



OUTCOME OF MONKEYPOX INFECTION IN GRAVIDA: A LITERATURE REVIEW

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Abstract

Background: Monkeypox is a smallpox-like disease which is an important globally emerging infectious disease caused by the monkeypox virus. WHO declared monkeypox a public health emergency on 23 July 2022. Most research on monkeypox infection in humans has not included pregnant people. However, previous studies in pregnancy on the outcome of infection with smallpox viruses belonging to the Poxviridae family have reported high mortality rates. This literature review aims to determine the effects of monkey pox on pregnancy. **Methods:** Writing literature reviews is done by searching the Pubmed, Science direct, Web of Science, and Scopus databases. A literature search was carried out using the keywords "outcome", "monkeypox", and "pregnancy". Searches using these keywords are limited to 2014 – 2023 (the last 10 years) and then screening according to inclusion and exclusion criteria. **Results:** A total of three included literature were reviewed using a qualitative descriptive method. The three literatures reinforce each other by finding signs and symptoms of monkeypox in neonates, besides that there are also pregnant women who experience miscarriages. However, there is one literature which states that there is no monkeypox transmission from pregnant women with monkeypox to neonates. **Conclusion:** The findings from this literature review indicate that the impact of monkeypox on pregnancy is closely associated with a high risk of miscarriage, intrauterine fetal death, vertical transmission, and complaints in pregnant women due to monkeypox infection. Health workers are advised to be more alert to monkeypox cases in pregnancy due to the relatively high risk of fetal death in pregnant women in endemic areas and during monkeypox epidemics.

Keyword: outcome, monkeypox, pregnancy

INTRODUCTION

Monkey pox or monkeypox which is classified as a zoonotic virus, was identified in 1958 in a monkey colony used for research purposes. Monkeypox is a smallpox-like disease that is a globally important emerging infectious disease caused by the monkeypox virus. The infection is a serious public health problem in Central and West Africa and is endemic. The disease is most prevalent in the Democratic Republic of Congo where most reported cases are found (Kisalu et al., 2017).



Active surveillance of monkeypox by WHO in the Democratic Republic of Congo from 1976 to 1980 led to a significant reduction in surveillance efforts after WHO determined that monkeypox was no longer a major global health threat. Since 1990, the incidence of reported human monkeypox cases has increased dramatically in the Democratic Republic of Congo, for 3 obvious reasons: (1) an increase in the unvaccinated population due to the elimination of smallpox vaccination as it has been since the late 1970s, (2) a slope of immunity in previously vaccinated adults, and (3) a potential increase in the frequency of contact between humans and animal reservoirs of MPXV (Monkeypox Virus) due to continued forestry for new lodging lands and recurrent civil wars, forcing the population to move deeply in the forest (Mbala et al., 2017).

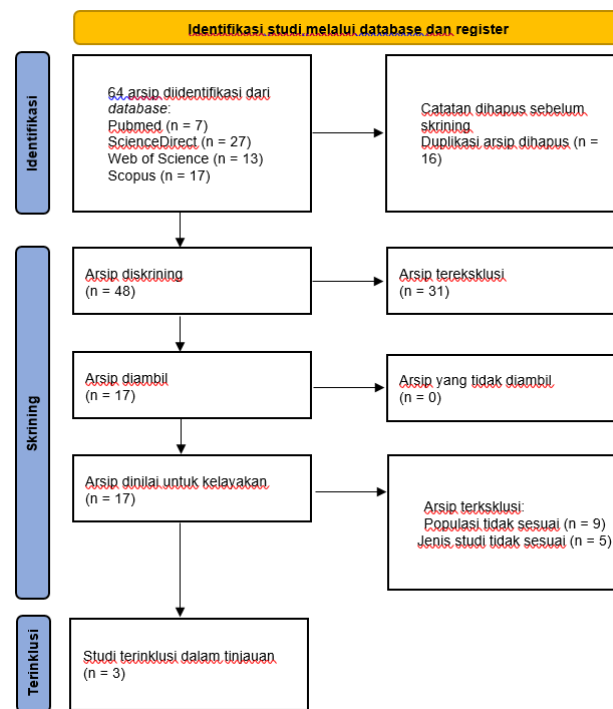
WHO confirmed 2103 cases of monkey pox spread across 10 non-endemic countries between 1 January and 15 June 2022. WHO declared monkey pox a public health emergency on 23 July 2022 (WHO., 2022). Although monkeypox has a moderate clinical course in the majority of cases, the case fatality rate ranges between 3% and 11% and can be higher in vulnerable groups, such as patients with autoimmune diseases, children and pregnant women (Pomar et al., 2022).

Most studies on human monkeypox infection exclude pregnant people. However, previous studies in pregnancy on the outcome of infection by viral pox belonging to the poxviridae family have reported high mortality rates for the first infection acquired in pregnancy, especially when it was acquired in the third trimester of pregnancy or in patients with bleeding diseases (D'Antonio et al., 2023). Based on the description above, this article review aims to determine the consequences caused by monkey pox in pregnancy with a systematic review approach.

METHOD

The literature review was conducted by searching the Pubmed, Science direct, Web of Science, and Scopus databases. The literature search was conducted using the keywords "outcome", "monkeypox", and "pregnancy". The search using these keywords was limited to the years 2014 - 2023 (the last 10 years). In addition, the literature search was limited to literature that used English and could be accessed in full text. The search results obtained 7 articles from Pubmed, 27 articles from Science direct, 13 articles from Web of Science, and 17 articles from Scopus so that a total of 64 articles were obtained from the four databases. From the search results, the deduplication process was then carried out. The deduplication process using the Rayyan application removed 16 articles that were identified as the same and left 48

articles. Next, the title and abstract of the article were screened according to the inclusion and exclusion criteria. In this process 31 articles were excluded because they did not meet the inclusion and exclusion criteria, leaving 17 articles. All 17 articles are fully accessible text by researchers. Further full text screening was carried out and a total of 5 articles were excluded with details of 9 articles excluded because they discussed unsuitable populations and 5 articles excluded because they used unsuitable research designs. The extracted data were summarised and presented narratively, using text and tables. Analyses and discussions were conducted descriptively based on the extracted data and/or other relevant references to answer the research objectives.



Gambar 1. PRISMA diagram cycle

RESULT AND DISCUSSION

A total of 3 literatures that have been included have the characteristics of being published from 2014 - 2023. The three literatures used English and the full texts of the three literatures were accessible to researchers. The three included literatures were case series, case report, systematic review and meta analysis. This literature review design analysed the literature in a qualitative descriptive manner by examining the results and discussion of each included literature. The researcher created a table to extract the data needed according to the points to be discussed in this literature review. The data listed in the table included the title of the study, the author of the article, the year the article was published, and the results of the study.

Although all studies contained keywords such as monkeypox, outcome, pregnant or pregnancy, some of the included studies did not specifically discuss these issues, only one study focused on the impact of monkey pox on pregnancy. However, all studies still had the data that the researchers were looking for.

Table 1. Data extraction of literature search results

No	Judul Jurnal	Author dan Tahun	Jenis Studi	Hasil Penelitian
1	<i>Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo</i>	Mbala PK; Huggins JW; Riu-Rovira T; Ahuka SM; Mulembakani P; Rimoin AW; Martin JW; Muyembe JT; (2017)	<i>Cohort study</i>	3 out of 4 pregnant women identified as infected with MPXV experienced foetal death. Two pregnancies ended in spontaneous abortion during the first trimester of pregnancy, with moderate to severe disease with no evidence of fetal contamination, as the products of miscarriage were not tested. Pathological findings for the stillborn fetus of case 4 consisted of diffuse cutaneous maculopapillary lesions involving the scalp; body, including abdomen, back, and chest; and extremities, including palms and soles and feet. There was extensive postmortem autolysis, consistent with intrauterine foetal death. The products of conception (excluding the foetus) showed placental haemorrhage on the maternal cotyledon surface, which was profuse, punctate, and diffuse; no other obvious abnormalities of the placenta, placental membranes, or umbilical cord were seen. Maternal MPXV viremia levels increased rapidly and abruptly, from 102 to 106 genomes/mL, coinciding with the cessation of fetal movements from day 21 to day 23 after fever onset
2	<i>Monkeypox infection in pregnancy: a</i>	D'Antonio F; Pagani G; Buca D; Khalil A; (2023)	<i>Systematic review dan meta-analysis</i>	There were no cases of maternal death. Miscarriage occurred in 39% of cases (95% confidence interval, 0-89.0), while intrauterine foetal death occurred in 23.0% (95% confidence

	<i>systematic review and meta analysis</i>			interval, 0-74.0) of cases. The overall incidence of fetal and late perinatal death was 77.0% (95% confidence interval, 26.0-100), while only 23% (95% confidence interval, 0-74.0) of the fetuses were included in the live to birth. The incidence of preterm birth before 37 weeks' gestation was 8.0% (95% confidence interval, 0-62.0). Vertical transmission occurred in 62.0% (95% confidence interval, 3.0-100) of cases. When clustering the analysis according to gestational age at infection, foetal death was found to occur in 67.0% (95% confidence interval, 9.0-99.0) of cases with first trimester infection and in 82.0% (95% confidence interval, 17.0-100) of those with infection in the second trimester.
3	<i>Mpox Cases Among Cisgender Women and Pregnant Persons - United States, May 11- November 7, 2022.</i>	Oakley LP; Hufstetler K; O'Shea J; Sharpe JD; McArdle C; Neelam V; Roth NM; Olsen EO; Wolf M; Pao LZ; Gold JAW; Davis KM; Perella D; Epstein S; Lash MK; Samson O; Pavlick J; Feldpausch A; Wallace J; Nambiar A; Ngo V; Halai UA; Richardson CW; Fowler T; Taylor BP; Chou J; Brandon L; Devasia R; Ricketts EK; Stockdale C; Roskosky M; Ostadkar R; Vang Y; Galang RR; Perkins K; Taylor M; Choi MJ; Weidle PJ; Dawson P; Ellington S; (2022)	<i>Case series</i>	Among the 10 cases in pregnant people with information about the trimester of pregnancy, three occurred during the first trimester, four during the second trimester, and three during the third trimester. The rash was present in all. Genital lesions were reported by four people who were pregnant or newly pregnant. Genital lesions in pregnant people pose a risk of monkey pox virus transmission to the foetus during vaginal delivery. As there may be an increased risk of severe disease in the newborn, breastfeeding should be temporarily suspended until the criteria for termination of isolation have been met (lesions have healed, scabs have fallen off, and a new layer of intact skin has formed). Three outcomes have been reported, including two



				uncomplicated full-term deliveries (including no transmission to the baby) and one spontaneous abortion at 11 weeks gestation. Two pregnant individuals developed symptoms of mpox within 3 days of delivery; their newborns developed lesions within 1 week of symptom onset.
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The impact of monkey pox on pregnancy varies from signs and symptoms, vertical transmission, to foetal death. In a study conducted by Oakley et al. 23 pregnant women studied all had rashes, six had fever and pruritus, four had genital and breast lesions, two had myalgia, and three had lymphadenopathy. One newly pregnant woman who was breastfeeding developed lesions four days postpartum, including under the breasts. The newborn showed symptoms with facial and chest lesions 6 days later. Of the 21 people who received a diagnosis of monkey pox during pregnancy, three have reported outcomes, two uncomplicated full-term deliveries (including no transmission to the baby) and one spontaneous abortion at eleven weeks gestation (Oakley et al., 2023). The next study conducted by Mbala et al. found that three of the four dead fetuses had pathological findings consisting of diffuse cutaneous maculopapillary lesions involving skin from the head, the entire body including the abdomen, back, and chest, and extremities, including the palms and soles of the hands and feet. As for haematology and fetal clinical chemistry findings, there was hepatomegaly and peritoneal effusion with implication of severe hepatic damage and increased vascular permeability due to MPXV-induced cellular injury. Very high viral levels release placental proinflammatory cytokines resulting in cellular injury mechanisms. Confirmation of virology by PCR and histopathological evaluation of fetal tissue revealed high virus levels with >10⁷ genome copies/mL in some tissue samples. Smallpox case studies report severe disease in pregnant women, with higher case fatality rates and increased risk of developing haemorrhagic smallpox, compared to non-pregnant women (Mbala et al., 2017).

The study conducted by Fransisco et al. with a sample of seven pregnant women, all of whom experienced severe signs and symptoms of monkey pox and three of them had vertical transmission. Of the seven pregnant women, three of them experienced miscarriage, two experienced stillbirth, the remaining two neonates remained alive. Based on the above, accurate fetal surveillance is required when maternal monkey pox infection is confirmed, especially when the infection is severe and requires hospitalisation. After diagnosis of the infection by PCR analysis, the patient should be carefully monitored to identify early signs of progression of disease severity. Tecovirimat and immunoglobulin vaccines may be considered for those who are severely ill while cidofovir and brincidofovir show evidence of teratogenic effects in animal studies. Modified Vaccinia Ankara Bavarian Nordic (MVABN) is a third generation smallpox vaccine that has been approved in the United States, Canada and the European Union. The vaccine is considered relatively safe as it contains non-replicating virus and should be given to pregnant people who are in close contact with individuals with confirmed monkeypox infection. (D'Antonio et al., 2023).



CONCLUSION AND SUGGESTION

The findings of this literature review indicate that the effects of monkey pox in pregnancy are closely associated with a high risk of miscarriage, intrauterine foetal death, vertical transmission, and complaints in pregnant women due to monkey pox infection. Health workers are advised to be more alert to cases of monkey pox in pregnancy due to the relatively high risk of fetal death in pregnant women in endemic areas and during monkey pox epidemics.

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