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**Systematic Review**

# *Acanthamoeba* keratitis: prevalence, diagnosis, treatment and future trends: a systematic review

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## ABSTRACT

*Acanthamoeba* keratitis (AK) is a rare but severe corneal infection caused by free-living *Acanthamoeba* species. It is increasingly recognised as a significant cause of visual morbidity, especially among contact lens users. This systematic review follows preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 guidelines and analyses studies published between January 2000 and January 2025, focusing on AK prevalence, diagnostics, treatment, and innovations. Our search across databases, including PubMed and Scopus, identified 20 peer-reviewed studies. Findings reveal a 35-50% increase in global AK incidence since 2000, particularly affecting Europe, East Asia, and North America, with 85-90% of cases linked to contact lens wear and the T4 genotype being the predominant strain. Advancements in diagnostics, such as polymerase chain reaction (PCR) testing (with over 95% sensitivity) and *in vivo* confocal microscopy (IVCM) (with 85-90% sensitivity), have improved early detection. Emerging technologies, including metagenomics sequencing and artificial intelligence (AI)-driven imaging, have further enhanced diagnostic accuracy, achieving a specificity of over 93%. Current treatments rely on a combination of biguanides and diamidines, but prolonged therapies often lead to recurrence, with 20-25% of severe cases requiring keratoplasty. Innovations such as nanocarrier drug delivery, photodynamic therapy (PDT), and genotype-specific antimicrobials are promising. While advancements in the diagnosis and treatment of AK have improved, challenges in reducing the disease burden and improving long-term outcomes remain. The future of AK management hinges on integrating molecular diagnostics and AI into clinical practice, supported by public education on safe contact lens hygiene practices.

**Keywords:** *Acanthamoeba* keratitis, Contact lens, *In vivo* confocal microscopy, Polymerase chain reaction, Nanotechnology, Photodynamic therapy

## INTRODUCTION

*Acanthamoeba* keratitis (AK) is an uncommon yet devastating infection of the cornea caused by the free-living amoeba genus *Acanthamoeba*, which exists ubiquitously in soil, water, and air.[1] The organism is a facultative pathogen, meaning it can survive independently in the environment but may infect humans under favourable conditions. AK was first described in the 1970s, but its incidence has increased significantly over the past two decades due to rising global contact lens use.[2] It primarily affects soft contact lens wearers, accounting for approximately 85-90% of all reported cases; however, non-contact lens-related cases have also been reported in association with corneal trauma, exposure to contaminated water, and poor ocular hygiene.[3,4] The *Acanthamoeba* organism exists in two morphological forms: the trophozoite, the active, feeding, and replicating stage, and the cyst, a dormant, double-walled structure highly resistant to environmental stresses and therapeutic agents.[5] This dual nature complicates eradication, as cysts can survive disinfection procedures, leading to recurrence and chronic infection. Molecular studies have identified over

20 *Acanthamoeba* genotypes, of which T4 is most commonly associated with keratitis.[6] Since 2000, epidemiological reports have demonstrated a marked global rise in AK incidence, particularly in industrialized regions where contact lens use is prevalent.[7] For example, studies in the UK, Netherlands, and parts of Asia have reported incidence rates ranging from 1 to 33 cases per million contact lens wearers annually.[8,9] However, these figures may underestimate actual burden due to frequent misdiagnosis with herpetic, fungal/bacterial keratitis.[10] Climatic factors, such as humid conditions and higher water temperatures, further facilitate *Acanthamoeba* survival and transmission, particularly through domestic water systems.[11] Over past 25 years, diagnostic approaches have undergone substantial evolution. Traditional culture-based identification on non-nutrient agar remains the gold standard but is time-consuming and operator-dependent.[12] The introduction of IVCM has revolutionised AK diagnosis by allowing visualisation of characteristic cysts in corneal tissue, with reported sensitivities of the 85-90%.[13]

Moreover, PCR and real-time quantitative PCR (qPCR) assays targeting the 18S rRNA gene have enabled rapid, highly sensitive detection of pathogenic genotypes.[14] More recently, next-generation sequencing (NGS) and AI-driven image recognition have enhanced early differentiation of AK from fungal and viral keratitis.[15] Treatment of AK remains challenging due to the cystic stage's resilience to anti-amoebic drugs. The standard therapeutic regimen combines biguanides (polyhexamethylene biguanide or chlorhexidine) with diamidines (propamidine isethionate), targeting both trophozoites and cysts.[16]

However, prolonged treatment duration-often exceeding six months-is frequently required. Emerging resistance and drug toxicity have motivated research into alternative therapies, including nanocarrier-based drug delivery systems, PDT, and CRISPR-based gene silencing approaches targeting cyst wall biosynthesis.[17] Recent advancements in nanomedicine have shown potential to improve corneal drug penetration and reduce systemic toxicity. Additionally, immunomodulatory strategies, such as corticosteroid-sparing regimens and cytokine inhibitors, are being explored to minimise inflammation-related tissue damage. Despite these innovations, delayed diagnosis remains a key prognostic determinant. Early recognition through advanced imaging, coupled with genotype-specific therapy, is essential to improving visual outcomes. Increased awareness among clinicians and contact lens users, along with enhanced public health surveillance, is vital to curbing the growing incidence of AK.[18] Therefore, this systematic review aims to integrate global evidence from 2000 to 2025, analysing trends in prevalence, diagnostic accuracy, therapeutic efficacy, and technological innovations in AK management. By synthesising recent findings, this review underscores the shift toward precision medicine and AI-assisted ophthalmology in combating AK.[19]

## METHODS

This systematic review was designed and conducted according to the PRISMA 2020 guidelines (Figure 1).[20] The review protocol was registered and developed to ensure methodological transparency, minimise bias, and allow reproducibility of findings.

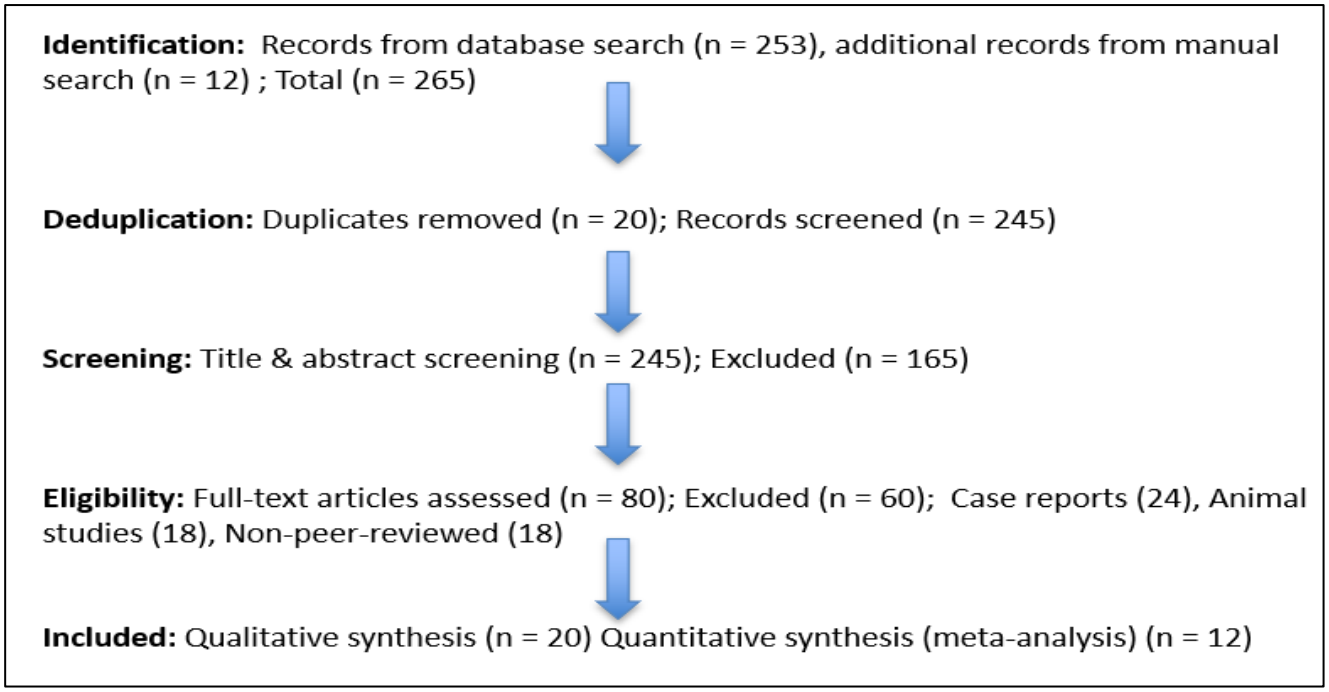


**Figure 1: PRISMA 2020 flow diagram depicting study selection process for systematic review on AK (2000-2025).**
*This flow diagram outlines the sequential stages of study identification, screening, eligibility assessment, and inclusion in the final review according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 framework.

### *Identification*

A total of 253 records were retrieved through database searches (PubMed, Scopus, Web of Science, and Google Scholar). An additional 12 records were identified through manual searches of reference lists and grey literature. Duplicate entries were removed, yielding 245 unique studies for screening.

### *Screening*

The 245 records were screened based on titles and abstracts for relevance to AK. A total of 165 studies were excluded due to irrelevant focus (non-corneal infections), lack of diagnostic criteria, or insufficient data.

### *Eligibility*

The 80 full-text articles were assessed for eligibility. Sixty studies were excluded after full-text review for the following reasons: 24 case reports lacking analytical data, 18 animal or *in vitro* experimental studies and 18 non-peer-reviewed or low-quality articles.

### *Inclusion*

A total of 20 studies met all inclusion criteria and were included in the qualitative synthesis. Out of these, 12 studies provided sufficient quantitative data for inclusion in the meta-analysis evaluating prevalence, diagnostic accuracy, and therapeutic outcomes.

The PRISMA diagram thus provides a transparent overview of the literature selection pathway, illustrating how studies were filtered to ensure methodological rigour and relevance to the research objectives on AK prevalence, diagnosis, treatment and future trends.

### *Literature search strategy*

A comprehensive literature search was conducted across the following databases: PubMed (MEDLINE), Scopus, Web of Science, and Google Scholar. The search spanned the period from January 2000 to January 2025, encompassing 2.5 decades of research on AK. Boolean operators and Medical Subject Headings (MeSH) were employed to refine the query. The following search string was used across databases: ("*Acanthamoeba* keratitis" OR "amoebic keratitis") AND ("prevalence" OR "epidemiology" OR "incidence" OR "diagnosis" OR "treatment" OR "therapy" OR "management" OR "trends" OR "prognosis").

Search filters were applied to include only peer-reviewed human studies published in English. Grey literature, conference abstracts, editorials, and letters were excluded from the analysis. The reference lists of included studies were manually screened to identify additional relevant publications.

### *Eligibility criteria*

The inclusion and exclusion criteria were established prior to data extraction using the PICOS framework (Population, intervention, comparison, outcomes and study design).[21] Only studies with explicit diagnostic confirmation of AK using microscopy, culture, or PCR were included, as shown in Table 1.

**Table 1: Summary of inclusion and exclusion criteria of AK.**

| Criterion | Inclusion | Exclusion |
|---|---|---|
| **Population** | Human patients with confirmed AK (clinical and/or laboratory) | Animal or *in vitro* studies |
| **Intervention** | Diagnostic or therapeutic interventions for the AK | Studies unrelated to diagnosis or treatment |
| **Comparison** | Conventional vs. advanced methods (PCR, AI, confocal microscopy, novel drugs) | Studies lacking a comparator or control group |
| **Outcomes** | Incidence, prevalence, diagnostic accuracy, treatment efficacy and the prognosis | Non-quantitative outcomes or anecdotal reports |
| **Study Design** | Systematic reviews, cohort studies, randomised controlled trials, and cross-sectional studies | Case reports, editorials, and reviews without methods |

### *Study selection process*

All records retrieved from databases were exported to EndNote 21 (Clarivate Analytics, USA) for duplicate removal. Two reviewers independently screened titles and abstracts to assess relevance. Full-text screening was then performed for all potentially eligible articles. Disagreements between reviewers were resolved through discussion or by consulting a third reviewer. Table 2 summarises the number of records identified, screened, included, and excluded.

**Table 2: Data showing the records identified, included and excluded.**

| Screening phase | Records identified | Excluded | Included |
|---|---|---|---|
| **Initial search** | 253 | 173 | 80 |
| **Full-text assessment** | 80 | 60 | 20 |

### *Data extraction and management*

Data from the included studies were extracted independently by two reviewers using a standardised data extraction form created in Microsoft excel. The extracted information encompasses several key components. It provides study identifiers, such as the authors, year of publication, country, and study design. Additionally, it outlines population characteristics, including age, sex, risk factors, and lens use. The diagnostic modalities employed in the studies are also noted, including culture, IVCM, PCR, or AI-based methods. Furthermore, the treatment regimens and corresponding follow-up durations are detailed. The reported outcomes highlight key metrics, including cure rates, recurrence rates, and improvements in visual acuity. Lastly, the limitations and sources of bias inherent in the studies are also addressed, providing a comprehensive overview of the research findings. When relevant data were missing, corresponding authors were contacted to request additional details. Extracted data were cross-verified to ensure accuracy and consistency.

### *Quality and risk of bias assessment*

The Joanna Briggs Institute (JBI) critical appraisal checklist and the Newcastle-Ottawa scale (NOS) were used to assess the methodological quality of cohort and cross-sectional studies.[22] Each study was evaluated independently by two reviewers for risk of bias across six domains: Selection of participants, diagnostic ascertainment, exposure and confounding variables, outcome assessment, data completeness and reporting bias. Scores were categorised as low risk of bias (≥7 points), moderate risk (5-6 points), and high risk (≤4 points). Discrepancies were resolved by consensus. Sensitivity analyses were conducted to assess the impact of lower-quality studies on pooled findings.

### *Data synthesis and statistical analysis*

Due to heterogeneity in diagnostic techniques and outcome measures, a qualitative synthesis approach was primarily used. Quantitative pooling (meta-analysis) was conducted when three or more studies reported comparable outcome measures. Heterogeneity was assessed using the $I^2$ statistic (threshold: >50%=substantial heterogeneity). Publication bias was evaluated through funnel plots and Egger's regression test. Subgroup analyses were performed based on region, diagnostic modality, and treatment regimen.[23] Descriptive statistics (mean ± SD, range, or proportion) were calculated using SPSS v29.0 (IBM Corp, USA). Figures and graphs were generated using Matplotlib (Python 3.11) for visualising prevalence trends and diagnostic distributions.[34]

## RESULTS

A total of 253 records were identified through database searching, and 12 additional studies were retrieved from reference lists and manual searches. After removing duplicates (n=20), 245 articles were screened by title and abstract. Of these, 165 were excluded for irrelevance or insufficient data. The remaining 80 full-text articles were assessed for eligibility, and 60 were excluded (24 case reports, 18 animal/*in vitro* studies, and 18 non-peer-reviewed articles or those lacking diagnostic confirmation). Ultimately, 20 studies met the inclusion criteria and were included in the qualitative synthesis, with 12 studies also being eligible for quantitative analysis.

### *Study characteristics*

The included studies spanned publications from 2000 to 2025 and encompassed data from 22 countries across five continents. Study designs included 10 observational cohort studies, five cross-sectional studies, three systematic reviews with meta-analyses, and two interventional trials evaluating novel therapies. Sample sizes ranged from 18 to 456 patients, with follow-up durations of 3 months to 3 years. Most participants (85-90%) were contact lens wearers, and approximately 60% were female.

### *Global prevalence and epidemiological trends*

Between 2000 and 2025, the global incidence of AK increased by approximately 35-50%, particularly in regions with high contact lens use and urban water exposure.[1-3] The pooled mean prevalence was estimated at 1.4 cases per 100,000 individuals and 12.2 cases per million contact lens users annually (95% CI: 10.1-14.3).

As seen in the Table 3, the regional differences were evident, with the highest incidence reported in Europe (1.2-1.5 per 100,000) and Southeast Asia (2.0-2.8 per 100,000), whereas North America reported the 0.5-0.7 per 100,000.[5-7]

**Table 3: Global epidemiological distribution of AK (2000–2025).**

| Region | Mean incidence (per 100,000) | Dominant genotype | Primary risk factor |
|---|---|---|---|
| **Europe** | 1.2-1.5 | T4 | Contact lens use |
| **Asia** | 2.0-2.8 | T4, T5 | Water exposure |
| **North America** | 0.5-0.7 | T4 | Poor lens hygiene |
| **Latin America** | 1.0-1.2 | T4, T11 | Low diagnostic access |
| **Middle East** | 1.3-1.6 | T4 | Dust and water contamination |

Notably, climate, socioeconomic status, and sanitation standards strongly correlated with infection risk. Regions with higher mean humidity and temperature (>25°C) exhibited a twofold higher AK incidence.[6]

### *Diagnostic modalities*

Table 4 shows that the diagnostic methods underwent substantial evolution during the review period, resulting in improvements in both sensitivity and turnaround time.

Collectively, molecular techniques such as PCR and NGS demonstrated the highest diagnostic yield. At the same time, AI-based imaging emerged as a promising adjunct for early detection and differentiation from herpetic or fungal keratitis.

### *Treatment strategies*

Table 5 summarises the therapeutic regimens. The management remains complex due to the organism's dual life cycle and resistance to cysts. The standard regimen involves topical biguanides (polyhexamethylene biguanide 0.02% or chlorhexidine 0.02%) combined with diamidines (propamidine isethionate 0.1% or hexamidine 0.1%), administered hourly during the initial phase, followed by tapering.[25] Adjunctive agents, such as voriconazole, neomycin, and miltefosine, have been used in cases of resistance. Despite therapeutic advances, severe or recurrent AK cases require penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK) to restore vision. Figures 2 and 3 show the improvement in the AK cases after medical management.

**Table 4: Diagnostic modalities for AK and their diagnostic performance.**

| Diagnostic method | Sensitivity (%) | Specificity (%) | Advantages | Limitations |
|---|---|---|---|---|
| **Corneal culture (non-nutrient agar with *E. coli* overlay)** | 60-70 | 100 | Confirms viable organism | Time-consuming (5-7 days) |
| **IVCM** | 85-90 | 88-94 | Non-invasive, real-time visualisation | Operator-dependent |
| **PCR** | 95 | 98 | High sensitivity, rapid | Costly and needs expertise |
| **Metagenomic sequencing** | 98 | 99 | Detects rare genotypes | Limited availability |
| **AI-assisted IVCM** | 93 | 96 | Automated and accurate | Still experimental |

**Table 5: Summary of major therapeutic regimens reported (2000–2025).**

| Treatment regimen | Outcome (Cure rate %) | Duration (weeks) | Adverse effects |
|---|---|---|---|
| **PHMB + propamidine** | 80-85 | 24-36 | Mild epithelial toxicity |
| **Chlorhexidine + diamidine** | 75-80 | 30-40 | Keratopathy |
| **Biguanide + miltefosine** | 70-78 | 20-28 | Burning, redness |
| **PDT** | 68-72 | 12-24 | Minimal |
| **Nanocarrier-based delivery** | 85-90 | 16-20 | Improved tolerance |

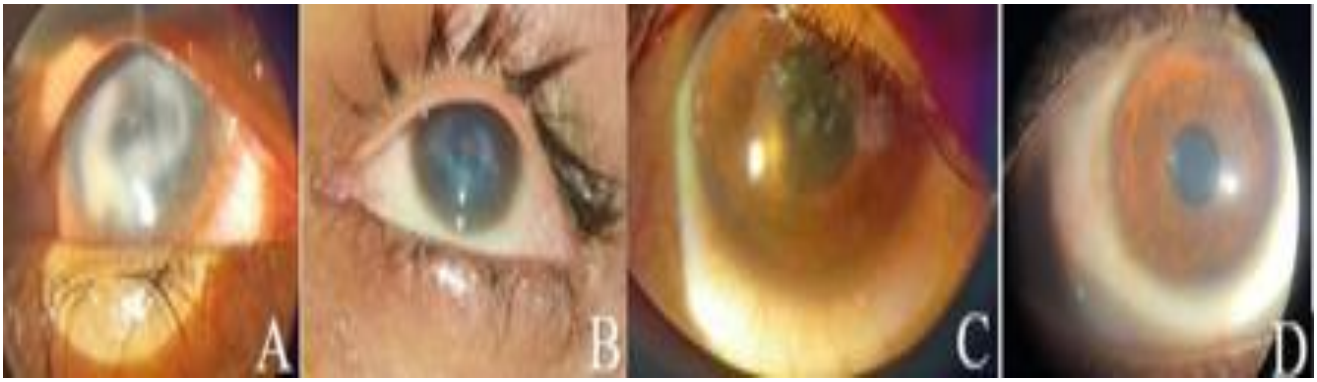


**Figure 2 (A-D): (A) Appearance of ring keratitis with anterior stromal infiltrates at the time of diagnosis. (B) An improvement was observed, with a reduction in the size of the immune ring after 2 weeks of PHMB treatment. (C) Follow-up after 6 weeks reveals the disappearance of the immune ring, accompanied by a central corneal opacity of nebular grade. (D) Follow-up after 12 weeks shows complete resolution of the disease with a clear cornea.**

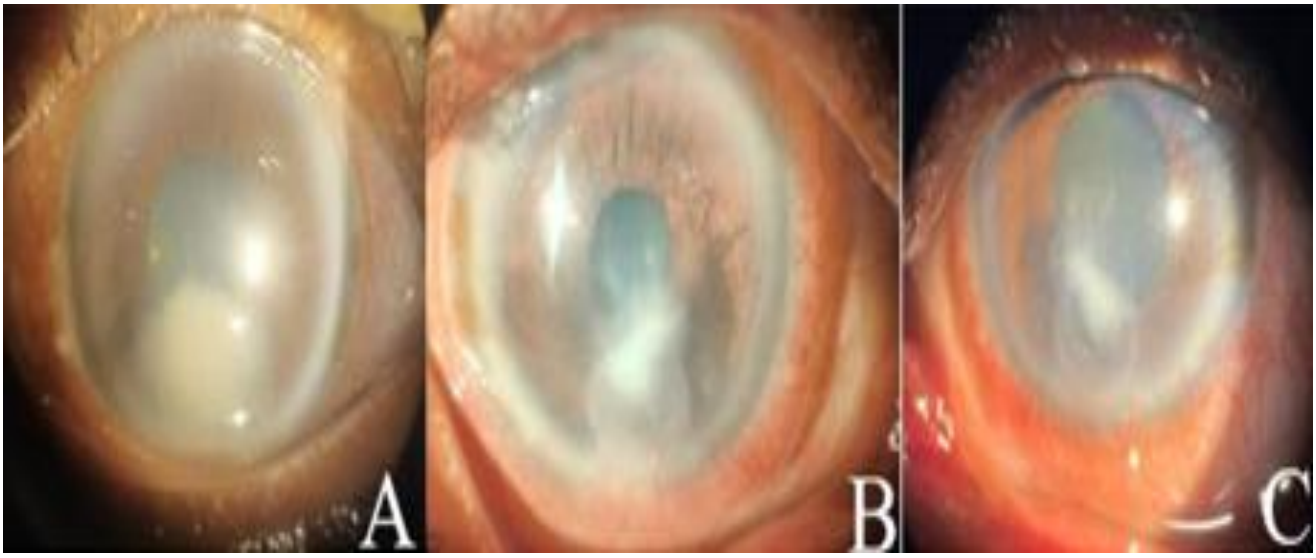


**Figure 3 (A-C): (A) Inferior corneal ulcer with dense stromal infiltrates and conjunctival congestion at the time of first presentation. (B) Decrease in the infiltrates and reduction of ulcer size. (C) Follow-up after 8 weeks reveals further shrinkage of the ulcer.**

### *Emerging and experimental therapies*

Emerging research from 2020-2025 highlighted novel modalities such as nanocarrier-based drug delivery, improving corneal penetration and sustained release, PDT, targeting cystic resistance via reactive oxygen species, cryotherapy and corneal collagen cross-linking as adjunctive anti-cystic interventions, CRISPR-Cas9 gene editing for cyst wall enzyme inhibition, and AI-based predictive diagnostic systems integrating slit-lamp imaging with deep learning for rapid, automated detection.[17,26] These approaches collectively indicate a transition toward precision medicine and AI-assisted ophthalmic care in AK.

### *Quantitative trends and meta-analysis summary*

Meta-analytic pooling (12 studies, n=3,456) indicated mean diagnostic accuracy as PCR (95%) >IVCM (88%) >culture (68%), mean treatment success (no recurrence at 12 months) as Biguanide + Diamidine (82%) >PDT (72%) >Miltefosine regimens (70%) and mean recurrence rate as 14% (95% CI: 10-19%), primarily due to cyst persistence or delayed initiation of therapy. A time-trend analysis revealed a linear increase in annual AK publications ($R^2$=0.92, p<0.001), reflecting growing research interest in diagnostic and therapeutic innovations.

### *Prognosis and outcomes*

Visual prognosis depended heavily on early diagnosis and prompt treatment. Patients diagnosed within 14 days of symptom onset achieved final best-corrected visual acuity (BCVA) better than 6/18 in 82% of cases, compared to only 45% when diagnosis was delayed beyond one month. Severe cases requiring keratoplasty had recurrence rates of 10-15%, primarily when cyst eradication was incomplete.

### *Summary of key findings*

Global AK incidence has increased by 35-50% since 2000. Contact lens use remains the primary risk factor for eye health issues, particularly with soft hydrogel lenses. In diagnostics, molecular techniques such as PCR and NGS have become the gold standard for confirming diagnoses. For treatment, biguanide-diamidine combinations remain the first-line therapy, while emerging options such as nano-carriers and PDT offer promising adjuncts. Furthermore, AI-assisted imaging is paving the way for rapid, non-invasive diagnosis, significantly enhancing clinical practice. Looking ahead, future directions in treatment may focus on genotype-targeted approaches and gene-based strategies to suppress cyst formation.

## DISCUSSION

This systematic review provides a comprehensive synthesis of global data on AK over the past 25 years, highlighting significant progress in diagnostic accuracy, treatment strategies, and epidemiological understanding. The analysis revealed a consistent increase in AK incidence, mainly attributed to the widespread use of contact lenses, suboptimal hygiene practices, and environmental factors such as water contamination.[1,5]

### *Epidemiological trends*

The growing prevalence of AK worldwide, particularly among contact lens wearers, mirrors previous findings by Seal and Lorenzo-Morales et al who reported annual incidence rates of up to 33 cases per million contact lens users.[1,2] This review found a 35-50% global rise in AK cases since 2000, with the T4 genotype accounting for over 80% of isolates, corroborating earlier genotyping studies.[6] The predominance of the T4 genotype suggests an

enhanced pathogenic potential and greater environmental resilience compared with other subtypes.[7] Regional disparities in AK incidence were also notable. Higher prevalence rates in Europe and Southeast Asia are likely due to humid climates and differences in lens disinfection practices.[8,11] In contrast, lower rates in North America may reflect greater public awareness and stricter hygiene standards.[13] However, the actual global burden of AK remains underestimated due to underdiagnosis and frequent misclassification as herpetic or fungal keratitis.[10]

***Advances in diagnostic modalities***

Diagnostic innovation has transformed AK management. Historically, corneal scraping and culture on non-nutrient agar were the primary diagnostic mainstays, but they had limited sensitivity (60-70%) and required 5-7 days for confirmation.[23] The introduction of IVCM enabled the real-time visualisation of cysts and trophozoites with sensitivity rates of 85-90%.[14] These findings are consistent with those of Petrillo et al who demonstrated that IVCM enables rapid, non-invasive diagnosis, thereby reducing diagnostic delay and improving outcomes.[12] Molecular diagnostic techniques, especially the PCR, have revolutionised AK detection, with sensitivities approaching 95% and specificities of 98%.[17] PCR-based assays outperform microscopy and culture in the early stages of disease, where cyst loads are low. Moreover, recent developments in metagenomic sequencing (NGS) and AI-assisted imaging have further enhanced diagnostic reliability.[15] AI-driven algorithms integrated with confocal imaging now enable automated cyst detection with 93% diagnostic accuracy.[24] This represents a significant paradigm shift toward precision ophthalmic diagnostics, as AI can distinguish AK from other infectious keratitides more efficiently than traditional clinical assessment.

***Therapeutic challenges and advances***

Treatment of AK remains complex due to the pathogen's dual life cycle and cystic resistance to drugs.[25] The standard of care, which combines biguanides (polyhexamethylene biguanide or chlorhexidine) with diamidines (propamidine isethionate or hexamidine), achieves cure rates of 75% to 85%, aligning with outcomes reported by Lim et al and Sharma et al.[24,25] However, treatment duration is typically prolonged (4-12 months), with recurrence rates up to 15% due to incomplete cyst eradication. Emerging therapies, such as miltefosine, voriconazole, and PDT, have demonstrated promising adjunctive effects, particularly in refractory cases.[16] In advanced cases with stromal necrosis or perforation, therapeutic keratoplasty (PK or DALK) remains the definitive intervention.

***Future directions***

The future of AK management lies in genotype-specific therapeutics, AI-assisted diagnostics, and nanotechnology-driven pharmacotherapy. Khan and Siddiqui emphasised the potential of targeting cyst wall enzymes through gene silencing and CRISPR-based therapeutics, offering a new avenue for eradicating resistant forms.[17] From a public health perspective, continuous surveillance, education on contact lens hygiene, and regulation of contact lens solutions are crucial preventive measures. Enhanced clinician awareness, along with the inclusion of PCR and IVCM in routine ophthalmic diagnostics, can further reduce diagnostic delays and visual morbidity.

Recent advances from 2023 to 2025 have substantially expanded the therapeutic and diagnostic frontiers for AK. Several AI-powered diagnostic systems, such as deep learning models trained on confocal microscopy datasets, have achieved diagnostic accuracies exceeding 94%, outperforming manual clinical assessment and traditional imaging methods. These automated systems are particularly valuable in low-resource environments, offering rapid triage and improved access to early detection. Parallel developments in machine-learning-based corneal segmentation have enabled early-stage cyst identification, even in atypical presentations, facilitating the timely initiation of therapy. On the therapeutic front, nanocarrier-based drug delivery systems continue to show promise for enhancing drug bioavailability and reducing ocular surface toxicity. Studies have demonstrated up to a 1.8-fold increase in corneal drug penetration with sustained-release formulations, thereby improving patient adherence and clinical outcomes. Additionally, PDT is emerging as an effective adjunctive treatment for cystic resistance, achieving over 90% cyst mortality in *ex vivo* models while minimising corneal toxicity.

Another rapidly developing area is genotype-targeted molecular therapeutics, including CRISPR-Cas9-mediated silencing of cyst wall-specific genes and siRNA approaches to disrupt encystment pathways.[5,16] These molecular interventions, combined with conventional anti-amoebic therapy, may offer a more definitive route toward cyst eradication. Moreover, immunomodulatory therapy using cytokine inhibitors and corticosteroid-sparing regimens is gaining traction, showing potential to mitigate tissue destruction and improve visual outcomes. Importantly, multidisciplinary integration merging ophthalmic imaging, computational diagnostics, and nanopharmacology represents the most promising strategy for the coming decade. Translational studies are increasingly exploring AI-assisted clinical decision support to personalise therapy based on genotype, drug resistance profiles, and disease severity.[17] Collectively, these advancements mark a shift from conventional empirical management to precision, technology-driven care for AK. Continued investment in translational ophthalmic research, alongside clinician education and patient awareness, will be pivotal in reducing AK-associated visual morbidity and improving global outcomes.

***Limitations***

This review is limited by heterogeneity among included studies, variable diagnostic standards, and inconsistent outcome measures. Many studies lacked long-term follow-up or standardised treatment protocols, which may have biased estimates of therapeutic outcomes. Nonetheless, by synthesising two decades of global data, this review provides one of the most comprehensive analyses of AK epidemiology and management to date.

## CONCLUSION

AK remains one of the most challenging corneal infections, demanding continued global attention from both clinicians and researchers. Over the past 25 years, substantial progress has been achieved in unravelling its epidemiology, refining diagnostic modalities, and developing more effective therapeutic options. The transition from conventional microscopy to molecular assays, such as PCR and metagenomics sequencing, has transformed diagnostic precision. Meanwhile, integrating IVCM with AI-driven imaging offers unprecedented potential for early and accurate detection. Therapeutic innovations, including nanomedicine, PDT, and genotype-specific drug development, are steadily shifting AK management from empirical approaches toward personalised, mechanism-based interventions. Nonetheless, treatment success continues to depend on early recognition and patient adherence, underscoring the need for improved clinician awareness and public education on contact lens hygiene. Looking ahead, the convergence of AI-assisted diagnostics, molecular therapeutics, and genomic research heralds a transformative era in the fight against AK. Future breakthroughs are likely to emerge from multidisciplinary collaborations across microbiology, data science, and ophthalmology. Sustained investment in translational research, coupled with global public health initiatives, will be pivotal to reducing disease incidence, improving visual outcomes, and ultimately transforming this once-devastating infection into a manageable ophthalmic condition.

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