Monkeypox Viral Detection In Semen Specimens of Confirmed Cases: A Systematic Review and Meta-Analysis

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Abstract

Background The current literature shows increasing concerns about potential seminal transmission of monkeypox virus (MPV). Accordingly, we aimed to understand better the potential presence of MPV in the seminal fluids and others specimens obtained from monkeypox (MPX) cases.

Methods On June 26, 2022, a systematic search of the literature was conducted across PubMed, Scopus, Web of Science, EMBASE, ScienceDirect, ProQuest, EBSCOHost-Academic Search Complete, and Google Scholar to find articles that examine the presence of MPV in seminal fluid of confirmed cases . The search was updated on August 12 to include newly published articles. The prevalence of MPV DNA presence in the seminal fluid and other specimens was pooled in a meta-analysis and results were presented as effect sizes and their corresponding 95% confidence intervals (CI). The quality of included articles was assessed using the National Institute of Health tool.

Results Eight articles (including 585 MPX-confirmed patients) were included. Only four studies were eligible for a meta-analysis, and the individual positivity rate of MPV DNA in semen specimens ranged from 61.11% to as high as 90.62%, while the pooled rate was 78% (95% CI: 62-93%; I2=61.93%) among 91 examined patients. Moreover, the pooled positive rate of MPV DNA was the highest in rectal samples (100%; 95%CI: 94-100%), followed by urinary (31%; 95%CI: 1-61%), nasopharyngeal (28%; 95%CI: 24-32%), and blood/plasma (8%; 95%CI: 6-10%) samples, respectively. Furthermore, two articles also investigated the infectivity of MPV particles detected in seminal specimens by testing their replication competence. Culturing MPV was successful in one out of three patients included in these studies. Also, based on available evidence, the positivity of MPV in semen specimens can be observed early and up to 19 days after symptoms onset.

Conclusions MPV is highly prevalent in seminal specimens of MPX cases, further corroborating the role of sexual transmission of the disease. However, further evidence is still needed to shed more light on the replication competence of these particles.

Introduction

Due to the current, rapid, and widespread monkeypox virus (MPV), the World Health Organization declared this multi-country outbreak a public health emergency of international concerns. The number of confirmed monkeypox (MPX) cases reached 31,799 cases in 89 countries, being the highest in the United States (9,491 cases), Spain (5,162 cases), Germany (2,982 cases), and the United Kingdom (2,914 cases), respectively [1].

Evidence from previous MPX outbreaks shows that the disease is characterized by the widespread of characteristic rash with multiple lesions affecting different body parts, including the legs, arms, and face, and less commonly, in the soles, palms, and genitalia [2-4]. On the other hand, evidence from the current outbreak shows that the rash shows an atypical pattern to the previously reported one, spreading mainly on the genital and perianal regions [5, 6]. Such events have been concerning since different reports indicated that most MPX cases are individuals that identify themselves as men who have sex with men (MSM) [7-9]. Therefore, the widespread of rashes and MPX lesions in the genital and perianal regions might suggest viral transmission in this population. The transmission of MPV has been recorded in different ways, including close contact with MPX cases (mainly when contacting an MPX active lesion), contacting animals directly or infected materials, and prolonged contact with infected individuals by droplet transmission [9-12].

Moreover, there have been concerns about the potential viral transmission among seminal fluids since most cases were reported among MSM. However, no cumulative evidence was found in the literature to indicate this hypothesis, and data is scattered among single reports with insufficient highlights regarding positive MPV DNA in seminal specimens [8, 13-16]. Accordingly, we aimed to conduct the current systematic review to understand better the potential presence of MPV in the seminal fluids of infected patients, while comparing it to the presence of MPV in other specimens.

Methods

Study design and search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17], where prior registration of a review protocol is not mandatory. On June 26, 2022, eight databases were searched including PubMed, Scopus, Web of Science, EMBASE, ScienceDirect, ProQuest, EBSCOHost-Academic Search Complete, and Google Scholar. In this regard, the following keywords were used to retrieve relevant articles: monkeypox AND (semen OR seminal). We also used Medical Subject Headings (MeSH) terms whenever possible. The search keywords were adjusted as per the database's guidelines. A full description of the used search strategy in each database is provided in (**Supplementary Table 1**). Noteworthy, the database search was updated on August 12, 2022, yielding five more relevant studies [6, 13, 15, 18, 19]. Additionally, we adopted a manual search strategy to retrieve any relevant article that was missed during the electronic database search. This strategy was conducted by: (1) screening the references of included studies, (2) searching "similar articles" of finally included studies on PubMed, and (3) conducting a random search on Google engine with the keywords "monkeypox" + "semen". No restrictions regarding year, country, or the language of publication were applied.

Eligibility criteria

This systematic review was conducted according to the PICO framework, where the population included MPX cases, no interventions, no comparisons, and the primary outcome included estimating the positivity rate of MPV in collected semen specimens. Secondary outcomes included (1) estimating the time interval between symptom onset and MPV DNA positivity in seminal specimens and (2) estimating the positivity rate of MPV in other collected specimens (urine, fecal, oropharynx, genitalia, and blood/plasma).

Since we aim to investigate the presence and prevalence of MPV in the seminal specimens of MPX cases, we included studies that (1) were original regardless of their design (i.e., case reports and series, cohort, cross-sectional studies), (2) included human individuals, (3) examined the presence of MPV in the seminal fluids of infected MPX cases. On the contrary, we excluded studies that (1) were not original (reviews, editorials, and letters to editors with no original data, commentaries, thesis, abstract-only articles, and posters), (2) animal, *in vivo*, and *in vitro* studies, (3) did not collect seminal specimens from recruited cases, (4) studies that did not include MPX cases, and (5) duplicated records.

Screening and study selection

After completing the search strategy, a senior member collected all the search results into a single Endnote library, which was used to remove all duplicates among the various databases considered in the search strategy. An excel sheet was then drafted with article reference, title, abstract, DOI, URL, journal, and link to full-text to start the screening process, which was done in two steps: title/abstract and full-text screening. These steps were done in a blind approach by at least two reviewers who discussed their differences to reach a final decision under the supervision of the senior authors. Finally, all included studies were grouped and prepared for data extraction.

Extraction and quality assessment

Data extraction was conducted in a similar approach to that of screening. A senior author drafted a pilot sheet on Excel that included three main tabs, a baseline characteristics tab, another one for intended outcomes, and the third one for quality assessment. Extracted baseline characteristics included reference, country, study design, sample size, age, gender, symptoms, travel history, previous smallpox vaccination, sexual transmission (through MSM or not), and diagnostic method. The outcome tab included events of sexually transmitted infections, lesion site, and diagnostic sample (including semen, urine, blood/plasma, skin, genital/anal, fecal, and oral/nasopharyngeal). Events of positive MPV DNA, time of onset of symptoms, and viral loads were extracted for each of these samples.

The quality of included case series was assessed using the National Institute of Health (NIH) quality assessment tool. The tool assesses the quality of each study at the level of seven domains/questions. Each domain, as well as the overall quality, is given a rating of good, fair, or poor. Two reviewers assessed the quality of included studies, and any discrepancies among them were solved by consulting one of the senior authors.

Data Synthesis

The quantitative synthesis was conducted using STATA Software (Version 17). The overall prevalence of positivity rate of MPV viral PCR in different specimens was estimated using the metaprop command. The random-effects and fixed-effects models were used according to the presence or absence of heterogeneity, respectively. Heterogeneity was measured using the I^2 statistic, where a value of >50% or a P-value of <0.05 indicates significant heterogeneity. The exact cimethod was used to pool the effect size (ES) along with its 95% confidence interval (CI). The assessment of publication bias was not feasible due to the lack of a sufficient number of studies (10 studies).

Results

Search results

The results of the initial and updated database searches are illustrated in **Figure 1**. The initial database search yielded 573 articles, out of which 70 duplicates were identified and excluded through EndNote Software. The title and abstracts of 503 articles were screened, resulting in 13 articles eligible for full-text screening. Three studies were included with the initial database search [8, 14, 20], five were added with the updated search on August 12, 2022 [6, 13, 15, 18, 19], and none was added through manual search. Finally, seven studies were included in the qualitative synthesis and four studies were included in the quantitative synthesis.

Baseline characteristics

The baseline characteristics of included studies are presented in **Table 1**. Six studies were case series [6, 13-15, 18, 20] and two were case reports [8, 19]. The number of included patients in each study ranged from 1 [20] to as high as 528 MPX-confirmed cases [6]. Most cases were adults with age >18 years. In terms of presenting symptoms and/or complaints, the majority of patients presented with rash, fever, lethargy, myalgia, or headache. Six studies reported the history of travel of MPX-confirmed cases, where 158 cases (out of 549, 28.77%) reported traveling to an MPX-endemic region in the past few months prior to contracting the infection. A minority of patients reported being previously vaccinated with smallpox vaccines (56 out of 547 MPX-confirmed cases). MSM was evident in almost all of the reported cases, where six studies reported that all of these cases were MSM [8, 13, 15, 18-20]. Meanwhile, in the largest case series of Thornhill et al., 99.80% (509 out of 528) of MPX-confirmed cases were MSM [6]. As for the diagnostic method used to confirm the diagnosis of MPX, RT-PCR was the diagnostic method reported in all of the included studies.

The history of previous or concurrent sexually-transmitted infections (STIs) among MPX-confirmed cases in included studies is highlighted in **Table 2**. These STIs included human immunodeficiency virus (overall, 243/585 cases) [6, 8, 13-15, 18, 19], Herpes simplex virus (4/378 cases) [6, 19], Chlamydia trachomatis (21/389) [6, 15], Neisseria gonorrhea (33/389) [6, 15], syphilis (39/394) [6, 15], hepatitis C virus (9/532) [6, 8], hepatitis B virus (7/532) [6, 8], hepatitis A virus (1/4) [8], and lymphogranuloma (2/377) [6].

Quality Assessment

The quality of included studies across different domains is presented in **Table 3**. Overall, five case series were assessed [6, 8, 14, 15, 18], all of which had good quality.

The positivity rate of MPV DNA in seminal specimens

Out of eight studies, only four studies were eligible for a meta-analysis (examined at least 5 semen specimens of MPX cases) [6, 13, 15, 18]. The remaining studies were not analyzed because of their design (case reports and series <3 cases) [8, 13, 14, 20]. Among included studies, the individual positivity rate of MPV DNA in semen specimens ranged from 61.11% [18] to as high as 90.62% [6]. The meta-analysis included a total number of 91 examined patients (69 showed positivity), revealing an overall positivity rate of MPV in seminal specimens of 78% (95% CI: 62-93%; I^2=61.93%) (**Figure 2**). Of note, the analyzed population is not reflective of the overall population included in these studies (**Table 1**) since only a minority of these populations were examined and analyzed.

Replication competence of MPV detected in seminal specimens

Only two included studies, which included three MPX patients reported this outcome. Lapa et al. [13] showed the cytopathic effect after viral inoculation in the cell growth medium for 48-96 hours after inoculating the viral specimen detected on the sixth day after the onset of symptoms in Vero E6 cells (ATCC; Manassas VA, USA). On the other hand, Noe et al. [14] reported that using the same culture media, no cytopathic effects were found for MPV particles obtained from seminal specimens in their two patients. This was also indicated for urine and plasma specimens, but not for particles obtained from pustules, which showed a cytopathogenic effect typical of orthopoxviruses two days after inoculation.

The time interval between symptoms onset and the positivity of MPV viral PCR in seminal fluid

Five studies [8, 13-15, 20] reported the time from symptom onset until the MPV viral PCR results of the collected semen specimens of MPX-confirmed cases (**Table 4**). Although available data in this regard are scarce, the positivity of MPV DNA PCR in the seminal fluid can be detected as early as within the first day of presentation [15] and remain positive up to 19 days following symptom onset [13].

The comparison of MPV DNA positivity rate among different collected specimens

The comparison between different specimens in terms of MPV positivity rate through viral detection with PCR is illustrated in **Table 5**. Three studies [6, 15, 18] compared the positive rate of MPV viral PCR tests among different specimens including salivary, oropharyngeal, nasopharyngeal, plasma, cutaneous, urinary, fecal, rectal, and genital samples. In our meta-analysis, compared to seminal samples (positivity rate of 78%), the positive rate of MPV viral PCR was the highest in rectal samples (100%; 95%CI: 94-100%), followed by urinary (31%; 95%CI: 1-61%), nasopharyngeal (28%; 95%CI: 24-32%), and blood/plasma (8%; 95%CI: 6-10%) samples, respectively. The prevalence rates of MPV viral PCR in oral (100%), oropharyngeal (100%), skin (96.96%), fecal (66.66%), and genital (100%) specimens. However, we could not conduct a meta-analysis because reported data were limited to an individual report per specimen site (**Table 5**).

Discussion

The main aim of the current study is to provide more insight into MPV transmission through seminal fluids of infected individuals. Our findings indicate the high prevalence of positive MPV DNA in the seminal fluid samples obtained from infected patients. This might strongly indicate the epidemiological evidence why most MPX cases are detected among MSM.

The study by Lapa et al. [13] was the only one to report that MPV detected in the semen samples of their MPX patient within the acute phase of the infection might contain a replication-competent virus. The replication competency in this study was indicated by the cytopathic effect after viral inoculation in the cell growth medium for 48-96 hours. The authors furtherly suggested that MPV might have a genital reservoir because of the prolonged viral shedding, even at low viral copies, in seminal samples. On the other hand, Noe et al. [14] showed that on growing the MPV seminal samples of their two MPX patients in cell culture (VeroE6), no growth was observable, unlike pustule materials, which showed a cytopathogenic effect typical of orthopoxviruses. MPV DNA presence in the seminal fluids might be due to local genital replication or passive diffusion from urine, blood, or genital lesions [21]. However, the exact mechanism of this event remains controversial in the literature. Although Lapa et al. [13] reported that cross-contamination from other sources (blood and urine) is unlikely (due to the absence of viral DNA in their specimens), our findings show the high prevalence of positive MPV DNA from different specimens, like the rectal, urinary, skin, and fecal ones, which might attribute to cross-contamination in some studies. Moreover, we found that only 8% of the blood/plasma specimens were positive for MPV DNA. However, MPX viremia was established in previous reports [14, 22], which might also be another reason for MPV presence in the seminal fluids of MPX patients.

MPX transmission through seminal fluids depends on the ability of the virus to replicate within this media. Accordingly, although the current study demonstrated a high prevalence rate of MPV in the tested seminal samples, this rate does not indicate viral infectivity since we could not provide more evidence regarding viral replication competence [16]. Therefore, the infectivity of seminal MPV remains controversial and needs further investigations. It should be noted that Noe et al. [14] furtherly demonstrated that skin swabs had the highest viral concentrations in their patients. This strengthens the fact that contact transmission through MPX-related lesions is another main route of infection. This does not exclude the role of sexual activities in spreading the disease. In fact, if the infection is not transmitted through seminal fluids, it might also spread through other ways, like contacting skin lesions.

Compared with other pandemics, previous studies also indicated that COVID-19 patients have SARS-CoV-2 in their seminal and feco-anal specimens [23]. However, the rates reported for the presence of SARS-CoV-2 viral RNA detection in semen samples are remarkably lower than the currently estimated rate for MPV DNA in the current study. This furtherly indicates that sexual transmission is the main route of viral transmission in the current outbreak. However, the current evidence is not definitive since contact transmission is also a common route for MPV transmission. Moreover, lesions reported in patients in the current outbreak are mostly detected in the anogenital region [16, 24, 25], which can significantly contribute to transmitting the infection since contacting such lesions during sexual activities is inevitable. Accordingly, future studies might be needed to explain further the pathogenesis of MPV presence in the seminal fluid. Moreover, most countries affected by the current MPX outbreak support LGBTQ+ activities, while transmission in other countries has been reported among individuals having a history of travel to endemic regions or having contact with animals. This furtherly indicates that sexual transmission is the main route of spreading the current MPX outbreak.

Importantly, our study has some limitations. First, the current number of relevant studies and the sample size per study are small. Accordingly, the currently reported rates might not be the best estimation since pooling is based on a low number of patients, and some data were obtained from case series studies. Moreover, data regarding the prevalence of positive MPV DNA in seminal specimens obtained from Lapa et al. [13] is preliminary, which might also limit the current estimation due to improper design. However, a random effect model was used whenever we encountered heterogeneity among the pooled outcomes. Second, we could estimate the prevalence rates of positive PCR samples from different specimens. However, we could not determine the infectivity of MPV detected in urine samples, although the prevalence rate is high among them, because of lacking proper data investigating the replication-competence of the virus in this medium. Although the high prevalence rate of positive MPV DNA in seminal samples potentially excludes cross-contamination, the current evidence is not definite and needs further strengthening.

Conclusion

This is the first study to provide cumulative evidence regarding the prevalence of positive MPV DNA in the seminal fluids of MPX patients. Our findings indicate the high prevalence of positive MPV DNA in these specimens. However, the infectivity of these specimens is yet to be determined due to current insufficient evidence regarding viral replication competence.

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Tables

Table 1. Baseline characteristics of studies examining MPV positivity in seminal fluid (N=7)

Author/YOP	Country	Study Design	Sample	Age	Gender (%)	Presenting Symptoms/Complaints		History of Travel (N/T)	Previous Smallpox Vaccination (N/T)	Sexual Transmission (N/T)	Diagnostic Method
						Systemic (N)	Non-systemic (N)				
Antinori et al., (2022)	Italy	Case report	4	30-39	100%	Fever (N=1), Myalgia (N=1)	Lymphadenopathy (N=2)	(4/4)	(1/4)	MSM=(4/4)	RT-PCR from various samples (skin, anogenital lesions, serum, plasma, semen, feces, and nasopharynx), viral quantification cycle (Cq), and DNA sequencing
Mileto et al., (2022)	Italy	Case Series	1	33	100%	Fever, asthenia, malaise, and anorexia	Lymphadenopathy, faryngodynia, and sneezing	(1/1)	NR	MSM=(1/1)	RT-PCR from different sites (pharynx, skin lesions, anal ulcer, seminal fluid)
Noe et al., (2022)	Germany	Case Series	2	26, 32	100%	Fever (N=2), fatigue (N=1), malaise (N=1), back/muscle/joint/anal pain (N=1), and headache (N=1)	Lymphadenopathy (N=2), dysphagia (N=1), and cough (N=1)	(1/2)	None	MSM=(1/2)	RT-PCR from different sites (urine -semen-blood-skin swap-oral lesion swap-Swab wrist pustule- swap head pustule), and DNA sequencing, viral quantification cycle (Cq)
Thornhill et al., (2022)	Multi-country (N=16)	Case Series	528	38 (18–68)[#]	99.81%	Rash (95%), fever (62%), lethargy (41%), myalgia (31%), headache (27%), and low mood (10%)	Lymphadenopathy (56%), pharyngitis (21%), proctitis or anorectal pain (14%)	(147/528)	(49/528)	MSM= (509/528); Bisexual= (10/528)	RT-PCR from different sites (skin or anogenital lesion -nose or throat swab- Blood -Urine -Semen)
Lapa et al., (2022)	Italy	Case Series	2	39, NR	100%	Fever (N=1)	NR	(1/2)	(1/2)	MSM=(2/2)	RT-PCR from different sites (skin lesion-urine- semen- plasma samples)- MPXV DNA concentration was measured using quantification cycles
Peiró-Mestres et al., (2022)	Spain	Case Series	12	38.5 (32-52)[#]	100%	Fever (N=4), Myalgia (N=6), fatigue (N=1), headache (N=1), general malaise (N=8)	Odynophagia (N=2), proctitis (N=3), and proctalgia (N=1)	(4/12)	(4/12)	MSM= (12/12)	RT-PCR from different sites (saliva, rectal and nasopharyngeal swab, semen, urine and fecal samples)
Raccagni et al., (2022)	Italy	Case Series	36	31.5 (31.25-35.5)[*]	100%	NR	NR	NR	NR	MSM= (36/36)	RT-PCR from different sites (serum/plasma, seminal fluids, genitalia, skin, rectum, and urine)
Tan et al., (2022)	Canada	Case report	1	40	100%	Fever, myalgia, and headache	Submandibular lymphadenopathy	NR	(0/1)	MSM=(1/1)	PCR from different sites (blood, pharynx, urine, and semen)

[#]median and range. [*]median and interquartile range. NR: not reported; N: number; T: total sample; MSM: men who have sex with other men; RT-PCR: reverse-trascriptase polymerase chain reaction; YOP: year of publication.

Table 2. Reported sexually-transmitted infections among MPX-confirmed cases in included studies

Author (YOP)	HIV (N/T)	HSV (N/T)	Chlamydia trachomatis (N/T)	Neisseria gonorrhea (N/T)	Syphilis (N/T)	HCV (N/T)	HBV (N/T)	HAV (N/T)	Lymphogranuloma (N/T)	Previous STIs	Concurrent STIs
Antinori et al., (2022)	(2/4)	NR	NR	NR	(3/4)	(1/4)	(1/4)	(1/4)	NR	NR	NR
Mileto et al., (2022)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Noe et al., (2022)	(1/2)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
thornhill et al., (2022)	(218/528)	(3/377)	(20/377)	(32/377)	(33/377)	(8/528)	(6/528)		(2/377)	NR	NR
Lapa et al., (2022)	(2/2)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Peiró-Mestres et al., (2022)	(4/12)	NR	(1/12)	(1/12)	(2/12)	NR	NR	NR	NR	NR	NR
Raccagni et al., (2022)	(15/36)	NR	NR	NR	NR	NR	NR	NR	NR	(36/36)	(4/36)
Tan et al., (2022)	(1/1)	(1/1)	NR	NR	(1/1)	NR	NR	NR	NR	NR	NR

HIV: Human immunodeficiency virus; HSV: Herpes simplex virus; HCV: Hepatitis C virus; HBV: Hepatitis B virus; HAV: Hepatitis A virus; STI: Sexually-transmitted infection; NR: Not reported; N: Number of cases with STIs; T: Total number of examined MPX-confirmed cases; YOP: Year of publication.

Table 3. The quality of included studies using the NIH tool for case series

Author (YOP)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Overall Rating
Thornhill et al., (2022)	Y	Y	NR	Y	NA	Y	Y	Y	Y	Good
Peiró-Mestres et al., (2022)	Y	Y	NR	Y	NA	Y	Y	NA	Y	Good
Noe et al., (2022)	Y	Y	NR	Y	NA	Y	Y	NA	Y	Good
Antinori et al., (2022)	Y	Y	N	Y	NA	Y	Y	NA	Y	Good
Roberto Raccagni et al., (2022)	Y	Y	N	Y	NA	Y	Y	NA	Y	Good

YOP: year of publication; Y: yes; N: no; NA: not applicable; NIH: National Institute of Health.

Q1: Was the study question or objective clearly stated?
Q2: Was the study population clearly and fully described, including a case definition?
Q3: Were the cases consecutive?
Q4: Were the subjects comparable?
Q5: Was the intervention clearly described?
Q6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?
Q7: Was the length of follow-up adequate?
Q8: Were the statistical methods well-described?
Q9: Were the results well-described?

Table 4. Number of cases that showed postivie MPV viral PCR result based on seminal analysis according to the day of assessment following symptom onset

Author (YOP)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 19
Antinori et al., (2022)					(1/2)	(1/1)		(1/1)	(2/4)								
Mileto et al., (2022)									N/A	(0/1)	N/A	N/A			N/A		N/A
Noe et al., (2022)				(0/1)													
Lapa et al., (2022)					(1/1)	(1/1)	(1/1)	N/A	N/A	N/A	N/A		N/A	(1/1)	(1/1)	N/A	(1/1)
Peiró-Mestres et al., (2022)	(1/12)	(0/12)	(0/12)	(2/11)	(0/11)	(1/12)	(2/12)	(1/11)	(0/12)	(1/12)	(0/10)	(0/11)	(1/11)	(1/12)	N/A	(1/12)	

Data are presented as (number of cases with positive seminal fluid for MPV/ total number of assessed patients). YOP: Year of publication; N/A: Not assessed during that day. Blank cells mean that semen specimens were not collected that day.

Table 5. MPV viral PCR positivity according to the site of collected specimen

Site of positive MPX viral PCR	Studies (N)	Patients (N)	Pooled ES [95% CI]	Model/Method	I^2
Saliva					
	1	12	100%	N/A	N/A
Oro-pharynx					
	1	36	100%	N/A	
Nasopharynx					
	2	540	28% [24-32%]	Fixed-effects/ cimethod(exact)	0%
Blood/Plasma					
	2	564	8% [6-10%]	Fixed-effects/ cimethod(exact)	0%
Skin					
	1	12	96.96%		
Urine					
	3	576	31% [1-61%]	Fixed-effects/ cimethod(exact)	0%
Feces					
	1	12	66.66%	N/A	
Recutm					
	2	48	100% [94-100%]	Fixed-effects/ ftt	0%
Genitalia					
	1	36	100%	N/A	
Semen					
	4	91	78% [62-93%]	Random-effects/ cimethod(exact)	61.93%

MPX: monkeypox; MPV: monkeypox virus; ES: effect size; N/A: not applicable; PCR: polymerase chain reaction; CI: Confidence interval; I^2: heterogeneity measure.

Figures

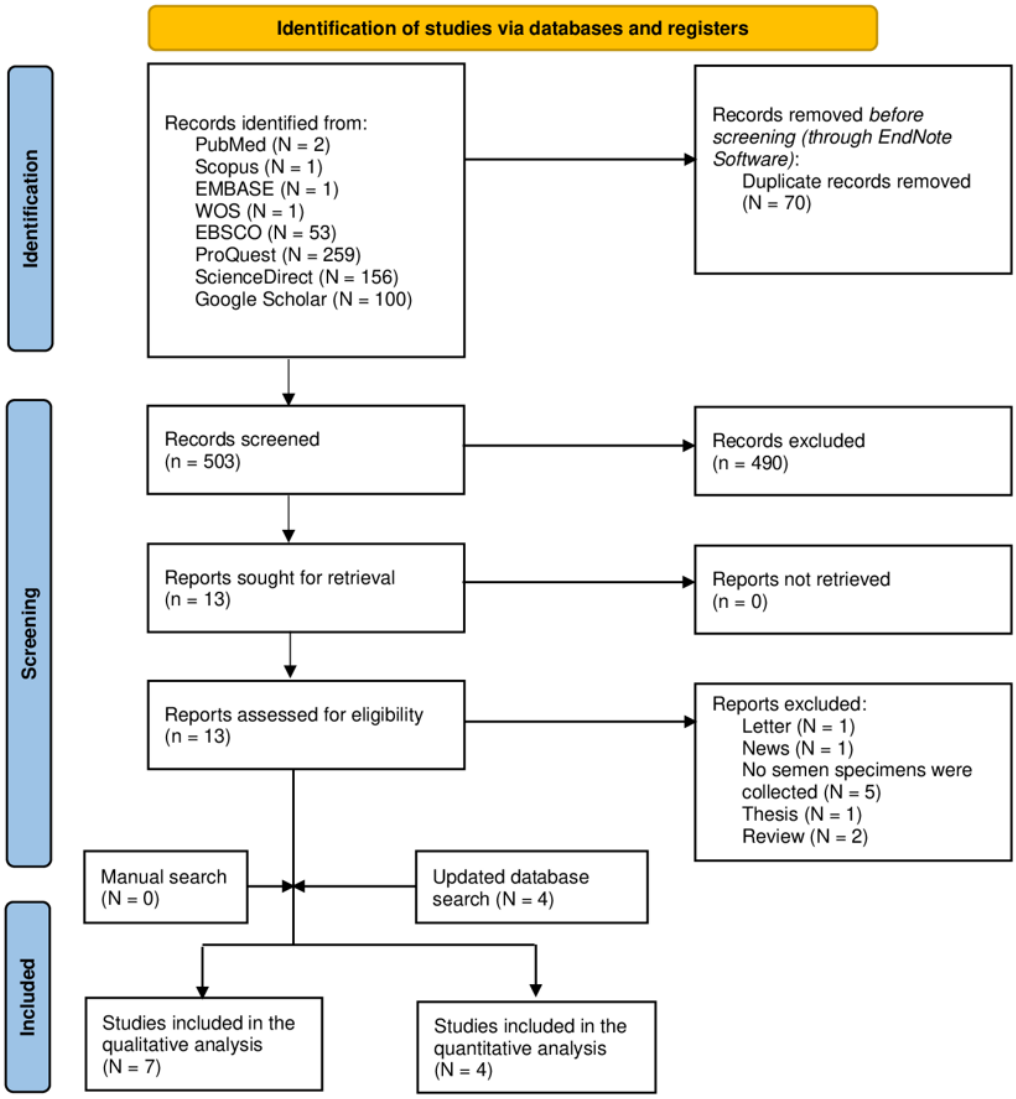

Figure 1

PRISMA flow diagram of the database search and screening processes

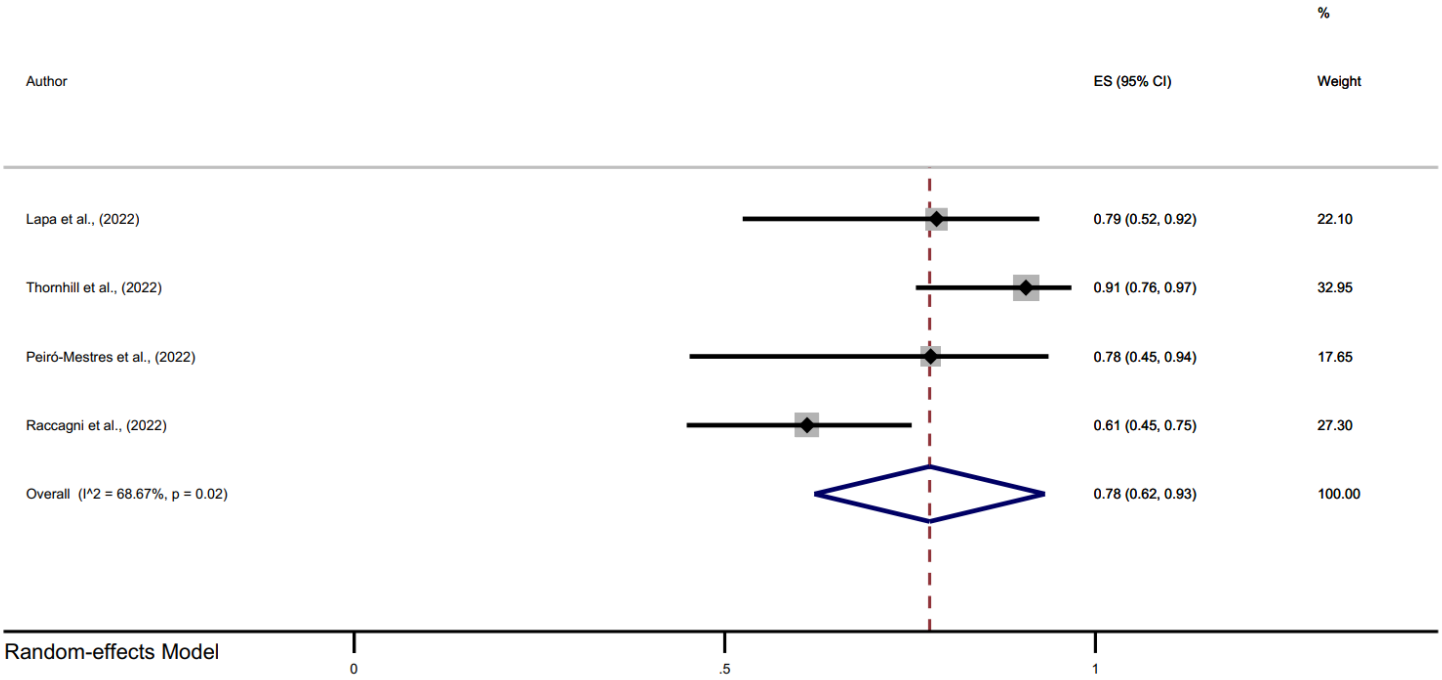

Figure 2

A forest plot showing the pooled rate of positive MPV viral PCR results in semen specimens of MPX-confirmed cases.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.docx