treatment failure. Beyond biological considerations, delayed presentation, repeated exposure in high-transmission settings, and challenges in achieving effective household and environmental control -particularly in older age people and in crowded living conditions- may facilitate sustained infestation and reinfestation [15]. In addition, immunocompetent hosts are not immunologically homogeneous; functional variability in host immune responses may facilitate nymphal stages survival and maturation into adult mites. These factors likely interact with biological mite characteristics to shape the observed high-load phenotype.

From a biological standpoint, mite burden represents the outcome of life-cycle efficiency. Although we did not perform quantitative motility assays, video recordings(Videos 1–3) showed vigorous mite activity, characterised by rapid cheliceral movements and efficient burrow extension (delta-wing/jet-with-contrail sign). These observations surprised our team when compared with our previous personal experience and suggested that mites in high-load patients exhibit greater vitality, which may facilitate faster burrow progression and reproductive success even in the absence of overt host immunosuppression. This hypothesis-generating finding warrants confirmation in future controlled microscopy studies.

Interpretation and clinical implications

Recent evidence suggests that "treatment failure" often stems from operational factors rather than drug resistance alone [3–5]. Our data propose that high mite load serves as a valuable clinical marker in this context. While we cannot definitively state that high load causes the failure of topical monotherapy without a control group, the presence of such a high burden may pose practical challenges to topical application coverage; however, transmission dynamics were not directly assessed in this study. While awaiting more definitive studies, for patients meeting this high-load definition, we describe the routine-care approach used across centers, which involved front-loading combined oral ivermectin plus topical therapy alongside rigorous household and environmental management. Importantly, this strategy reflects pragmatic clinical practice and cannot be inferred as superior to topical monotherapy without comparative or controlled studies. This approach is consistent with guidance for heavier-burden phenotypes [7] and offers a proactive strategy to reduce the risk of ongoing transmission.

Limitations

Strengths include a prospective, multicenter design and standardized dermoscopic enumeration. Our study has limitations inherent to its pragmatic design, which preclude definitive causal inferences regarding treatment failure. The primary limitation is the absence of a concurrent control group; we did not analyze the 3,240 screened patients who did not meet the high-load criteria or who responded to initial therapy. Consequently, we cannot statistically compare "responders" against "non-responders" to definitively establish high load as an independent risk factor for failure. Additionally, potential selection bias exists as the cohort represents a specific subset of patients presenting to tertiary centers, which may not fully reflect primary care prevalence. Methodologically, we used dermoscopic burrow counts as a practical proxy for total mite load; however, this approach may underestimate the true burden compared to ex vivo extraction methods. In addition, formal inter-observer reliability testing was not performed, and although a standardized dermoscopic protocol was used across centers, some degree of observer-related variability cannot be excluded. Similarly, video recordings of mites were descriptive and hypothesis-generating; no quantitative assessment of motility or formal comparison with low-burden specimens was performed. In addition, Day-14 retreatment data—specifically the number of patients requiring an additional treatment cycle and their subsequent outcomes—were not systematically recorded as a separate analytic variable, precluding a per-protocol subgroup analysis of retreated versus non-retreated patients. Baseline photographic documentation was limited to representative cases; Day-28 assessment of new burrows therefore relied on anatomic-site-level dermoscopic re-examination rather than individual burrow-level comparison. Additionally, adherence to prior topical regimens and environmental measures was self-reported and could not be objectively verified, which may have influenced the characterization of treatment-refractory cases.

Conclusion

We operationalized a pragmatic high-load non-crusted scabies phenotype (≥50 dermoscopically counted burrows) that clinically sits between classic and crusted disease. Identification of this high-load subgroup via routine dermoscopy describes a pragmatic approach used in routine care, in which combined oral and topical therapy was associated with high clearance rates in this cohort; however, as some patients required additional treatment cycles at Day 14, future studies should report the number of cycles needed for clearance. Future controlled studies are needed to prospectively validate this threshold, directly compare outcomes against low-load populations, and determine whether this approach should be adopted as a universal treatment algorithm.

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Author contributions Conceptualization: A.Y, G.Ş.Investigation: A.Y, M.D, S.A.T, I.D.O, S.A, Ü.G, Ö.S.K, B.A, S.K, F.U, İ.C, S.D, E.T.A, T.T, İ.M, M.Ö, G.Ş.Formal analysis: A.Y, M.D, S.A.T.Visualization: A.Y, Ö.S.K, Ü.G, S.A.T.Writing—original draft: A.Y, M.D, S.A.T, I.D.O, S.A, Ü.G, Ö.S.K, G.Ş.Writing—review & editing: A.Y, G.ŞSupervision: A.Y, M.D, S.A.Project administration: A.Y, M.D, S.A.T.All authors approved the final version and agree to be accountable for all aspects of the work.

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Data availability The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval and consent to participate Ethics committee approval was received from the Bezmialem University Ethics Committee (Approval No. [2024/30]; [February 2024]) and the study was conducted in accordance with the Helsinki Declaration.

Informed consent Written informed consent obtained for participation in the study and for publication of images/videos was obtained.

Consent for publication Permission granted by all authors.

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