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Review article

Spectrum of ophthalmic manifestations in monkeypox virus infection worldwide: Systematic review and meta-analysis

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ABSTRACT

Mpox virus infection is a significant public health concern worldwide due to its potential severity and the likelihood of outbreaks occurring across different regions. Ophthalmic manifestations of the disease have been linked with more severe cases, leading to the need for hospitalization and antiviral therapy. A systematic review and meta-analysis were conducted following PRISMA guidelines to summarize the literature available on this topic. The review revealed that ophthalmic manifestations, such as conjunctivitis and periocular umbilicated lesions, are the most common in Mpox virus infections. However, severe manifestations, such as corneal opacity, that can potentially cause blindness may also occur. Antiviral treatment with tecovirimat and topical management for conjunctivitis can be considered for severe cases. However, the evidence quality is poor due to the predominance of case reports and imprecise characterization of the ophthalmic manifestations. Overall, ophthalmologists and healthcare professionals should be aware of these manifestations for early diagnosis and timely treatment.

1. Introduction

Mpox virus is part of the Poxiviridae family, from the subfamily of the *Chordopoxvirinae* of the genus *Orthopoxvirus* [1,2]. It was discovered in 1958 and is considered a neglected tropical disease with some outbreaks in several regions of Africa [3–5]. Until the current outbreak, the international organization recognized it as a disease of global public health importance [6].

Mpox virus primarily circulates among certain rodent species, including African rope squirrels, Gambian rats, and dormice, which are believed to be the natural reservoirs [7]. Human infections can result from direct contact with blood, bodily fluids, or lesions of infected animals or humans [8]. Furthermore, human-to-human transmission can occur through large respiratory droplets during close contact and through intimate sexual contact (kissing; oral, anal, or vaginal sex) [9]. Susceptibility to mpox spans all ages, but children, particularly those under age 10, appear to be more vulnerable [10]. Populations residing in or near tropical rainforests, especially

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those with increased levels of rodent-human interaction, are at a significantly higher risk [11]. During the 2022 outbreak, most of the infections have occurred in men who have sex with men, although any individual who has been in close contact with a person who has mpox is at risk of infection [9].

The most common symptoms of this condition are the development of a rash or skin lesions, fever, and lymphadenopathy. Typically, the prognosis is good, and treatment is usually symptomatic, with only 4% of patients requiring antiviral medication [12]. However, some patients may experience severe infections affecting organs such as the eyes [13].

Indeed, this is a potentially blinding disease of one or both eyes, mainly reported in pediatric populations [13–15]. Thus, it is crucial to characterize the ophthalmic manifestations of Mpox virus infection because these are associated with a more severe presentation of the disease, being indications for antiviral therapy and hospitalization [16]. Although multiple reports described that this infection could cause ophthalmic manifestation, commonly conjunctivitis, the literature in this field is still insufficient. Therefore, we aimed to systematically review the ophthalmic manifestations of Mpox virus infection in humans and their treatment to provide clinical guidance on diagnosing and managing these patients.

2. Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17] (**Supplemental appendix 1**). In addition, it was registered in the "International prospective register of systematic reviews" (PROSPERO ID: CRD42022359027).

2.1. Information sources, search strategy, and selection criteria

We conducted a systematic literature search on February 28, 2023, in the following databases: PubMed, Embase, VHL (Virtual Health Library), and MedxRiv. We used "MeSH," "Emtree, and "DeCS" terms accordingly. The search strategy can be found in **supplemental appendix 2**. We also searched reference lists of key journals to identify more information on mpox and ophthalmic manifestations. We identified and deleted duplicated articles with the assistance of Zotero and Excel filters. We reviewed all articles that provide data on any ocular manifestations of the Mpox virus infection. We included all patients with mpox confirmation presenting any ophthalmic manifestation [18,19]. Patients with ophthalmic manifestations unrelated to mpox (sign, symptom, or chronic ophthalmic disease before the diagnosis of mpox) were excluded.

2.2. Selection process and data extraction

Two authors (CC, WR) reviewed the titles and abstracts independently. Each author screened titles and abstracts separately to exclude unrelated ones based on the selection criteria. Subsequently, the independent decision was compared with the pair, and any disagreements were discussed. A third investigator (AD or RA) resolved the discrepancies. The level of agreement was: 91·4%. Two independent investigators (CC, WR) extracted and entered data into a standardized and validated Excel form (Microsoft, Redmond, Washington, USA), including first author, year of publication, country, study design, number of participants and cases, case confirmation, ocular manifestation, laterality, type of systemic treatment (dose), topical treatment (dose), time of resolution, and answers to the question "Was this the first manifestation?" (Yes/No), "Do they describe any post-treatment visual outcome?" (Yes/No), post-treatment visual outcome (BCVA).

2.3. Risk of bias assessment

The checklist provided by the Clinical Advances Through Research and Knowledge Translation (CLARITY) group of McMaster University was used to assess the risk of bias for cohorts and case-control studies [20]. This tool classifies the risk as (Low Risk of Bias, Probably Yes, Probably no, High Risk of Bias). We scored each domain of the corresponding question with 1 (Low Risk of Bias, Probably Yes) and 0 (Probably no, High Risk of Bias) to obtain a weighted mean of the bias risk. Additionally, the ROBINS-I tool was used to assess non-randomized studies of interventions with its seven domains. Moreover, we used the Hoy et al. tool for cross-sectional studies, where a score $\leq$4 is considered a low risk of bias, between 5 and 7 moderate risk, and $\geq$8 high risk of bias [21]. Finally, for the quality assessment of case series and case reports, the tool proposed by Hassan Murad et al. was used [22].

2.4. Data analysis and synthesis

First, we performed a qualitative synthesis and created tables summarizing the demographic information, ophthalmic manifestations, treatments used, and complications reported in all the articles included. Then, we performed a meta-analysis of proportions for the clinical manifestations in which sufficient literature was available. We excluded the case reports and case series with less than ten patients from the meta-analysis. A random effects model was used for all analyses, considering the significant heterogeneity of data. Only variables that were reported by at least two included studies underwent meta-analysis. We used the I2 statistics test to assess the heterogenicity. It was interpreted as follows: 30% to 60% moderate heterogeneity and 60% to 100% substantial heterogeneity. All meta-analyses were conducted using the R Package (dmetar version 0.0.9000), and the interventional was done on Review Manager (RevMan 5.4) [23]. Additionally, publication bias was evaluated using funnel plots if there were more than ten studies. Significance was set at the level of a *P*-value less than 0.05.

3. Results

3.1. Studies characteristics and risk of bias

After completing the selection process(Fig. 1), 60 articles reporting ocular manifestations of Mpox virus infection were retrieved. That included 23 case reports (8 from USA, 4 from Brazil, 3 from Italy, 2 from Spain, 2 from United Kingdom (UK), 1 from Switzerland, 1 from Colombia, 1 from Canada, and 1 from Australia), 11 cases series (3 from the USA, 2 from the UK, 1 from the Democratic Republic of the Congo, 1 from Portugal, 1 from the Republic of the Congo and 3 multinational (1 of 16 countries worldwide, 1 of several countries of Africa, and 1 from Brazil and Colombia), 18 cross-sectional (3 multinational, 1 from France, 1, Brazil, 3 from USA, 1 from Sudan, 1 from Spain, 1 from France, 2 from Nigeria, and 6 from the Democratic Republic of the Congo, of which 2 where abstracts and 1 preprint), 6 cohorts (2 from the Democratic Republic of the Congo, 1 from Mexico, 1 from UK, 1 from Brazil, and 1 from Nigeria), 1 case control study from UK and 1 quasi-experimental study from USA.

4. Findings

In most cases, those affected were young men under 40 years old. However, mpox can affect people from 9 months to 79 years [24,25]. In most cases the diagnosis was confirmed through rt-PCR in conjunctival, skin lesion, nose, tissue, or serum samples. Some patients had serum IgM and IgG in addition to the PCR [26,27] (Table 1).

Ophthalmic manifestations of mpox could be present in up to 40% of cases [75], varying from skin eyelid compromise to corneal opacity and blindness. Generally, they are unilateral and appear as the first manifestation of the disease [12,55,75] or until 7 days after systemic manifestations [45]. Depending on the type of manifestation, it may take between 3 days [45] and 2 months to resolve [49,53]. However, in some cases, the complications are severe and take a chronic course [5,14].

4.1. Eyelids, blepharoconjunctivitis, and conjunctivitis

The most common ophthalmic manifestations of mpox are external, compromising the eyelids and ocular surface. Eyelids can present single or multiple umbilicated papules in the 3% of patients with mpox (Fig. 2 A) [45,50], which can lead to eyelid deformation [75]. In some cases, this blepharitis evolves into a blepharoconjunctivitis with a compromise of the tarsal and bulbar conjunctiva, the fornix, and the temporal limbus [45,46]; severe cases of skin necrosis have been reported [31]. The weighted prevalence of conjunctivitis was 6% (Fig. 2 B and Fig. 3). However, it has been reported in up to 60% of patients with Mpox virus infection in some

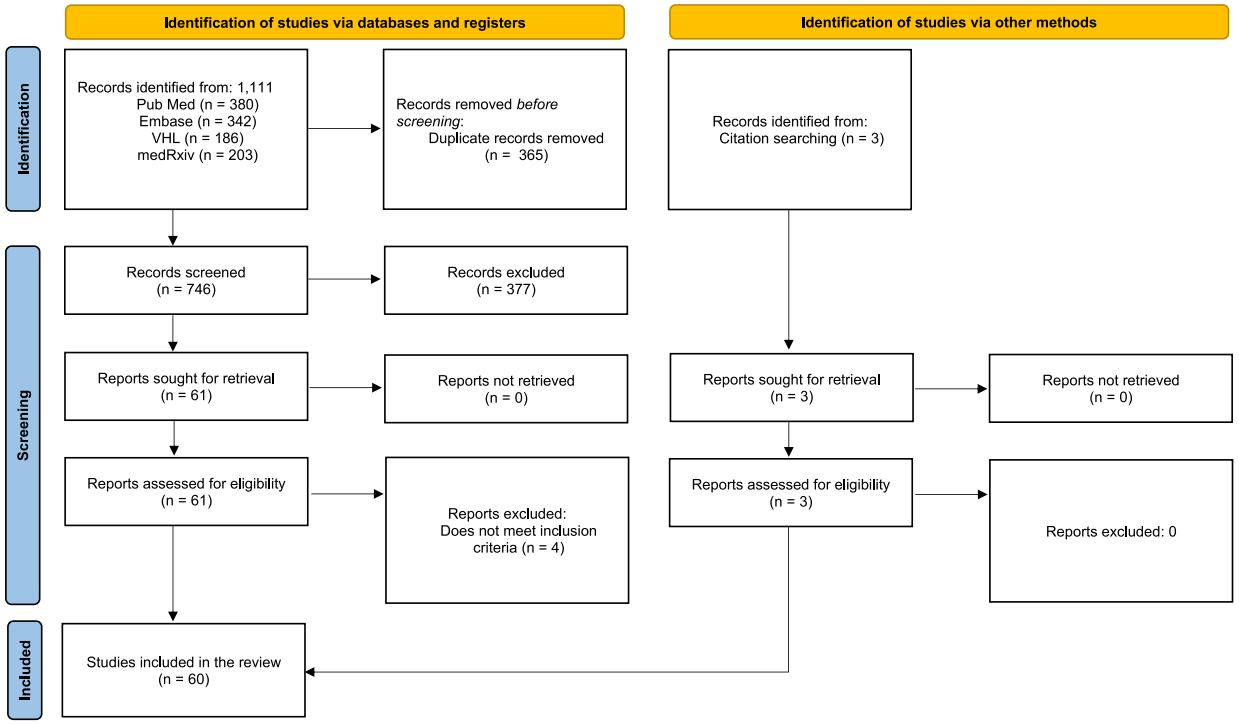

Fig. 1. PRISMA flow diagram for selected studies included in the systematic review.

Table 1
Summary of the ocular findings reported in the included studies.

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Uner (2023) [28]	USA	Case report	1	47 y, male	PCR	Preseptal cellulitis, membranous Keratoconjunctivitis with Transient Corneal Hypoesthesia.	Unilateral	Yes. Periocular edema, conjunctival follicles, subconjunctival hemorrhage, watery discharge, and left preauricular lymphadenopathy, with absence of membranes, pseudomembranes, and vesicles.
Bhamray-Sanchez (2023) [29]	USA	Case report	2	Patient 1: 28 y, male Patient 2: 36 y, male	rt-PCR	Patient 1: Corneal scarring and opacification; 2+ injection of the conjunctiva/sclera; peripheral inferior keratolysis with stromal keratitis of the cornea, and peripheral ulcerative keratitis with superimposed stromal keratitis, and elevated intra ocular pressure 36 mmHg. Patient 2: mild eyelid edema and mild conjunctivitis, stromal interstitial keratitis, and an inferior corneal ulcer.	Unilateral	Patient 1: No, he reported a rash on his lower back and right shoulder which resolved, and an ulcerative lesion on his penile shaft. Patient 2: Yes
Perzia (2023) [30]	USA	Case report	1	36 y, male	NR	Photophobia, Vesicular eyelid lesions, a single conjunctival lesion.	Unilateral	No, seven days after the first symptom presented the manifestations.
Carrubba (2023) [31]	USA	Case report	2	Patient 1: 33 y, male Patient 2: 45 y, male	PCR	Patient 1: Confluent necrotic skin rash spanning the bilateral periorbital, nasal, malar, and submalar areas; after the worsening of the clinical condition right eye revealed only necrotic tissue and no identifiable structures, left eye large, total thickness, a central corneal defect/perforation that was plugged by the prolapsed iris. Patient 2: Ulcerated papules with necrotic centers right upper eyelid, preseptal cellulitis, a necrotic rash of the face, expanding outward from initial foci and becoming confluent, restricting lid function.	Patient 1 and 2: Bilateral	Patient 1: NR Patient 2: No, a month after the symptoms and empirical treatment.

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Vasquez-Perez (2023) [32]	United Kingdom	Case report	1	63 y, male	PCR	Conjunctival hyperemia with purulent discharge and corneal edema, and a 4-mm central epithelial defect. Diffuse preseptal soft tissue thickening on MRI (Preseptal cellulitis). On day 4 of admission, a more detailed examination revealed white discharge, fibrotic membranes, and significant necrosis on the bulbar and tarsal conjunctiva. Corneal epithelial defect, edema, stromal keratitis, and a small 2-mm central nonsuppurative infiltrate without corneal melting or perforation.	Unilateral	Yes. 5-day history of worsening left eye redness, itching, discharge, and painful swelling of the upper and lower eyelid as well as fever and malaise 2 days after the onset of his eye symptoms.
Quites (2023) [33]	Brazil	Case report	1	31 y, male	qPCR	Ocular hyperemia, keratoconjunctivitis, photophobia and blurred vision of the left eye. Two semicircular fluorescein-staining lesions. 1 week later: Wessley immune ring and two corneal ulcerations of 2.5 and 1 mm.	Unilateral	No. Ophthalmic symptoms appeared 1 week after systemic vesicles.
Carvalho (2023) [34]	Brazil	Case report	1	28 y, male	PCR	Hyperemia and vesicles in the bulbar conjunctiva. small keratic precipitates, +1 anterior chamber cells, and discrete cells in the anterior vitreous were observed.	Unilateral	No. Genital lesions appeared 2 weeks earlier.
Ayala-Rivera (2023) [35]	Colombia	Case report	1	28 y, male	PCR	Bilateral tearing and eyelid swelling. Bilateral follicular conjunctivitis and mucous discharge without keratitis. One week later, umbilicated papules and pustular lesions were seen on the margin of the upper eyelids.	Unilateral	No. Body maculopapular lesions appeared 4 weeks before.
Alsarhan (2022) [36]	Canada	Case report	1	36 y, male	PCR	Red eye, blurred vision, and photophobia. Diffuse conjunctival injection of the left eye and a corneal epithelial ridge that stained with fluorescein, 1+ grade of anterior chamber cellular reaction with no flare.	Unilateral	Simultaneous onset with body lesions and systemic symptoms.

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Rai et al. (2022) [37]	USA	Case report	1	30 y, male	PCR	Trace injection, an ulcer on the right lower palpebral conjunctiva, an ulcer on the right caruncle, and a papule on the right upper eyelid.	Unilateral	No. Penile papules appeared first.
Alexis (2022) [38]	Australia	Case report	1	38 y, male	PCR	-Upper and lower lid edema and erythema. -Conjunctival hyperaemia without tarsal papillae or follicle blepharoconjunctivitis. -A small vesicle at the medial canthus of the lower lid was present. -The cornea demonstrated minimal superficial punctate epithelial erosions but was otherwise clear.	Unilateral	No, it appears ten days after the onset of the initial symptoms, he developed a conjunctival injection of his right eye with associated epiphora, foreign body sensation and intermittent blurring of vision.
Weppelmann (2022) [39]	USA	Case report	1	34 y, transgender female	PCR	Temporal conjunctival injection, engorgement of the episcleral vessels, and a raised papule with conjunctival ulceration.	Unilateral	No, they appeared after two weeks of treatment with Tecovirimat for MPX and bictegravir-emtricitabine-tenofovir for a new diagnosis of AIDS
Ly-Yang (2022) [40]	Spain	Case report	1	42 y, male	PCR	Ulcer lesions on the eyelid margin, mucoid discharge, and conjunctival whitish, serpinginous, infiltrative lesions with conjunctival thickening.	Unilateral	Yes. Left-eye lacrimation, pain, and photophobia.
Kontos and Micheletti (2022) [41]	United Kingdom	Case report	1	27 y, male	PCR	Dome-Shaped Eyelid Nodule. A vesicular lesion was also present on the caruncle and there was global conjunctival hyperemia, mostly pronounced nasally and around the lesions.	Unilateral	No. He developed a skin rash affecting his trunk, limbs, and genitalia within the previous week.
Finamor (2022) [42]	Brazil	Case report	1	27 y, male	PCR	Diffuse anterior scleritis, serpiginous epithelial elevation in the corneal periphery with an underlying whitish stromal infiltrate and thinned out epithelium. Decreased corneal sensitivity was observed. keratic precipitates and 1+ cells in the anterior chamber.	Unilateral	No. The first genital lesion appeared 24 days before.
Lamas-Francis (2022) [43]	Spain	Case report	1	45 y, male	rtPCR	Keratitis with epithelial corneal ulcer, superior limbitis and anterior chamber 0.5+ cells.	Unilateral	No. Genital and perioral lesions appeared 20 days before.

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Nogueira Filho (2022) [44]	Brazil	Case report	1	30 y, male	PCR	Conjunctivitis with three ulcerated epithelial conjunctival lesions.	Unilateral	No. Ocular lesions appeared 5 days after body lesions and systemic symptoms.
Scandale et al. (2022) [45]	Italy	Case report	1	35 y, male	rt-PCR of ocular lesions and other four tissues lesions.	Multiple (>10) umbilicated papules on the tarsal and bulbar conjunctiva, the fornix, and at the temporal limbus.	Unilateral	No. Ocular lesions appeared 7 days after body lesions and systemic symptoms.
Benatti (2022) [46]	Italy	Case report	1	36 y, male	PCR from viral swabs from the cutaneous (perianal) and ocular vesicles, and from the oropharynx.	Conjunctivitis with a small vesicle on the lower eyelid. The left eye blepharoconjunctivitis evolved into a single whitish ulcer (10 mm) on the medial bulbar conjunctiva, with regular edges. Neither corneal, nor anterior chamber involvement, were found on ophthalmologic examination.	Unilateral	No. Ocular lesions appeared 4 days after body lesions and systemic symptoms.
Meduri (2022) [47]	Switzerland	Case report	1	39 y, male	PCR from cutaneous and conjunctival swabs	Conjunctival follicular reaction and the presence of small white vesicles on the nasal bulbar conjunctiva.	Unilateral	No. Ocular lesions appeared 5 days after body lesions and systemic symptoms.
Foos (2022) [48]	USA	Case report	1	36 y, female	Diagnosis confirmed by the CDC not specified.	Eye redness and discomfort. A fluorescein-staining subconjunctival nodule with sectoral hyperemia and an adjacent left upper eyelid umbilicated nodule with central crusting. The hyperemic lesion did not blanch with administration of topical phenylephrine.	Unilateral	No
Mazzotta (2022) [49]	Italy	Case report	1	26 y, male	rt-PCR and MPXV isolation in cell culture.	Multiple papular lesions in the eyelid with progressive periorbital and conjunctival involvement.	Unilateral	No. Ocular lesions appeared 2 days after body lesions and systemic symptoms.
Anderson (2003) [50]	USA	Case report	1	Scholar age	Epidemiological link with an MPX-infected prairie dog confirmed by PCR	One vesicle on the eye lash edge of the right inferior palpebral fissure, without conjunctival involvement.	Unilateral	No
CASE SERIES								
Curi et al. (2023) [51]	Brazil and Colombia	Case series	7	30.2 (SD ± 4.57) y, 100% male	PCR	Two had skin lesions in the eyelids, and the other five had conjunctival lesions with conjunctivitis.	Unilateral	No

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
de Sousa (2022) [52]	Portugal	Case series	47	Mean 35.1 (SD 8.7) y, 100% were males	rtPCR	1/47 had palpebral conjunctiva ulceration.	Unilateral	NR
Cash-Goldwasser (2022) [53]	USA	Case series	5	Four patients had 30-39 y, one had 20-29 y, male 4/5 (80%)	PCR	A: Symptoms: Ocular redness, pain, itching, swelling, discharge, foreign body sensation, photosensitivity, and vision changes. Sings: conjunctivitis, conjunctival lesion, and keratitis B: Symptoms: Ocular redness, pain, itching, and photosensitivity. Sings: medial canthus lesion, conjunctivitis, conjunctival lesion, and corneal lesion C:Symptoms:redness, pain, and discharge. Sings: conjunctivitis. D: Symptoms: Ocular redness, pain, and periorbital swelling. Sings: eyelid lesion, conjunctivitis, conjunctival lesion, and preseptal cellulitis E: Symptoms: Ocular redness and pain. Sings: eyelid lesion, conjunctivitis, conjunctival lesion, and subconjunctival nodule	A: Unilateral B: Unilateral C: Bilateral D: Unilateral E: Unilateral	A: NR B: No C: No D: No E: No
Adler et al. (2022) [54]	UK	Case series	7	30-40 y, female	PCR from nose or throat and eye swabs.	1 had suspected bacterial conjunctivitis.	Unilateral	No
Thornhill et al. (2022) [12]	Multinational (16 countries)	Case series	528	Median 38 y (IQR 18 - 68y), Males (99%)	PCR in a specimen from any anatomical site.	3 had conjunctivitis	NR	Yes, in the 3 cases conjunctivitis
Patel et al. (2022) [55]	UK	Case series	197	NR (Median 38 y (IQR 32–42). 100% males.	PCR	2 had conjunctivitis	NR	Yes, in 2 cases of conjunctivitis
Huhn et al. (2005) [56]	USA	Case series	34	NR (Median 26 y (IQR 6 - 47y). 53% Males	PCR	3 had conjunctivitis	NR	No
Learned (2005) [57]	Republic of Congo	Case series	11	<18 y	PCR and EDTA-whole blood specimens	1 had severe conjunctivitis, erythematous sclera, corneal edema, and opacity.	Unilateral	No
Sejvar (2004) [27]	USA	Case series	3	33 y, male	Viral culture, PCR and serum ELISA (IgM and IgG).	Small raised nonpruritic vesicle on his right palm, followed 2 days later by a similar lesion over his left eyebrow.	Unilateral	No. Ocular lesions appeared 2 days after body lesions and systemic symptoms.

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Jezek et al. (1988) [14]	Congo	Case series	338	Mean 6·9 y; Median 4·4 y (Range 3 months-69 y) 53·8% Males	Serological absorption test	Conjunctival lesions (In 45 patients with infection from animal source; 15 patients with infection from human source) Complications: Keratitis (8 patients with infection from animal source; 3 patients with infection from human source)	NR	NR
Breman et al. (1980) [5]	Africa (Congo, Nigeria, Ivory Coast, Liberia and Sierra Leone)	Case series	47	Mean 8 y; Median 4y (Range 7-35y) (83% were <10y) 55·3% Males	Serological absorption test	1 had corneal opacities 1 had blindness unilateral 2 had eyelid margin lesions	-Unilateral corneal opacities -Bilateral eyelid margins lessons	NR
CROSS SECTIONAL								
Mitjà (2023) [58]	Multinational	Cross sectional	382	35 y (IQR 30–43). 367 cisgender men, four cisgender women, and ten transgender women.	PCR	20 (5%) had ocular involvement: Conjunctivitis 6 (2%) Periorbital edema 1 (0%) Keratitis 5 (1%) Periorbital cellulitis 8 (2%)	NR	NR
Thornhill (2022) [59]	Multinational	Cross sectional	136	34 y (range 19–84). 62 trans women, 69 cis women, and five non-binary individuals.	PCR	1 cis woman had keratitis	NR	NR
Pascom (2022) [60]	Brazil	Cross-sectional	8167	Median age 32 y (IQR 27–38 years), 91.8% were male	PCR	81 had conjunctivitis	NR	NR
Hennessee (2022) [61]	USA	Cross sectional	83	66.2% children between 13 and 17 y, 80% males.	PCR	Three cases: -Two children between 0 and 4 eyelid involvement -One child 5–12 periorbital cellulitis and conjunctivitis	NR	NR
Miller (2022) [62]	USA	Cross sectional	57	Median 34 y (range 20–61), Males 54 (94.7%)	PCR	12 (21.21% of all) had eyelid lesions or conjunctivitis.	NR	NR
Kyaw (2022) [63]	USA	Cross sectional	704	Median 35 y (31–41), Male 704 (97.9%)	PCR	−38 (6.2% of all) Includes eye lesion, conjunctivitis, red eyes, or eye discharge −3 (0.5%) had eye lesions	NR	NR

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Harrison, et al. (2023) [64]	Multinational	Cross sectional	226	37 y (range 18–68; IQR 32–43). 100% male	PCR	2 (1%) patients had red eyes due to conjunctivitis or keratitis.	NR	Yes, in 1 case
Català et al. (2022) [65]	Spain	Cross-sectional	185	Mean 38·7 y (SD 8·7y) 100% Males	PCR	2 pustules or pseudo pustules on the eyelids. NR the number Conjunctivitis.	NR	NR
Mailhe et al. (2022) [66]	France	Cross-sectional	264	Median 35 y (IQR 30-41y). 99% Males	rt-PCR	10 had complications: Ocular disease (Not specified) 1 case Bell's palsy 2 were hospitalized: 2 had palpebral lesions 1 had blepharitis, conjunctivitis, and keratitis.	NR	NR
Pittman (2022) [67]	Democratic Republic of the Congo	Preprint-Cross-sectional	216	Mean 14 y, median 13 y, (range 0–61 y). 63·9% Males	PCR	Symptoms: Conjunctiva redness, eye pain, eye discharge, etc. n = 20 (9·3%) Signs: Conjunctival and other eye lesion n = 14 (6·5%)	NR	NR
Whitehouse (2021) [25]	Democratic Republic of the Congo	Cross-sectional	1054	Median 14 y (IQR, 6·0–23·9 y; range, 1 month to 79 y). 53·7% males	rt-PCR or isolation of MPXV in culture from ≥1 specimen.	20·7% had conjunctivitis and 33·2% had photophobia Conjunctivitis by age group (n: %) 0-4 y = 59/250: 30·1% 5-9 y = 53/250: 27·5% 10-19 y = 41/250: 14·2% 20-29 y = 38/250: 21·1% 30-29 y = 9/250: 9·7% >40 y = 10/210: 15·4%	NR	NR
Hughes (2021) [68]	Democratic Republic of the Congo	Cross-sectional	40	MPX alone Mean 15·9 y, median 13·8 y, (range 0·1–67·7) 52·9% males Coinfection with VZV Mean 15·5 y, median 11·0 y, (range 0·5–79 y) 51·1% males	PCR	22·4% conjunctivitis (patients with MPX and VZV coinfection)	NR	NR
Ogoina (2020) [69]	Nigeria	Cross-sectional	40	Median 32 y (28 days to 54 y) 77·5% males	Following the previously described protocols used by Yinka-Ogunleye et al.	22·5% conjunctivitis and photophobia. 25% skin rash in the eyelids.	NR	NR
Ogoina et al. (2019) [70]	Nigeria	Cross-sectional	21	4 cases of ocular manifestations (9	rt-PCR, serology and culture from at least two	4 had conjunctivitis.	NR	NR

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Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
				y male; 6y male; 28y male; 30y Male)	specimens (blood, swab or crust).			
Osadebe et al. (2017) [24]	Democratic Republic of the Congo	Cross-sectional	333	Mean 5·77y; Median 13.82y (Range 0·08-67y) 53·4% males	Orthopoxvirus-specific assay or rt-PCR.	24·1% had conjunctivitis and 32·5% preseted sensitivity to light.	NR	NR
Mbala (2017) [71]	Democratic Republic of the Congo	Abstract - Cross-sectional	229	NR	NR	1·3% (3 cases) presented keratitis, of these: 1 developed a staphyloma approximately 20 months later after the onset of keratitis 1 developed caseation of eye lesions in confluent lesions spreading in the sclera	NR	NR
Formenty (2010) [26]	Sudan	Cross-sectional	19	Range 8 months to 32 y (79% were <20 y). 48% males	Blood PCR, IgM, IgG, or Tissue PCR	60% had conjunctivitis.	NR	NR
Hughes (2014) [13]	Democratic Republic of the Congo	Abstract - Cross-sectional	294	61.8% < 10 y. 61·7% males	rt-PCR	23·1% had conjunctivitis.	NR	NR
COHORTS								
Núñez (2022) [72]	Mexico	Cohorts orEpidemiological report	536	Males median age 34 y (30–41), 549 cases (97.12%), Females median age 36 y (29–42), 16 cases (2.8%)	PCR	- Five females Conjunctivitis (0.9% of all patients; 1.9% of no HIV patient; 43.8% of females) - Two male children presented Conjunctivitis (No HIV, 50% of children) - One male Photophobia (0.2% of all patients, 0.3% of HIV patients)	NR	NR
Fink (2022) [73]	United Kingdom	Cohort	156	Median 35 y (IQR 30–44 y). 98% males	PCR	Ocular or periocular disease 6 patients, four with conjunctivitis, two of whom had peri-orbital cellulitis, one patient presented necrotizing conjunctivitis	NR	NR
Martins-Filho (2022) [74]	Brazil	Cohorts or Epidemiological report	9729	Decennium 20–39 y (73.6%), 92,2% were males	NR	Of patients that have reported 36/7518 (0.5%) patients have conjunctivitis, and 73/7518 (1.0%) have photosensitivity	NR	NR
Mande et al. (2022) [75]	Democratic Republic of the Congo	Cohorts	21	Median 18 y (IQR 7-29y) 66·7% Males	rt-PCR of a lesion	38% had ocular lesions/corneal opacities	Unilateral 2 Bilateral 6	Almost 40% patients with confirmed monkeypox and chickenpox presented with ocular lesions/corneal opacities.

(*continued on next page*)

Table 1 (*continued*)

Author (Year)	Country	Type of Study	Study population	Age	Case confirmation	Ocular Manifestation (n/N)	Laterality	Was the first manifestation?
Yinka-Ogunleye et al. (2019) [76]	Nigeria	Cohorts or Epidemiological report	92	Median 29 y (IQR14 - 50y) 69% males	rt-PCR, serology, and culture were done on the samples	21·7% had conjunctivitis 20·6% had sensitivity to light	NR	NR
Jezek et al. (1987) [15]	Democratic Republic of the Congo	Cohorts	282 32 vaccinated to smallpox 250 not vaccinated	90% < 15 y.50·7% males	electron microscopy and cultured on chicken embryo chorioallantoic membrane and in tissue culture. Sera were tested by HAl test, fluorescent-antibody test, ELISA, RIA, and RIA adsorption test.	Conjunctival lesions and along the eyelid margins lessons in 4 vaccinated patients and 42 ± 1 unvaccinated patients. Complications: Keratitis and Corneal Ulceration [1 vaccinated (3·1%); 11 unvaccinated (4·4%)] Bilateral Blindness (1 patient unvaccinated) Unilateral Blindness (3 unvaccinated) Corneal opacities [1 vaccinated (3·1%); 6 unvaccinated (2·4%)] Deformed eyelid (5 unvaccinated)	NR	No
OTHERS								
Rimmer (2023) [77]	United Kingdom	Case control	70	Median age 36 y (Range 21–75), 99% males	PCR	One case presenting unspecified ocular involvement	NR	No
Farrar (2023) [78]	USA	quasi-experimental study	6,605 cases Unvaccinated 6,329 Vaccinated 276	Unvaccinated Mean 36,9, median 36; Male 5,408 (90.8%) Vaccinated Mean 35,3 and median 34, Male (84.1%)	PCR	Unvaccinated: Conjunctivitis 148/2,703 (5.5%) Vaccinated: Conjunctivitis 2/65 (3.1%)	NR	NR

CDC: Centers for Disease Control and Prevention; y: years.

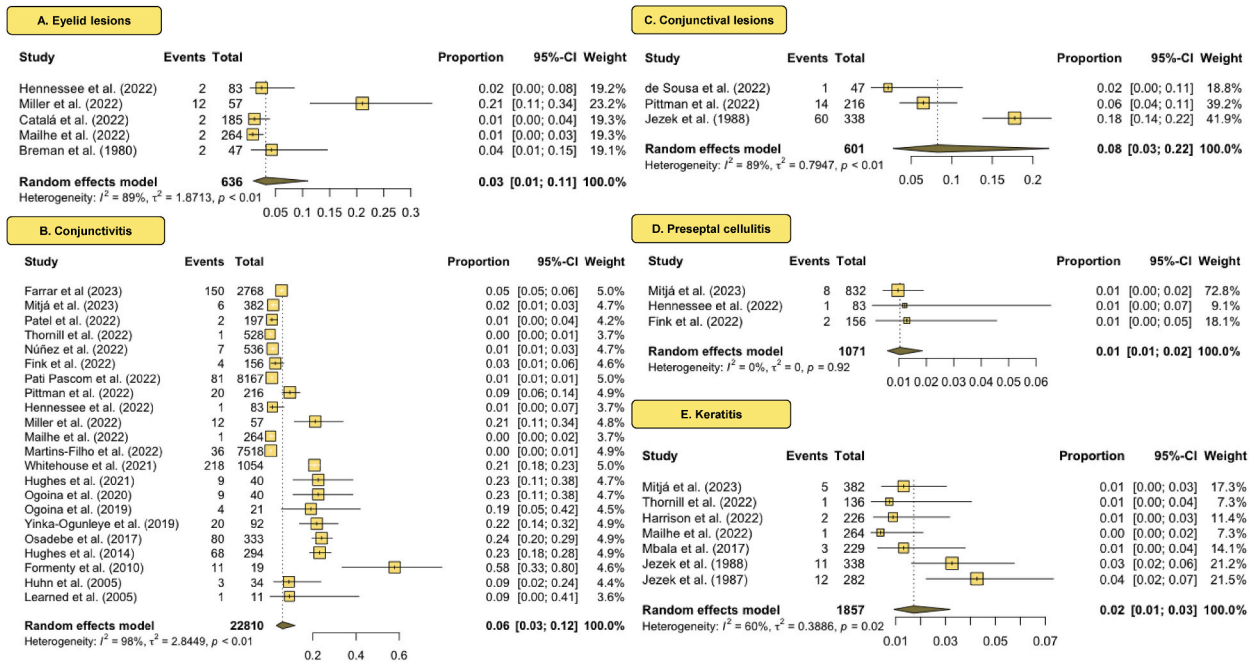

Fig. 2. Meta-analysis of proportion for the more common ophthalmic manifestations of mpox. A. Eyelid lesions. B. Conjunctivitis. C. Conjunctival lesions. D. Preseptal cellulitis. E. Keratitis.

latitudes [24,26,69]. It is generally diffuse with follicular reaction [12,47,54,56], but the presence of small vesicles, umbilicated papules, and whitish ulcers have been reported and can affect until 8% of patients (Fig. 2C). In several cases, the eyelid lesions were associated with progressive periorbital involvement, even leading to preseptal cellulitis [49,58,61,73]. However, this complication is unusual and represents just 1% of cases (Fig. 2 D). For more detailed information of the frequency of the ocular manifestations reported, sorted by the type of study conducted, see Table 2.

4.2. *Scleral involvement*

Just three studies reported cases of scleral involvement. One was a case of severe conjunctivitis with erythematous sclera, corneal edema, and opacity [57]. However, it was not described whether the scleral congestion was relieved with phenylephrine to discard the diagnosis of scleritis. The second was a case of keratitis, which developed confluent corneal lesions spreading into the sclera [71]. And

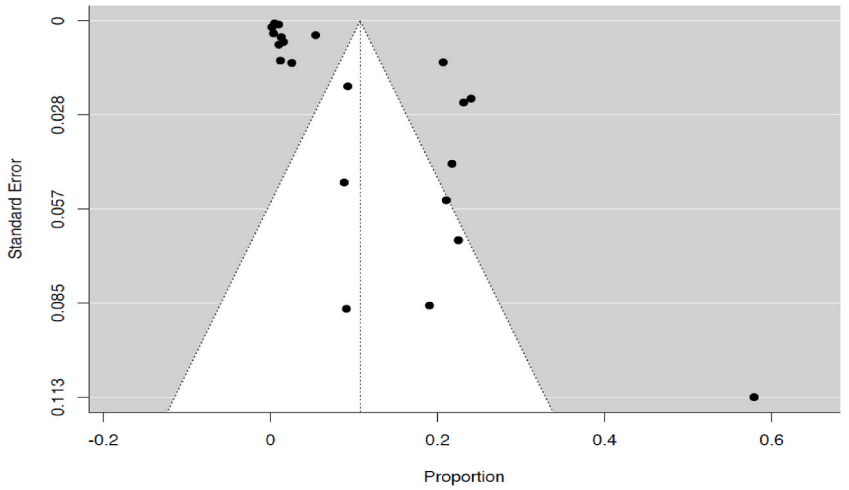

Fig. 3. Funnel Plot for the meta-analysis of conjunctivitis. Fail-safe N analysis (Fail-safe N = 4143.000, p < 0.001), Rank Correlation Test (Tau = 0.278, p = 0.071), Asymmetry (Z = 4.988, p < 0.001).

Table 2
Ocular manifestations of mpox reported in the literature.

	Ocular manifestation	Case report n cases = 25[a]	Case series[b]	Cross-sectional[b]	Others[b]
Eyelids	Preseptal cellulitis	3	1/5	8/382, 1/83, 2/156	
	Periorbital or eyelid edema	3		1/382	
	Eyelid lesions	10	2/7, 3/5, 1/3, 2/47	2/83, 12/57, 2/185, 2/264	
	Eyelid nodule	1			
	Blepharitis	1		1/264	
Cornea	Corneal edema	2	1/11		
	Corneal Hypoesthesia	2			
	Corneal ulcer or epithelial defect	7			
	Corneal staphyloma			1/229	
	Corneal perforation	3			
	Corneal scarring or opacities	1	1/11, 1/47	7/282	
	Limbitis	1			
	Keratitis	6 One of them with PUK	2/5, 11/338	5/382, 1/136, 2/226, 1/264, 3/229, 12/282	
	Keratic precipitates	2			
Conjunctiva	Keratoconjunctivitis	2 One with membranous keratoconjunctivitis			
	Subconjunctival nodule	1	1/5		
	Conjunctivitis	12	5/7, 5/5, 1/7, 2/528, 2/197, 3/34, 1/11	6/382, 81/8167, 14/216, 1/83, 12/57, 1/264, 218/1054, 9/40, 9/40, 4/21, 80/333, 11/19, 68/294, 7/536, 4/156, 36/7518, 20/92	150/2768
	Conjunctival lesions	10	5/7, 1/47, 4/5, 60/338	14/216	
Sclera	Anterior scleritis	1	1/11		
Uvea	Anterior uveitis	4			
IOP	Intraocular hypertension	1			

[a] For the column of case reports, the number in each cell represents the total number of cases that presented with ophthalmic manifestations.
[b] For the other columns (cross-sectional studies, case series, and other studies), each proportion represents the number of patients who presented with ophthalmic manifestations in the numerator and the total number of patients with monkeypox included in the study in the denominator. Each proportion represents one study.

the third case was that of a fluorescein-staining subconjunctival nodule with sectoral hyperemia and an adjacent left upper eyelid umbilicated nodule with central crusting. The hyperemic lesion did not blanch with the administration of topical phenylephrine, indicating scleral inflammation [48]. For more detailed information regarding the frequency of scleral involvement by type of study, see Table 2.

4.3. Uveitis

Four case reports described anterior uveitis [34,36,42,43]. All had mild inflammation (0.5 or 1+ of cells) and were accompanied by corneal compromise. Two had keratic precipitates [34,42], and one had keratitis with epithelial corneal ulcer and superior limbitis [43]. For more detailed information regarding the frequency of uveitis by type of study, see Table 2.

4.4. Corneal involvement

The most common corneal manifestation was keratitis, representing 2% of all cases (Fig. 2 E) [5,14,15,57,66,71,75]. In a cohort from DRC, keratitis was reported in 4·4% of smallpox-unvaccinated patients with mpox and 3·1% of vaccinated patients [15]. Another cohort reported a 1.3% of keratitis, corresponding to 3 cases, of which one developed a staphyloma approximately 20 months after the onset of keratitis and one developed caseation of eye lesions in confluent lesions spreading in the sclera [71]. Moreover, corneal ulcers and epithelial defects were reported in 7 case reports [15,29,31–33,36,43], and corneal perforation was reported in 3 [31,32]. Although uncommon, corneal involvement led to severe complications and was refractory to antiviral treatment in several cases. Three studies reported cases of blindness due to corneal opacity [5,14,15]. For more detailed information regarding the frequency of corneal involvement by type of study, see Table 2.

Table 3
Treatment approaches used for the treatment of mpox and its ocular manifestations, and HIV status of patients.

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
CASE REPORTS						
Uner (2023) [28]	Preseptal cellulitis, membranous keratoconjunctivitis with transient corneal hypoesthesia	Oral tecovirimat and IV vancomycin and piperacillin/tazobactam for presumed superimposed bacterial preseptal cellulitis.	Erythromycin ointment, preservative-free artificial tears, and topical moxifloxacin, all 4 times daily. a cryopreserved amniotic membrane ring. topical prednisolone after acute	20 to 29 days	Late Symblepharon Formation (20/25)	Negative
Bhamray-Sanchez (2023) [29]	Patient 1: Corneal scarring and opacification; conjunctival and scleral injection; peripheral inferior keratolysis with stromal keratitis, and peripheral ulcerative keratitis with superimposed stromal keratitis, and elevated intra ocular pressure 36 mmHg. Patient 2: Mild eyelid edema and mild conjunctivitis, stromal interstitial keratitis, and an inferior corneal ulcer.	Patients 1 and 2: Tecovirimat 600 mg twice a day for 30 days.	- Both patients Topical trifluridine -Just patient 1Topical moxifloxacin - Just patient 2 Topical tobramycin -Both patients Topical prednisolone acetate	Patient 1: One week Patient 2: Six weeks	Patient 1 presented a resolution of keratitis and ulceration, photophobia, and in both patients, the visual impairment persists. Patient 1 OS in hand motion Patient 2 OD visual impairment not specified	1/2 had HIV
Perzia (2023) [30]	-Photophobia - Vesicular eyelid lesions - Single conjunctival lesion.	Oral Tecovirimat 600 mg twice a day for 14 days.	- Topical Trifluridine 1% for 10 days - Topical Moxifloxacin for 10 days - Erythromycin ointment for 10 days - Artificial tears as required	Three weeks	Complete resolution of all lessons and no visual impairment. (20/20)	Positive
Carrubba (2023) [31]	Patient 1: Bilateral periorbital skin necrosis, a central corneal defect that was plugged by the prolapsed iris. Patient 2: Ulcerated papules with necrotic centers right upper eyelid, preseptal cellulitis, a necrotic rash of the face, expanding outward from initial foci and becoming confluent, restricting lid function.	Patient 1: Oral tecovirimat 600 mg twice daily for two weeks, HAART, and pneumocystis prophylaxis after the worsening of the clinical condition received tecovirimat 200 mg twice daily, vaccinia immunoglobulin and broad-spectrum antibiotics (intravenous vancomycin and cefepime). Patient 2: Before ocular manifestations, tecovirimat (600 mg twice daily for two weeks) and vaccine	Patient 1: NR Patient 2: Trifluridine 1%	Patient 1: The patient died Patient 2: NR	Patient 1: Blindness of both eyes Patient 2: NR	2/2 patients had HIV

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
		JYNNEOS. After ocular manifestations, they used HAART, broad-spectrum antibiotics (intravenous daptomycin and levofloxacin). Finally, since the necrotic lessons started, he received vaccinia immunoglobulin, intravenous cidofovir 5 mg/kg, and tecovirimat 200 mg twice daily.				
Vasquez-Perez (2023) [32]	Conjunctival hyperemia with purulent discharge and corneal edema, and a 4-mm central epithelial defect. diffuse preseptal soft tissue thickening on MRI (Preseptal cellulitis). On day 4 of admission, a more detailed examination revealed white discharge, fibrotic membranes, and significant necrosis on the bulbar and tarsal conjunctiva, corneal epithelial defect, edema, stromal keratitis, and a small 2-mm central nonsupurative infiltrate without corneal melting or perforation	Initially: intravenous ceftriaxone, 2 g, once a day, and oral metronidazole, 500 mg, 3 times a day as well as oral doxycycline, 100 mg, After mpox confirmation: oral tecovirimat, 600 mg, twice	Initially: intensive topical guttae moxifloxacin, 0.5%, Moxifloxacin eye drops were replaced by unpreserved chloramphenicol, 0.5%, 4 times a day. After mpox confirmations: topical trifluorodine, 1%, eye drops 5 times per day, for 9 days. Necrotic tissue debridement with dry amniotic membrane (OmniGen) placement. on the sixth day after his hospitalization, hourly dexamethasone, 0.1%, eye drops were initiated.	4 weeks	Remaining dense central corneal scarring and blepharoptosis. (Count fingers)	Positive. HIV viral load of less than 50 copies/mL and CD4 count of 495 cells/μL.
Quites (2023) [33]	Ocular hyperemia, keratoconjunctivitis, photophobia and blurred vision of the left eye. 1 week later: Wessley immune ring and two corneal ulcerations of 2.5 and 1 mm.	Doxycycline, fluconazole, acyclovir, Oral tecovirimat 600 mg twice a day for 14 days	ciprofloxacin 3.5 mg/mL eye drop prophylactic acyclovir 400 mg five times a day for 5 days gatifloxacin 0.3% eye drop for 10 days.	15 days after starting tecovirimat	Corneal scaring (20/100)	Negative
Carvalho (2023) [34]	Hyperemia and vesicles in the bulbar conjunctiva. Small keratic precipitates, +1 anterior chamber cells, and discrete cells in the anterior vitreous were observed.	None	topical eye corticosteroids.	10 days	Small keratic precipitates (20/20)	Negative
Ayala-Rivera (2023) [35]	Bilateral tearing and eyelid swelling. Bilateral follicular conjunctivitis and mucous discharge	Herpes Simplex Keratitis (HSK) was suspected and systemic acyclovir and ganciclovir	Ocular lubricant management with 0.4% sodium hyaluronate, a short course of topical	Eyelid lesions resolved 4 weeks after the onset of ocular symptoms,	No.complications (20/20)	Positive. HIV viral load 87 copies/mL, CD4 count of 11 cells/mm3.

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
	without keratitis. One week later, umbilicated papules and pustular lesions were seen on the margin of the upper eyelids.	ointment 5 times per day were indicated.	azithromycin 1.5% and loteprednol 0.5% were indicated.			
Alsarhan (2022) [36]	Red eye, blurred vision, and photophobia. Diffuse conjunctival injection of the left eye and a corneal epithelial ridge that stained with fluorescein, 1+ grade of anterior chamber cellular reaction with no flare.	oral tecovirimat 600 mg twice daily	topical prednisolone acetate 1% 4 times a day was added 3 days after tecovirimat starting	17 days	Small subepithelial corneal opacity (20/40)	Negative
Rai et al. (2022) [37]	Conjunctival injection, an ulcer on the right lower palpebral conjunctiva, an ulcer on the right caruncle, and a papule on the right upper eyelid.	Tecovirimat, 600 mg, twice a day for 14 days	erythromycin ointment 4 times daily to the right eye. artificial tears given every 4 h	6 days	No. complications. (20/20)	Negative
Alexis (2022) [38]	Upper and lower lid edema and erythema. Conjunctival hyperaemia without tarsal papillae or follicle blepharoconjunctivitis. A small vesicle at the medial canthus of the lower lid. Minimal superficial punctate epithelial erosions in the cornea.	Tecovirimat 600 mgtwice a day for two weeks	-Preservative free lubricating eye drops (carmellose sodium 0.5%) six times a day and as required -Lubricating ointment (paraffin + retinol palmitate 135 mcg/g) at night. - Prophylactic antibacterial cover was provided with topical chloramphenicol drops 0.5% four times a day.	One week	Improvement of intermittent blurring of vision.	Negative
Weppelmann (2022) [39]	A healing ulcerated Mpox lesion on the glabella. Temporal conjunctival injection, engorgement of the episcleral vessels, and a raised papule with conjunctival ulceration.	Tecovirimat (NR)	Erythromycin ointment	Three weeks	NR	Positive
Ly-Yang (2022) [40]	ulcer lesions on the eyelid margin, mucoid discharge, and conjunctival whitish, serpinginous, infiltrative lesions with conjunctival thickening	600-mg tecovirimat every 12 h and intravenous acyclovir, 1 g every 8 h	Ocular topical treatment included chlorhexidine, 0.2%, eye drops; ganciclovir, 0.15%, drops; moxifloxacin eyedrops, and povidone iodine, 1%, eye drops, all 5 times a day. Then, topical fluorometholone treatment 4 times a day	4 weeks	NR	Positive
Kontos and Micheletti (2022) [41]	Dome-Shaped Eyelid Nodule. A vesicular lesion was also present	oral tecovirimat (600 mg twice daily)	None	10 days	No complications. (20/20)	NR

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
	on the caruncle and there was global conjunctival hyperemia, mostly pronounced nasally and around the lesions					
Finamor (2022) [42]	Diffuse anterior scleritis, serpiginous epithelial elevation in the corneal periphery with an underlying whitish stromal infiltrate and thinned out epithelium. Decreased corneal sensitivity was observed. keratic precipitates and 1+ cells in the anterior chamber	Initially oral valacyclovir (1 g 3 times daily). After confirming mpox, oral tecovirimat (600 mg twice daily) for 14 days was started.	eye drops (sodium hyaluronate, 0.2%, andmoxifloxacin, 0.5%). topical fluorometholone, 0.1%, twice daily was introduced 3 days after tecovirimat starting.	2 weeks, symptoms and positive PCR of an eye swab at 24 and 41 days after the first genital lesion	No complications. (20/30)	Negative
Lamas-Francis (2022) [43]	Keratitis with epithelial corneal ulcer, superior limbitis, and anterior chamber 0.5+ cells	Oral tecovirimat 600 mg was administered for 14 days.	ganciclovir gel (5 daily), as well as povidone iodine 0.6% and moxifloxacin eyedrops were prescribed.	20 days	A faint subepithelial haze remained in the superior peripheral cornea. (20/25)	Positive
Nogueira Filho (2022) [44]	Conjunctivitis with three ulcerated epithelial conjunctival lesions.	Symptomatic	preservative-free lubricating eye drops (0.15% sodium hyaluronate every 3/3 h) and as topical prophylaxis (tobramycin 0.3% eye drops every 8 h for 10 days).	NR	No complications. (20/20)	NR
Scandale et al. (2022) [45]	Multiple (>10) umbilicated papules on the tarsal and bulbar conjunctiva, the fornix, and at the temporal limbus.	Intravenous cidofovir (5 mg/kg, single dose)	NR	3 days for the ocular papules	NR	NR
Benatti (2022) [46]	Conjunctivitis with a small vesicle on the lower eyelid. The blepharoconjunctivitis evolved into a single whitish ulcer (10 mm) on the medial bulbar conjunctiva, with regular edges. Neither corneal, nor anterior chamber involvement, were found on ophthalmologic examination.	NR	neomycin (3500 IU/mL), polymixin B (6000 IU/mL), and dexamethasone (1 mg/mL) twice a day for 2 weeks	3 weeks from symptom onset	NR	Negative
Foos (2022) [48]	Eye redness and discomfort. A fluorescein-staining subconjunctival nodule with sectoral hyperemia and an adjacent left upper eyelid umbilicated nodule with central crusting. The hyperemic lesion did not blanch with administration of topical phenylephrine.	NR	Oral nonsteroidal anti-inflammatory medications	1 day	NR	NR
Mazzotta (2022) [49]	Multiple papular lesions in the eyelid with	Two doses of intravenous	anti-inflammatory and vitamin A-based	Two months	NR	NR

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
	progressive periorbital and conjunctival involvement.	cidofovir (5 mg/kg weekly associated with oral probenecid and fluid support)	eye drops topical steroid therapy was started along with intravenous antibiotic therapy.			
Anderson (2003) [50]	One vesicle on the eye lash edge of the inferior palpebral fissure, without conjunctival involvement.	NR	Bacitracin cream was applied to the lesions on her face to ameliorate scarring.	NA	NR	NR
CASE SERIES						
Curi et al. (2023) [51]	Two had skin lesions in the eyelids, and the other five had conjunctival lesions with conjunctivitis.	2 patients received Tecovirimat, 600 mg, twice a day for 14 days	topical treatment with ganciclovir at medical discretion in the emergency department.	7 to 30 days	No complications 20/20 in all cases	3 had HIV (42.8%)
de Sousa et al. (2022) [52]	Palpebral conjunctiva ulceration.	NR	NR	NR	NR	21 had HIV (44.7%)
Cash-Goldwasser et al. (2022) [53]	A: Symptoms: Ocular redness, pain, itching, swelling, discharge, foreign body sensation, photosensitivity, and vision changes. Signs: conjunctivitis, conjunctival lesion, and keratitis. B: Symptoms: Ocular redness, pain, itching, and photosensitivity. Signs: medial canthus lesion, conjunctivitis, conjunctival lesion, and corneal lesion. C: Symptoms: redness, pain, and discharge. Signs: conjunctivitis. D: Symptoms: Ocular redness, pain, and periorbital swelling. Signs: eyelid lesion, conjunctivitis, conjunctival lesion, and preseptal cellulitis. E: Symptoms: Ocular redness and pain. Signs: eyelid lesion, conjunctivitis, conjunctival lesion, and subconjunctival nodule.	A: 5 days of intravenous tecovirimat and 4 weeks of oral tecovirimat. B: 14 days of oral tecovirimat and intravenous tecovirimat for 10 days. C: Tecovirimat for 1 month D: 14 days of oral tecovirimat E: 14 days of oral tecovirimat and Naproxeno	A: Trifluridine B: Antibacterial drops for 5 days C:NR D: Trifluridine and Antibacterial drops for 5 days E: Trifluridine for 5 days	A: >55 days B: 10 days C:3 weeks D: 5 days E: 3 days	Patient A: Vision impairment (20/800) Patients B,C, D, E: No changes	2 had HIV
Adler et al. (2022) [54]	Suspected bacterial conjunctivitis	Brincidofovir 200 mg (two doses) orally	Chloramphenicol (one drop four times a day until infection resolved).	35 days	NR	All negative
Thornhill et al. (2022) [12]	Conjunctivitis	NR	NR	NR	NR	41% had HIV
Patel et al. (2022) [55]	Conjunctivitis	NR	NR	NR	NR	70 had HIV (35.9%)
Jezek et al. (1988) [14]	Conjunctival lesions with complications: Keratitis, corneal lesions (8 patients with infection from animal source; 3 patients with infection from human source)	NR	NR	NR	Unilateral or bilateral blindness (22 (10%) from animal source; 4 ± 1 (5%) from human source)	NR

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
Breman et al. (1980) [5]	Corneal opacities Blindness unilateral Eyelid margins lesions	NR	NR	NR	Unilateral Blindness due to corneal opacities (1 children)	NR
Mitjà et al. (2023) [58]	Conjunctivitis Periorbital edema Keratitis Periorbital cellulitis	NA	NA	NA	NA	349 had HIV (91%). Median CD4 cell count was 211 (IQR 117–291) cells per mm3. 85 (22%) individuals with CD4 cell counts of less than 100 cells per mm3. 193 (51%) had undetectable viral load.
CROSS SECTIONAL						
Pascom et al. (2022) [60]	Conjunctivitis	NR	NR	NR	NR	34.6% had HIV
Pittman et al. (2022) [67]	Conjunctiva redness, Eye pain, Eye discharge, etc. Visual changes not specified. Conjunctival and Other Eye Lesion.	NR	NR	More or less 10 days	NR	1 had HIV
Hennessee et al. (2022) [61]	eyelid involvement, periorbital cellulitis and conjunctivitis	Oral tecovirimat	3 children received trifluridine	NR	Complete recovery	2 children had HIV
Miller et al. (2022) [62]	Eyelid lesions Conjunctivitis	One patient with conjunctivitis received oral tecovirimat for 7 weeks	One patient with conjunctivitis used trifluridine and antibacterial eye drops	NR	NR	47 had HIV (82%)
Kyaw et al. (2022) [63]	Eye lesion, conjunctivitis, red eyes, or eye discharge	NR	NR	NR	NR	181 had HIV (25.2%)
Harrison et al. (2022) [64]	Red eyes due to conjunctivitis or keratitis.	NA	NA	NA	NA	92 patients had HIV (44%). Median CD4 count of 713 cells per mm3 (range 36–1659; IQR 500–885).
Català et al. (2022) [65]	Pustules or pseudopustules on the eyelids. Conjunctivitis.	NR	NR	NR	NR	42% had HIV
Mailhe et al.(2022) [66]	Palpebral lesions, blepharitis, conjunctivitis, and keratitis.	Two injections of cidofovir (5 mg/kg).	-Ocular tobramycine -Ocular dexamethasone -Ocular ganciclovir All treatments were used before the MPX confirmation	All patients but the one with the keratitis achieved full resolution of symptoms after 4 days of hospitalization.	NR	73 had HIV (29%)
Pittman (2022) [67]	Symptoms: Conjunctiva redness, eye pain, eye discharge, etc. Signs: Conjunctival and other eye lesion	NR	NR	NR	NR	1 had HIV
Ogoina (2020) [69]	Conjunctivitis and photophobia Skin rash in the eyelids.	NR	NR	NR	NR	9 had HIV (22,5%)

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Table 3 (*continued*)

Author (Year)(DOI)	Ocular Manifestation (n/N)	Systemic antiviral treatment	Topical and other treatments	Time of resolution	Post-treatment visual outcome (BCVA)	HIV status
Ogoina et al. (2019) [70]	Conjunctivitis	NR	NR	NR	NR	2 had HIV (9,5%)
Núñez (2022) [72]	Conjunctivitis and photophobia	NR	NR	NR	NR	54.5% had HIV
Fink (2022) [73]	Conjunctivitis, periorbital cellulitis, necrotizing conjunctivitis	Tecovirimat (NR)	NR	NR	One patient with necrotising conjunctivitis presented visual impairment	47 had HIV (30%)
Yinka-Ogunleye et al. (2019) [76]	Conjunctivitis and sensitivity to light.	NR	NR	NR	NR	According to information reported by the attending clinician, 4 of the people who died had HIV with features of AIDS.
Jezek et al. (1987) [15]	Conjunctival lesions and lesions along the eyelid margins. Keratitis and Corneal Ulceration.	NR	NR	22 to 24 days	All were children: Bilateral Blindness (1 patient unvaccinated) Unilateral Blindness (3 unvaccinated) Corneal opacities (6 unvaccinated and one vaccinated) Deformed eyelid (5 unvaccinated)	NR
OTHERS						
Rimmer (2023) [77]	One case presenting unspecified ocular involvement	Tecovirimat (NR)	NR	NR	NR	20 had HIV (35%)
Farrar (2023) [78]	Conjunctivitis	Vaccinated with JYNNEOS vaccine dose ≥14 days before illness onset	NR	NR	NR	1,074 unvaccinated patients had HIV (41.6%) 19 vaccinated patients had HIV (24.4%)

NR: No reported.

4.5. Visual outcomes and complications

Overall, the outcomes of most cases were positive, with the majority achieving full recovery and preserving a visual acuity of 20/25 or better [30,34,35,37,41,44]. However, serious complications were reported in some cases. Some patients experienced unilateral or bilateral blindness due to corneal opacities or perforation [29,31–33,53], while one developed late symblepharon formation [28].

4.6. Treatment regimens used

Regarding treatment, 27 studies reported on the management approach. The most common treatment used, when indicated, was tecovirimat. In some cases, cidofovir and brincidofovir were used [31,45,49,54,66], and less commonly, the treatment was limited to symptomatic relief. Interestingly, several patients received diverse antibiotics and antivirals, either topically or systemically, due to suspicion of herpes simplex infections or superimposed bacterial infections [33,35,51,66]. In several cases, empirical treatment was initiated before specific therapy for mpox due to a delay in diagnosis. Additionally, some patients received topical trifluridine 1% as an adjunctive therapy. In one case, vitamin A-based eye drops were used to maintain epithelial integrity [49]. More information about the treatment for ocular manifestations of mpox is available in Table 3.

Moreover, two studies reported a lower prevalence of ophthalmic manifestations in patients who had received smallpox vaccination (Fig. 4). However, this result did not achieve statistical significance in our meta-analysis, although a trend was evident. Thus, more studies are needed to determine the impact of vaccination on mpox ophthalmic manifestations.

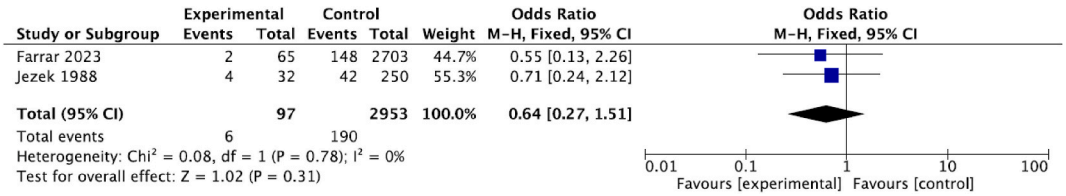

Fig. 4. Meta-analysis comparing the risk of ophthalmic manifestation between vaccinated and unvaccinated subjects.

5. Discussion

5.1. Ocular manifestations and temporality

Most cases reported eyelids or ocular surface involvement, while only a few reported intraocular inflammation. Ocular manifestations were diverse, but the most commonly reported were conjunctivitis, eyelid lesions, conjunctival lesions, keratitis, and preseptal cellulitis. The prevalence of these manifestations ranged from 1% to 8% (Fig. 2 A-E), and patients generally had a favorable visual outcome. However, the results demand a cautious interpretation as they are primarily based on observational studies. Moreover, a publication bias analysis could only be conducted in the meta-analysis of conjunctivitis (Fig. 3). Moreover, some severe manifestations, such as necrosis of palpebral skin and corneal perforations that led to unilateral or bilateral blindness, were reported in some cases.

Investigations conducted by Thornhill et al. (2022) [12], Patel et al. (2022) [55], and Mande et al. (2022) [75] have shown that ophthalmic may be the first manifestations of the disease. However, in other studies, the time interval between the onset of systemic and ophthalmic manifestations was approximately 7 days (as shown in Table 1) [27,45–47,49]. Moreover, ophthalmic compromise has been associated with a more severe Mpox virus infection [55,67], being a reason for hospitalization in some cases [65]. In a cohort study, patients with conjunctivitis had a higher frequency of other symptoms, such as nausea, chills/sweating, mouth ulcers, sore throat, lymphadenopathy, fatigue, and sensitivity to light compared to those with no reported conjunctivitis. Moreover, 47% of cases with conjunctivitis reported were considered as “bed-ridden”, compared to 16% of cases where conjunctivitis was not reported [13].

Some studies of the Clade I found that ophthalmic compromise seems to be more frequent in patients with infection from animal sources [14,15]. It could be related to the route of infection, because animal-source infection is primarily generated by direct contact with wild animals maintained in captivity or used as pets, such as prairie dogs and monkeys [50]. Probably, people become infected when they touch or pet animals and then touch their faces, allowing the virus to reach conjunctival tissue. However, most cases of the last outbreak correspond to Clase II/IIa/IIb [79], for which the risk factors differ, i.e. men who have sex with men or the known risk factor for severe disease that has been noted in HIV co-infected patients [62].

On the other hand, a critical aspect of the2022 outbreak (Clade IIa and IIb) is the milder severity of the presentation of illness and the lower rate of ocular manifestations compared with Clade I [79,80]. Likewise, ophthalmic manifestations seem to be more severe in smallpox-unvaccinated patients [14,15]. That can be explained because the Mpox virus belongs to the same smallpox family, and the immunity generated decreases the viral load. Interestingly, two articles found that ocular complications were less common in patients previously vaccinated for the smallpox virus [15,78]. We conducted a meta-analysis of both articles, which compared the frequency of conjunctivitis between vaccinated and unvaccinated patients and did not find a statistically significant reduction in ophthalmic manifestations (Fig. 4). However, it is important to note that the studies compared did not use the same vaccine.

5.2. HIV and ocular manifestations of mpox

The majority of mpox patients in the largest cohorts are males, with a significant proportion of them also living with HIV [61,64,74]. However, there are still uncertainties regarding the relationship between these two infections, beyond the fact that they share similar transmission mechanisms. Some studies suggest that HIV-positive patients tend to have a more severe disease course and require antiviral therapy more frequently [59,70]. Additionally, one study found that among HIV-positive patients with ocular involvement, most had mild CD4 counts of less than 100 cells per mm3 [58].

5.3. Complications and treatment

Ocular involvement in mpox is considered a complication that predicts worse clinical outcomes in a certain proportion, which require in-hospital management [16]. However, it leaves implications after the disease because it is also a potentially blinding disease, as we see in the studies of Breman et al. [5] and Jezek et al. [14,15], where it is highlighted that blindness is a common complication in the pediatric population studied and that it can become bilateral, so it should be a wake-up call to physicians who manage this disease, to provide appropriate education on hygiene, care of lesions and warning signs.

The most recent studies reported the use of antiviral agents when there were multiple complications or a severe presentation (Multiple papular lesions plus other manifestations); the antiviral most commonly used was tecovirimat, although cidofovir and brincidofovir were also used [45,49,54,66,81]. Tecovirimat is currently available for clinical use under an expanded-access protocol and seems to improve clinical outcomes in severe cases of mpox. However, its safety and efficacy in humans have not been completely established [82]. Additionally, the use of topical trifluridine 1% as an adjunctive therapy was reported in several cases. The use of

trifluridine is substantiated by the reports of use in ocular vaccinia, since both are orthopoxvirus and share several biological characteristics. Likewise, a single study in a rabbit model showed potential for corneal scarring when vaccinia keratitis was treated with vaccinia immune globulin intravenous (VIGIV) [83]. VIGIV could potentially offer passive immunity to specific individuals with compromised immune systems, providing temporary protection until their own immune system can eliminate the virus. Nonetheless, the frequency of favorable outcomes associated with medical countermeasures (MCMs) and whether improvements in patients' conditions were primarily a result of MCMs, natural recovery from the illness, or a combination of both, remains unknown [84]. Although there is not enough literature to recommend or not the use of these agents, the CDC has stated that "trifluridine may be considered in cases of Mpox virus conjunctivitis and is recommended in cases of Mpox virus keratitis, in consultation with an ophthalmologist." [85].

On the other hand, since the most common manifestation was conjunctivitis, a wide spectrum of management ranging from the use of antibiotics alone (chloramphenicol), antibiotics with corticosteroids (neomycin + dexamethasone), and even the combined use of eye drops and intravenous antibiotics were initiated before the confirmation of Mpox virus infection in the conjunctiva either to treat bacterial superinfection or as prophylactic therapy (Table 3) [46,48–50,54,66,86]. Clinicians should consider mpox in the differential diagnosis of conjunctivitis in patients with sociodemographic risk factors.

Finally, the resolution of ophthalmic manifestations can occur between the first three days and up to 2 months [15,46,48,49,54,66]. But as we saw previously, these can be permanent, generating corneal opacities, and unilateral or bilateral blindness, with a special predominance in unvaccinated children, associated with contact with animals [14,15].

6. Limitations

Although the literature on ophthalmic manifestations of mpox has been increasing recently, it remains scarce. Most of the information that comes from cross-sectional and cohort studies does not provide a detailed description of ophthalmic manifestations. Therefore, further studies are necessary to characterize better the frequency and implications of ophthalmic manifestations in Mpox virus infection. Additionally, more precise characterization is needed since the term "ocular disease" was used in several cases without precise descriptions. Given that this is a disease of global public health interest, reports should be more accurate regarding the temporality of manifestations and their treatment. Furthermore, the quality of the evidence available to date and the fact that it comes from different clades could limit the conclusions of our meta-analysis. With the emergence of new studies featuring larger sample sizes and more detailed descriptions of ophthalmological manifestations, the true prevalence of these can be more accurately determined.

7. Conclusions

The most commonly reported ophthalmic manifestations of Mpox virus infection are conjunctivitis and the presence of periocular umbilicated lesions. However, severe ophthalmic manifestations, that can potentially cause blindness, tend to occur in patients with more severe disease phenotypes, pediatric patients, and those who are unvaccinated. Therefore, if ocular involvement of the Mpox virus is suspected, it is highly recommended to seek ophthalmologic consultation for a comprehensive evaluation and ongoing monitoring of the patient's condition and the extent of the disease. Although some cases resolve spontaneously with symptomatic treatment, it is recommended to consider systemic antiviral therapy for all patients with severe Mpox virus disease, including those with ophthalmic manifestations. Tecovirimat is the preferred antiviral management in such scenarios, and topical management for conjunctivitis can be added if necessary.

Ethical approval statement

Due to the characteristics of the study, it does not require approval by the ethics committee; however, it was submitted for approval in PROSPERO (ID: CRD42022359027).

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18561.

References

[1] G. McFadden, Poxvirus tropism, Nat. Rev. Microbiol. 3 (2005) 201–213, https://doi.org/10.1038/nrmicro1099.
[2] B.N. Fields, Fields Virology, sixth ed., Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia, 2013.
[3] B.K. Titanji, B. Tegomoh, S. Nematollahi, M. Konomos, P.A. Kulkarni, Monkeypox: a contemporary review for healthcare professionals, Open Forum Infect. Dis. 9 (2022), https://doi.org/10.1093/ofid/ofac310 ofac310.
[4] P. von Magnus, E.K. Andersen, K.B. Petersen, A. Birch-Andersen, A POX-like disease in cynomolgus monkeys, Acta Pathol. Microbiol. Scand. 46 (2009) 156–176, https://doi.org/10.1111/j.1699-0463.1959.tb00328.x.
[5] J.G. Breman, Kalisa-Ruti, M.V. Steniowski, E. Zanotto, A.I. Gromyko, I. Arita, Human monkeypox, 1970-79, Bull. World Health Organ. 58 (1980) 165–182.
[6] World Health Organization, Monkeypox. https://www.who.int/news-room/fact-sheets/detail/monkeypox, 2022.
[7] L. Khodakevich, M. Szczeniowski, null Manbu-ma-Disu, Z. Jezek, S. Marennikova, J. Nakano, D. Messinger, The role of squirrels in sustaining monkeypox virus transmission, Trop. Geogr. Med. 39 (1987) 115–122.
[8] M.G. Reynolds, I.K. Damon, Outbreaks of human monkeypox after cessation of smallpox vaccination, Trends Microbiol. 20 (2012) 80–87, https://doi.org/10.1016/j.tim.2011.12.001.
[9] K. Walter, P.N. Malani, Update on mpox, 1892, JAMA 329 (2023), https://doi.org/10.1001/jama.2023.9142.
[10] L.D. Nolen, L. Osadebe, J. Katomba, J. Likofata, D. Mukadi, B. Monroe, J. Doty, C.M. Hughes, J. Kabamba, J. Malekani, P.L. Bomponda, J.I. Lokota, M.P. Balilo, T. Likafi, R.S. Lushima, B.K. Ilunga, F. Nkawa, E. Pukuta, S. Karhemere, J.-J.M. Tamfum, B. Nguete, E.O. Wemakoy, A.M. McCollum, M.G. Reynolds, Extended human-to-human transmission during a monkeypox outbreak in the democratic republic of the Congo, Emerg. Infect. Dis. 22 (2016) 1014–1021, https://doi.org/10.3201/eid2206.150579.
[11] A.W. Rimoin, P.M. Mulembakani, S.C. Johnston, J.O. Lloyd Smith, N.K. Kisalu, T.L. Kinkela, S. Blumberg, H.A. Thomassen, B.L. Pike, J.N. Fair, N.D. Wolfe, R. L. Shongo, B.S. Graham, P. Formenty, E. Okitolonda, L.E. Hensley, H. Meyer, L.L. Wright, J.-J. Muyembe, Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo, Proc. Natl. Acad. Sci. USA 107 (2010) 16262–16267, https://doi.org/10.1073/pnas.1005769107.
[12] J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, F. Maggi, A.-B.E. Hansen, C. Hoffmann, J.I. Lezama, C. Mussini, A. Cattelan, K. Makofane, D. Tan, S. Nozza, J. Nemeth, M.B. Klein, C.M. Orkin, Monkeypox virus infection in humans across 16 countries - april-june 2022, N. Engl. J. Med. 387 (2022) 679–691, https://doi.org/10.1056/NEJMoa2207323.
[13] C. Hughes, A. McCollum, E. Pukuta, S. Karhemere, B. Nguete, R. Shongo Lushima, J. Kabamba, M. Balilo, J.-J. Muyembe Tamfum, O. Wemakoy, J. Malekani, B. Monroe, I. Damon, M. Reynolds, Ocular complications associated with acute monkeypox virus infection, DRC, Int. J. Infect. Dis. 21 (2014) 276–277, https://doi.org/10.1016/j.ijid.2014.03.994.
[14] Z. Jezek, B. Grab, M. Szczeniowski, K.M. Paluku, M. Mutombo, Clinico-epidemiological features of monkeypox patients with an animal or human source of infection, Bull. World Health Organ. 66 (1988) 459–464.
[15] Z. Jezek, M. Szczeniowski, K.M. Paluku, M. Mutombo, Human monkeypox: clinical features of 282 patients, J. Infect. Dis. 156 (1987) 293–298, https://doi.org/10.1093/infdis/156.2.293.
[16] Centers for Disease Control and Prevention, Patient's Guide to Monkeypox Treatment with TPOXX, Monkeypox, 2022. https://www.cdc.gov/poxvirus/monkeypox/if-sick/treatment.html.
[17] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shamseer, J.M. Tetzlaff, E.A. Akl, S.E. Brennan, R. Chou, J. Glanville, J. M. Grimshaw, A. Hróbjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, L.A. Stewart, J. Thomas, A.C. Tricco, V.A. Welch, P. Whiting, D. Moher, The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ (2021) n71, https://doi.org/10.1136/bmj.n71.
[18] A.M. McCollum, I.K. Damon, Human monkeypox, Clin. Infect. Dis. 58 (2014) 260–267, https://doi.org/10.1093/cid/cit703.
[19] D. Li, K. Wilkins, A.M. McCollum, L. Osadebe, J. Kabamba, B. Nguete, T. Likafi, M.P. Balilo, R.S. Lushima, J. Malekani, I.K. Damon, M.C.L. Vickery, E. Pukuta, F. Nkawa, S. Karhemere, J.-J.M. Tamfum, E.W. Okitolonda, Y. Li, M.G. Reynolds, Evaluation of the GeneXpert for human monkeypox diagnosis, Am. J. Trop. Med. Hyg. 96 (2017) 405–410, https://doi.org/10.4269/ajtmh.16-0567.
[20] CLARITY Group, Risk of bias assessment tools, Method. Resour. (2023). https://www.evidencepartners.com/resources. (Accessed 7 October 2022).
[21] D. Hoy, P. Brooks, A. Woolf, F. Blyth, L. March, C. Bain, P. Baker, E. Smith, R. Buchbinder, Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement, J. Clin. Epidemiol. 65 (2012) 934–939, https://doi.org/10.1016/j.jclinepi.2011.11.014.
[22] M.H. Murad, S. Sultan, S. Haffar, F. Bazerbachi, Methodological quality and synthesis of case series and case reports, BMJ Evid.-Based Med. 23 (2018) 60–63, https://doi.org/10.1136/bmjebm-2017-110853.
[23] M. Harrer, T. Furukawa, D. Ebert, R Package, 2019, version 0.0.9000. https://dmetar.protectlab.org/.
[24] L. Osadebe, C.M. Hughes, R. Shongo Lushima, J. Kabamba, B. Nguete, J. Malekani, E. Pukuta, S. Karhemere, J.-J. Muyembe Tamfum, E. Wemakoy Okitolonda, M.G. Reynolds, A.M. McCollum, Enhancing case definitions for surveillance of human monkeypox in the Democratic Republic of Congo, PLoS Neglected Trop. Dis. 11 (2017), e0005857, https://doi.org/10.1371/journal.pntd.0005857.
[25] E.R. Whitehouse, J. Bonwitt, C.M. Hughes, R.S. Lushima, T. Likafi, B. Nguete, J. Kabamba, B. Monroe, J.B. Doty, Y. Nakazawa, I. Damon, J. Malekani, W. Davidson, K. Wilkins, Y. Li, K.W. Radford, D.S. Schmid, E. Pukuta, E. Muyamuna, S. Karhemere, J.-J.M. Tamfum, E.W. Okitolonda, A.M. McCollum, M. G. Reynolds, Clinical and epidemiological findings from enhanced monkeypox surveillance in tshuapa province, democratic republic of the Congo during 2011-2015, J. Infect. Dis. 223 (2021) 1870–1878, https://doi.org/10.1093/infdis/jiab133.
[26] P. Formenty, M.O. Muntasir, I. Damon, V. Chowdhary, M.L. Opoka, C. Monimart, E.M. Mutasim, J.-C. Manuguerra, W.B. Davidson, K.L. Karem, J. Cabeza, S. Wang, M.R. Malik, T. Durand, A. Khalid, T. Rioton, A. Kuong-Ruay, A.A. Babiker, M.E.M. Karsani, M.S. Abdalla, Human monkeypox outbreak caused by novel virus belonging to Congo Basin clade, Sudan, 2005, Emerg. Infect. Dis. 16 (2010) 1539–1545, https://doi.org/10.3201/eid1610.100713.
[27] J.J. Sejvar, Y. Chowdary, M. Schomogyi, J. Stevens, J. Patel, K. Karem, M. Fischer, M.J. Kuehnert, S.R. Zaki, C.D. Paddock, J. Guarner, W.-J. Shieh, J.L. Patton, N. Bernard, Y. Li, V.A. Olson, R.L. Kline, V.N. Loparev, D.S. Schmid, B. Beard, R.R. Regnery, I.K. Damon, Human monkeypox infection: a family cluster in the midwestern United States, J. Infect. Dis. 190 (2004) 1833–1840, https://doi.org/10.1086/425039.
[28] O.E. Uner, D.C. 2nd Hubbard, C. Torres-Quinones, R. Pegany, L. Huang, M.K. Ponsetto, M. Fletcher, M.K. Sikka, A. Nanji, T.K. Redd, R.D. Stutzman, W. Chamberlain, D.H. Kim, Human MPox (monkeypox) virus membranous keratoconjunctivitis with transient corneal hypoesthesia and late symblepharon formation: a novel case and clinical implications, Cornea (2023), https://doi.org/10.1097/ICO.0000000000003231.
[29] D. Bhamray-Sanchez, S. Subramanian, L.L. Dever, D. Chew, Ocular MPox: a report of two cases, IDCases 31 (2023), e01706, https://doi.org/10.1016/j.idcr.2023.e01706.
[30] B. Perzia, D. Theotoka, K. Li, E. Moss, M. Matesva, M. Gill, M. Kibe, J. Chow, S. Green, Treatment of ocular-involving monkeypox virus with topical trifluridine and oral tecovirimat in the 2022 monkeypox virus outbreak, Am. J. Ophthalmol. Case Rep. 29 (2023), 101779, https://doi.org/10.1016/j.ajoc.2022.101779.
[31] S. Carrubba, A. Geevarghese, E. Solli, S. Guttha, J. Sims, L. Sperber, S. Meehan, A. Ostrovsky, Novel severe oculocutaneous manifestations of human monkeypox virus infection and their historical analogues, Lancet Infect. Dis. (22) (2023) S1473–S3099, https://doi.org/10.1016/S1473-3099(22)00869-6, 00869–6.
[32] A. Vasquez-Perez, T. Magan, G. Volpe, S.F. Osborne, K. McFaul, K. Vahdani, Necrotizing blepharoconjunctivitis and keratitis in human monkeypox, JAMA Ophthalmol (2023), https://doi.org/10.1001/jamaophthalmol.2022.6253.
[33] T. de O. Quites, L.F.L. Landeira, T.G.V. de Santana, C.L. Khouri, M.B. Arruda, P.A. da S. Baptista, S.P.C. Barroso, Monkeypox keratoconjunctivitis with associated Wessley immune ring in an immunocompetent patient, J. Med. Virol. 95 (2023), e28545, https://doi.org/10.1002/jmv.28545.
[34] E.M. Carvalho, M. Medeiros, V.G. Veloso, A.L. Biancardi, A.L.L. Curi, Monkeypox infection causing conjunctival vesicles and anterior uveitis, Ocul. Immunol. Inflamm. (2023) 1–2, https://doi.org/10.1080/09273948.2023.2174884.
[35] V.D. Ayala-Rivera, F.D. Padilla-Pantoja, Late ophthalmologic manifestations of monkeypox in a Latin American immunosuppressed patient, Int. J. STD AIDS (2023), 095646242311621, https://doi.org/10.1177/09564624231162180.

[36] W.K. Alsarhani, C.C. Chan, S.R. Boyd, M. Hasso, A. Almeer, D.H.S. Tan, Monkeypox-associated disciform keratitis, Cornea (2022), https://doi.org/10.1097/ICO.0000000000003171.

[37] R.S. Rai, E. Kahan, B. Hirsch, I. Udell, M. Hymowitz, Ocular pox lesions in a male patient with monkeypox treated with tecovirimat, JAMA Ophthalmol 140 (2022) 1244–1246, https://doi.org/10.1001/jamaophthalmol.2022.4568.

[38] J. Alexis, H. Hohnen, M. Kenworthy, B.K.J. Host, Ocular manifestation of monkeypox virus in a 38-year old Australian male, IDCases 30 (2022), e01625, https://doi.org/10.1016/j.idcr.2022.e01625.

[39] T.A. Weppelmann, H.P. Wadia, E.M. Espana, Large conjunctival ulceration from ocular monkeypox, Am. J. Ophthalmol. (2023) S0002–S9394, https://doi.org/10.1016/j.ajo.2023.01.027 (23)00043–0.

[40] F. Ly-Yang, A. Miranda-Sánchez, B. Burgos-Blasco, J.I. Fernández-Vigo, J.A. Gegúndez-Fernández, D. Díaz-Valle, Conjunctivitis in an individual with monkeypox, JAMA Ophthalmol 140 (2022) 1022, https://doi.org/10.1001/jamaophthalmol.2022.3743.

[41] G. Kontos, E. Micheletti, A dome-shaped eyelid nodule in a young white man, JAMA Ophthalmol 140 (2022) 1011–1012, https://doi.org/10.1001/jamaophthalmol.2022.3741.

[42] L.P.S. Finamor, D. de Freitas, G. Andrade, V.D. Bergamasco, L. Cunha, C. Lázari, C. Muccioli, Tecovirimat treatment for monkeypox virus keratouveitis, JAMA Ophthalmol 141 (2023) 210–212, https://doi.org/10.1001/jamaophthalmol.2022.5486.

[43] D. Lamas-Francis, M. Treviño, H. Pérez-Freixo, L. Martínez-Perez, R. Touriño, T. Rodríguez-Ares, Corneal ulcer due to monkeypox infection, Ocul. Immunol. Inflamm. (2022) 1–3, https://doi.org/10.1080/09273948.2022.2153343.

[44] P.A. Nogueira Filho, C.D.S. Lazari, C.F.H. Granato, M.A.R.D.V. Shiroma, A.L.D. Santos, M.S.D.Q. Campos, D. Freitas, Ocular manifestations of monkeypox: a case report, Arq. Bras. Oftalmol. 85 (2022) 632–635, https://doi.org/10.5935/0004-2749.2022-0281.

[45] P. Scandale, A.R. Raccagni, S. Nozza, Unilateral blepharoconjunctivitis due to monkeypox virus infection, Ophthalmology (22) (2022) S0161–S6420, https://doi.org/10.1016/j.ophtha.2022.08.013, 00632–7.

[46] S.V. Benatti, S. Venturelli, N. Comi, F. Borghi, S. Paolucci, F. Baldanti, Ophthalmic manifestation of monkeypox infection, Lancet Infect. Dis. 22 (2022) 1397, https://doi.org/10.1016/S1473-3099(22)00504-7.

[47] E. Meduri, A. Malclès, M. Kecik, Conjunctivitis with monkeypox virus positive conjunctival swabs, Ophthalmology (22) (2022) S0161–S6420, https://doi.org/10.1016/j.ophtha.2022.07.017, 00548–6.

[48] W. Foos, K. Wroblewski, S. Ittoop, Subconjunctival nodule in a patient with acute monkeypox, JAMA Ophthalmol (2022), e223742, https://doi.org/10.1001/jamaophthalmol.2022.3742.

[49] V. Mazzotta, A. Mondi, F. Carletti, B. Baldini, R. Santoro, S. Meschi, M. Moccione, S. Gebremeskel Teklé, C. Minosse, M. Camici, S. Vita, M. Matusali, E. Nicastri, E. Girardi, F. Maggi, F. Vaia, A. Antinori, C. Pinnetti, Ocular involvement in monkeypox: description of an unusual presentation during the current outbreak, J. Infect. (2022), https://doi.org/10.1016/j.jinf.2022.08.011.

[50] M.G. Anderson, L.D. Frenkel, S. Homann, J. Guffey, A case of severe monkeypox virus disease in an American child: emerging infections and changing professional values, Pediatr. Infect. Dis. J. 22 (2003) 1093–1096, https://doi.org/10.1097/01.inf.0000101821.61387.a5. ; discussion 1096-1098.

[51] A.L.L. Curi, W. Rojas-Carabali, C. Talero-Gutiérrez, C. Cifuentes-González, A.L. Biancardi Barreto, E.M. Carvalho, A. de-la-Torre, Ophthalmic manifestations of monkeypox virus infection: a cases series, Ocul. Immunol. Inflamm. (2023) 1–4, https://doi.org/10.1080/09273948.2023.2181823.

[52] D. de Sousa, J. Patrocínio, J. Frade, C. Brazão, D. Mancha, C. Correia, J. Borges-Costa, P. Filipe, Monkeypox diagnosis by cutaneous and mucosal findings, Infect. Dis. Rep. 14 (2022) 759–764, https://doi.org/10.3390/idr14050077.

[53] S. Cash-Goldwasser, S.M. Labuda, D.W. McCormick, A.K. Rao, A.M. McCollum, B.W. Petersen, J. Chodosh, C.M. Brown, S.Y. Chan-Colenbrander, C.M. Dugdale, M. Fischer, A. Forrester, J. Griffith, R. Harold, B.W. Furness, V. Huang, A.R. Kaufman, E. Kitchell, R. Lee, N. Lehnertz, R. Lynfield, K.J. Marsh, L.C. Madoff, N. Nicolasora, D. Patel, R. Pineda, T. Powrzanas, A. Roberts, M.T. Seville, A. Shah, J.M. Wong, J.M. Ritter, C.A. Schrodt, E. Raizes, S.B. Morris, J.A.W. Gold, , CDC Monkeypox Clinical Escalations Team, CDC Monkeypox Clinical Escalations Team, A. Asif, A. Beeson, R. Bhatia, B.F. Borah, K. Chatham-Stevens, R. Choudhary, E. Click, T.D. Filardo, R.R. Galang, J. Haston, S. Hsu, G. Kaur, A. Kimball, J.T. Lee, G. Marx, J. McNicholl, M.J. Miller, R. Noe, S. O'Connor, K. O'Laughlin, K. Padgett, G. Thompson, F. Tobolowsky, I. Zulu, Ocular monkeypox — United States, july–september 2022, MMWR Morb. Mortal. Wkly. Rep. 71 (2022) 1343–1347, https://doi.org/10.15585/mmwr.mm7142e1.

[54] H. Adler, S. Gould, P. Hine, L.B. Snell, W. Wong, C.F. Houlihan, J.C. Osborne, T. Rampling, M.B. Beadsworth, C.J. Duncan, J. Dunning, T.E. Fletcher, E. R. Hunter, M. Jacobs, S.H. Khoo, W. Newsholme, D. Porter, R.J. Porter, L. Ratcliffe, M.L. Schmid, M.G. Semple, A.J. Tunbridge, T. Wingfield, N.M. Price, Clinical features and management of human monkeypox: a retrospective observational study in the UK, Lancet Infect. Dis. 22 (2022) 1153–1162, https://doi.org/10.1016/S1473-3099(22)00228-6.

[55] A. Patel, J. Bilinska, J.C.H. Tam, D. Da Silva Fontoura, C.Y. Mason, A. Daunt, L.B. Snell, J. Murphy, J. Potter, C. Tuudah, R. Sundramoorthi, M. Abeywickrema, C. Pley, V. Naidu, G. Nebbia, E. Aarons, A. Botgros, S.T. Douthwaite, C. van Nispen Tot Pannerden, H. Winslow, A. Brown, D. Chilton, A. Nori, Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series, BMJ 378 (2022), e072410, https://doi.org/10.1136/bmj-2022-072410.

[56] G.D. Huhn, A.M. Bauer, K. Yorita, M.B. Graham, J. Sejvar, A. Likos, I.K. Damon, M.G. Reynolds, M.J. Kuehnert, Clinical characteristics of human monkeypox, and risk factors for severe disease, Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 41 (2005) 1742–1751, https://doi.org/10.1086/498115.

[57] L.A. Learned, M.G. Reynolds, D.W. Wassa, Y. Li, V.A. Olson, K. Karem, L.L. Stempora, Z.H. Braden, R. Kline, A. Likos, F. Libama, H. Moudzeo, J.D. Bolanda, P. Tarangonia, P. Boumandoki, P. Formenty, J.M. Harvey, I.K. Damon, Extended interhuman transmission of monkeypox in a hospital community in the Republic of the Congo, Am. J. Trop. Med. Hyg. 73 (2005) 428–434, 2003.

[58] O. Mitjà, D. Ogoina, B.K. Titanji, C. Galvan, J.-J. Muyembe, M. Marks, C.M. Orkin, Monkeypox, Lancet Lond. Engl. 401 (2023) 60–74, https://doi.org/10.1016/S0140-6736(22), 02075-X.

[59] J.P. Thornhill, R. Palich, J. Ghosn, S. Walmsley, D. Moschese, C.P. Cortes, R.M. Galliez, A.B. Garlin, S. Nozza, O. Mitja, A.E. Radix, J.L. Blanco, B. Crabtree-Ramirez, M. Thompson, L. Wiese, H. Schulbin, A. Levcovich, M. Falcone, A. Lucchini, E. Sendagorta, C.-J. Treutiger, R. Byrne, K. Coyne, E.A. Meyerowitz, A. M. Grahn, A.-B.E. Hansen, V. Pourcher, M. DellaPiazza, R. Lee, M. Stoeckle, A. Hazra, V. Apea, E. Rubenstein, J. Jones, A. Wilkin, A. Ganesan, A.F. Henao-Martínez, E.J. Chow, B.K. Titanji, J.E. Zucker, D. Ogoina, C.M. Orkin, Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series, Lancet Lond. Engl. 400 (2022) 1953–1965, https://doi.org/10.1016/S0140-6736(22)02187-0.

[60] A.R.P. Pascom, I.N. de Souza, A. Krummenauer, M.M.S. Duarte, J. Sallas, D.B. Rohlfs, G.M. Pereira, A.C. de Medeiros, A.E. Miranda, Epidemiological and clinical characteristics of monkeypox cases in Brazil in 2022: a cross-sectional study, Epidemiol. E Serv. Saude Rev. Sist. Unico Saude Bras. 31 (2022), e2022851, https://doi.org/10.1590/S2237-96222022000300036.

[61] I. Hennessee, V. Shelus, C.E. McArdle, M. Wolf, S. Schatzman, A. Carpenter, F.S. Minhaj, J.K. Petras, S. Cash-Goldwasser, M. Maloney, L. Sosa, S.A. Jones, A. T. Mangla, R.E. Harold, J. Beverley, K.E. Saunders, J.N. Adams, D.R. Stanek, A. Feldpausch, J. Pavlick, M. Cahill, V. O'Dell, M. Kim, J. Alarcón, L.E. Finn, M. Goss, M. Duwell, D.A. Crum, T.W. Williams, K. Hansen, M. Heddy, K. Mallory, D. McDermott, M.K.Q. Cuadera, E. Adler, E.H. Lee, A. Shinall, C. Thomas, E. K. Ricketts, T. Koonce, D.B. Rynk, K. Cogswell, M. McLafferty, D. Perella, C. Stockdale, B. Dell, M. Roskosky, S.L. White, K.R. Davis, R.S. Milleron, S. Mackey, L. A. Barringer, H. Bruce, D. Barrett, M. D'Angeli, A. Kocharian, R. Klos, P. Dawson, S.R. Ellington, O. Mayer, S. Godfred-Cato, S.M. Labuda, D.W. McCormick, A. M. McCollum, A.K. Rao, J.S. Salzer, A. Kimball, J.A.W. Gold, Epidemiologic and clinical features of children and adolescents aged <18 Years with monkeypox - United States, may 17-september 24, 2022, MMWR Morb. Mortal. Wkly. Rep. 71 (2022) 1407–1411, https://doi.org/10.15585/mmwr.mm7144a4.

[62] M.J. Miller, S. Cash-Goldwasser, G.E. Marx, C.A. Schrodt, A. Kimball, K. Padgett, R.S. Noe, D.W. McCormick, J.M. Wong, S.M. Labuda, B.F. Borah, I. Zulu, A. Asif, G. Kaur, J.M. McNicholl, A. Kourtis, A. Tadros, S. Reagan-Steiner, J.M. Ritter, Y. Yu, P. Yu, R. Clinton, C. Parker, E.S. Click, J.S. Salzer, A.M. McCollum, B. Petersen, F.S. Minhaj, E. Brown, M.P. Fischer, R.L. Atmar, A.R. DiNardo, Y. Xu, C. Brown, J.C. Goodman, A. Holloman, J. Gallardo, H. Siatecka, G. Huffman, J. Powell, P. Alapat, P. Sarkar, N.A. Hanania, O. Bruck, S.D. Brass, A. Mehta, A.W. Dretler, A. Feldpausch, J. Pavlick, H. Spencer, I. Ghinai, S.R. Black, L. N. Hernandez-Guarin, S.Y. Won, S. Shankaran, A.T. Simms, J. Alarcón, J.G. O'Shea, J.T. Brooks, J. McQuiston, M.A. Honein, S.M. O'Connor, K. Chatham-Stephens, K. O'Laughlin, A.K. Rao, E. Raizes, J.A.W. Gold, S.B. Morris, Severe monkeypox in hospitalized patients - United States, august 10-October 10, 2022, MMWR Morb. Mortal. Wkly. Rep. 71 (2022) 1412–1417, https://doi.org/10.15585/mmwr.mm7144e1.

[63] N.T.T. Kyaw, N. Kipperman, K.A. Alroy, J. Baumgartner, A. Crawley, E. Peterson, A. Ross, R.C. Fowler, V.E. Ruiz, M. Leelawong, S. Hughes, M. Juste-Tranquille, K. Lovingood, C.D. Joe, M. Chase, A. Shinall, J. Ackelsberg, C. Bergeron-Parent, B. Badenhop, S. Slavinski, V. Reddy, E.H. Lee, Notes from the field: clinical and epidemiologic characteristics of mpox cases from the initial phase of the outbreak - New York city, may 19-july 15, 2022, MMWR Morb. Mortal. Wkly. Rep. 71 (2022) 1631–1633, https://doi.org/10.15585/mmwr.mm715152a3.

[64] L.B. Harrison, G. Bergeron, G. Cadieux, H. Charest, J. Fafard, I. Levade, A.C. Blais, E. Huchet, B. Trottier, D. Vlad, J. Szabo, R. Thomas, S. Poulin, C. Greenaway, G.J. Zaharatos, M. Oughton, A. Chakravarti, R. Pilarski, A. Bui-Nguyen, K. Benomar, M.D. Libman, D.C. Vinh, A.T. Duggan, M. Graham, M.B. Klein, S. Barkati, Monkeypox in montréal: epidemiology, phylogenomics, and public health response to a large North American outbreak, ann, Intern. Med. 176 (2023) 67–76, https://doi.org/10.7326/M22-2699.

[65] A. Català, P. Clavo-Escribano, J. Riera-Monroig, G. Martín-Ezquerra, P. Fernandez-Gonzalez, L. Revelles-Peñas, A. Simon-Gozalbo, F.J. Rodríguez-Cuadrado, V. G. Castells, F.J. de la Torre Gomar, A. Comunión-Artieda, L. de Fuertes de Vega, J.L. Blanco, S. Puig, Á.M. García-Miñarro, E. Fiz Benito, C. Muñoz-Santos, J. B. Repiso-Jiménez, C. López Llunell, C. Ceballos-Rodríguez, V. García Rodríguez, J.L. Castaño Fernández, I. Sánchez-Gutiérrez, R. Calvo-López, E. Berna-Rico, B. de Nicolás-Ruanes, F. Corella Vicente, E.J. Tarín Vicente, L. de la Fernández de la Fuente, N. Riera-Martí, M.A. Descalzo-Gallego, M. Grau-Perez, I. García-Doval, I. Fuertes, Monkeypox outbreak in Spain: clinical and epidemiological findings in a prospective cross-sectional study of 185 cases, Br. J. Dermatol. (2022), https://doi.org/10.1111/bjd.21790.

[66] M. Mailhe, A.-L. Beaumont, M. Thy, D. Le Pluart, S. Perrineau, N. Houhou-Fidouh, L. Deconinck, C. Bertin, V.M. Ferré, M. Cortier, C. De La Porte Des Vaux, B.-C. Phung, B. Mollo, M. Cresta, F. Bouscarat, C. Choquet, D. Descamps, J. Ghosn, F.-X. Lescure, Y. Yazdanpanah, V. Joly, N. Peiffer-Smadja, Clinical characteristics of ambulatory and hospitalised patients with monkeypox virus infection: an observational cohort study, S1198-743X, Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis. (22) (2022), https://doi.org/10.1016/j.cmi.2022.08.012, 00428–1.

[67] P.R. Pittman, J.W. Martin, P.M. Kingebeni, J.-J.M. Tamfum, Q. Wan, M.G. Reynolds, X. Quinn, S. Norris, M.B. Townsend, P.S. Satheshkumar, B. Soltis, A. Honko, F.B. Güereña, L. Korman, J.W. Huggins, Clinical Characterization of Human Monkeypox Infections in the Democratic Republic of the Congo, Infectious Diseases (except HIV/AIDS), 2022, https://doi.org/10.1101/2022.05.26.22273379.

[68] C.M. Hughes, L. Liu, W.B. Davidson, K.W. Radford, K. Wilkins, B. Monroe, M.G. Metcalfe, T. Likafi, R.S. Lushima, J. Kabamba, B. Nguete, J. Malekani, E. Pukuta, S. Karhemere, J.-J.M. Tamfum, E.O. Wemakoy, M.G. Reynolds, D.S. Schmid, A.M. McCollum, A tale of two viruses: coinfections of monkeypox and varicella zoster virus in the democratic republic of Congo, Am. J. Trop. Med. Hyg. 104 (2021) 604–611, https://doi.org/10.4269/ajtmh.20-0589.

[69] D. Ogoina, M. Iroezindu, H.I. James, R. Oladokun, A. Yinka-Ogunleye, P. Wakama, B. Otike-Odibi, L.M. Usman, E. Obazee, O. Aruna, C. Ihekweazu, Clinical course and outcome of human monkeypox in Nigeria, Clin. Infect. Dis. 71 (2020) E210, https://doi.org/10.1093/cid/ciaa143. –E214.

[70] D. Ogoina, J.H. Izibewule, A. Ogunleye, E. Ederiane, U. Anebonam, A. Neni, A. Oyeyemi, E.N. Etebu, C. Ihekweazu, The 2017 human monkeypox outbreak in Nigeria-Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria, PLoS One 14 (2019), e0214229, https://doi.org/10.1371/journal.pone.0214229.

[71] K.P. Mbala, W.J. Huggins, R.T. Riu, M.P. Mulembakani, M.S. Ahuka, M.C. Kumakamba, W.J. Martin, T.J.J. Muyembe, The clinical characterization of human monkeypox infections in the Democratic Republic of Congo, Trop. Med. Int. Health 22 (2017) 31, https://doi.org/10.1111/(ISSN)1365-3156.

[72] I. Núñez, M. García-Grimshaw, S.E. Ceballos-Liceaga, C. Toledo-Salinas, G. Carbajal-Sandoval, L. Sosa-Laso, G. García-Rodríguez, R. Cortés-Alcalá, A. de la Torre, S. Fragoso-Saavedra, A. Quintero-Villegas, H. López-Gatell, G. Reyes-Terán, S.I. Valdés-Ferrer, Epidemiological and clinical characteristics of patients with human monkeypox infection in Mexico: a nationwide observational study, Lancet Reg. Health Am. 17 (2023), 100392, https://doi.org/10.1016/j.lana.2022.100392.

[73] D.L. Fink, H. Callaby, A. Luintel, W. Beynon, H. Bond, E.Y. Lim, E. Gkrania-Klotsas, J. Heskin, M. Bracchi, B. Rathish, I. Milligan, G. O'Hara, S. Rimmer, J. R. Peters, L. Payne, N. Mody, B. Hodgson, P. Lewthwaite, R. Lester, S.D. Woolley, A. Sturdy, A. Whittington, L. Johnson, N. Jacobs, J. Quartey, B. Ai Payne, S. Crowe, I.A. Elliott, T. Harrison, J. Cole, K. Beard, T.-P. Cusack, I. Jones, R. Banerjee, T. Rampling, J. Dunning, Clinical features and management of individuals admitted to hospital with monkeypox and associated complications across the UK: a retrospective cohort study, Lancet Infect. Dis. (22) (2022) S1473–S3099, https://doi.org/10.1016/S1473-3099(22)00806-4, 00806–4.

[74] P.R. Martins-Filho, R.R. Nicolino, K. da Silva, Incidence, geographic distribution, clinical characteristics, and socioeconomic and demographic determinants of monkeypox in Brazil: a nationwide population-based ecological study, Trav. Med. Infect. Dis. 52 (2022), 102517, https://doi.org/10.1016/j.tmaid.2022.102517.

[75] G. Mande, I. Akonda, A. De Weggheleire, I. Brosius, L. Liesenborghs, E. Bottieau, N. Ross, G.-C. Gembu, R. Colebunders, E. Verheyen, D. Ngonda, H. Leirs, A. Laudisoit, Enhanced surveillance of monkeypox in Bas-Uélé, Democratic Republic of Congo: the limitations of symptom-based case definitions, Int. J. Infect. Dis. IJID Off. Publ. Int. Soc. Infect. Dis. 122 (2022) 647–655, https://doi.org/10.1016/j.ijid.2022.06.060.

[76] A. Yinka-Ogunleye, O. Aruna, M. Dalhat, D. Ogoina, A. McCollum, Y. Disu, I. Mamadu, A. Akinpelu, A. Ahmad, J. Burga, A. Ndoreraho, E. Nkunzimana, L. Manneh, A. Mohammed, O. Adeoye, D. Tom-Aba, B. Silenou, O. Ipadeola, M. Saleh, A. Adeyemo, I. Nwadiutor, N. Aworabhi, P. Uke, D. John, P. Wakama, M. Reynolds, M.R. Mauldin, J. Doty, K. Wilkins, J. Musa, A. Khalakdina, A. Adedeji, N. Mba, O. Ojo, G. Krause, C. Ihekweazu, Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report, Lancet Infect. Dis. 19 (2019) 872–879, https://doi.org/10.1016/S1473-3099(19)30294-4.

[77] S. Rimmer, J. Barnacle, M.M. Gibani, M.-S. Wu, O. Dissanayake, R. Mehta, T. Herdman, M. Gilchrist, D. Muir, U. Ebrahimsa, B. Mora-Peris, O. Dosekun, L. Garvey, J. Peters, F. Davies, G. Cooke, A. Abbara, The clinical presentation of monkeypox: a retrospective case-control study of patients with possible or probable monkeypox in a West London cohort, Int. J. Infect. Dis. IJID Off. Publ. Int. Soc. Infect. Dis. 126 (2023) 48–53, https://doi.org/10.1016/j.ijid.2022.11.020.

[78] J.L. Farrar, N.M. Lewis, K. Houck, M. Canning, A. Fothergill, A.B. Payne, A.L. Cohen, J. Vance, B. Brassil, E. Youngkin, B. Glenn, A. Mangla, N. Kupferman, K. Saunders, C. Meza, D. Nims, S. Soliva, B. Blouse, T. Henderson, E. Banerjee, B. White, R. Birn, A.M. Stadelman, M. Abrego, M. McLafferty, M.G. Eberhart, M. Pietrowski, S.M. De León, E. Creegan, A. Diedhiou, C. Wiedeman, J. Murray-Thompson, E. McCarty, J. Marcinkevage, A. Kocharian, E.A. Torrone, L.C. Ray, D.C. Payne, Demographic and clinical characteristics of mpox in persons who had previously received 1 dose of JYNNEOS vaccine and in unvaccinated persons — 29 U.S. Jurisdictions, may 22–september 3, 2022, Am. J. Transplant. 23 (2023) 298–303, https://doi.org/10.1016/j.ajt.2023.01.003.

[79] National Institute of Allergy and Infectious Diseases, Mpox (Formerly Monkeypox), Mpox, 2022. https://www.niaid.nih.gov/diseases-conditions/mpox.

[80] Centers for Disease Control and Prevention, Science Brief: Detection and Transmission of Mpox (Formerly Monkeypox) Virus during the 2022 Clade IIb Outbreak, 2022 Outbreak Cases Data, 2023. https://www.cdc.gov/poxvirus/mpox/about/science-behind-transmission.html.

[81] A.R. Raccagni, C. Candela, E. Bruzzesi, D. Mileto, D. Canetti, A. Rizzo, A. Castagna, S. Nozza, Real-life use of cidofovir for the treatment of severe monkeypox cases, J. Med. Virol. 95 (2023), https://doi.org/10.1002/jmv.28218.

[82] A. Sherwat, J.T. Brooks, D. Birnkrant, P. Kim, Tecovirimat and the treatment of monkeypox — past, present, and future considerations, N. Engl. J. Med. 387 (2022) 579–581, https://doi.org/10.1056/NEJMp2210125.

[83] S. Altmann, C.R. Brandt, C.J. Murphy, R. Patnaikuni, T. Takla, M. Toomey, B. Nesbit, K. McIntyre, J. Covert, R. Dubielzig, G. Leatherberry, E. Adkins, S. Kodihalli, Evaluation of therapeutic interventions for vaccinia virus keratitis, J. Infect. Dis. 203 (2011) 683–690, https://doi.org/10.1093/infdis/jiq103.

[84] A.K. Rao, C.A. Schrodt, F.S. Minhaj, M.A. Waltenburg, S. Cash-Goldwasser, Y. Yu, B.W. Petersen, C. Hutson, I.K. Damon, Interim clinical treatment considerations for severe manifestations of mpox - United States, February 2023, MMWR Morb. Mortal. Wkly. Rep. 72 (2023) 232–243, https://doi.org/10.15585/mmwr.mm7209a4.

[85] Centers for Disease Control and Prevention, Interim Clinical Considerations for Management of Ocular Monkeypox Virus Infection, Mpox., 2023. https://www.cdc.gov/poxvirus/mpox/clinicians/ocular-infection.html#r5.

[86] M.G. Reynolds, A.M. McCollum, B. Nguete, R. Shongo Lushima, B.W. Petersen, Improving the care and treatment of monkeypox patients in low-resource settings: applying evidence from contemporary biomedical and smallpox biodefense Research, Viruses 9 (2017), https://doi.org/10.3390/v9120380.

Abbreviations

Mpox: Monkeypox disease
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO: International prospective register of systematic reviews
VHL: Virtual Health Library
BCVA: Best corrected visual acuity
CLARITY: Clinical Advances Through Research and Knowledge Translation
VIGIV: vaccinia immune globulin intravenous
MCMs: medical countermeasures
HIV: Human Immunodeficiency Virus
DRC: Democratic Republic of Congo
rt-PCR: Real time Polymerase Chain Reaction
ROBINS-I: Risk Of Bias In Non-randomised Studies - of Interventions
DeCS: Health Sciences Descriptors (in Spanish: Descriptores en Ciencias de la Salud)