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RESEARCH ARTICLE

SEROPREVALENCE AND RESEARCH GAPS IN CYTOMEGALOVIRUS STUDIES IN YEMEN: A COMPREHENSIVE REVIEW

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Abstract

Cytomegalovirus is a prevalent virus that poses significant public health challenges, especially in developing countries like Yemen. Despite its widespread occurrence, there is a substantial gap in understanding the true epidemiological burden due to diagnostic limitations and low awareness among healthcare professionals and the general public. This comprehensive review aimed to assess Cytomegalovirus seroprevalence across different regions and population groups in Yemen, critically analyze the diagnostic techniques used, and evaluate awareness levels among key stakeholders. The findings indicated consistently high seroprevalence rates, reaching up to 100% among pregnant women and 99.5% among cancer patients. However, the heavy reliance on serological methods, such as enzyme-linked immunosorbent assay and electrochemiluminescence immunoassay, without the use of molecular techniques, such as polymerase chain reaction, significantly hampers the accurate detection of active infections. Moreover, awareness among healthcare workers and the general population remains critically low, exacerbating the transmission risks. This review identifies critical research gaps, including a lack of molecular epidemiological studies and comprehensive awareness campaigns. Addressing these gaps requires an integrated approach that combines advanced diagnostic methods, enhanced healthcare training, and public education initiatives to mitigate Cytomegalovirus transmission and reduce its impact on health.

Keywords: Cytomegalovirus, Seroprevalence, Diagnostic techniques, Awareness, Yemen.

1. Introduction

Cytomegalovirus (CMV), a member of the Herpesviridae family, is one of the most common viral infections worldwide[1]. It is particularly prevalent in developing countries, where socioeconomic factors, poor hygiene, and limited access to health care contribute to its widespread transmission[2]. CMV infection typically occurs through direct contact with bodily fluids, such as saliva, urine, blood, breast milk, or genital secretions[3], [4]. In most immunocompetent individuals, CMV infection is either asymptomatic or mild[5]. However, it poses significant health risks to immunocompromised individuals, including transplant recipients and cancer patients, and pregnant women, which can lead to severe morbidity and mortality[6], [7].

In Yemen, CMV prevalence is notably high, with reported IgG seropositivity rates reaching 100% among pregnant women in Sana'a[8], 98.7% among pregnant women in Hodeidah[9], and 96.6% among healthy blood donors in Sana'a[10]. Similarly, high seroprevalence rates have been reported among healthcare workers, with 86.5% of female doctors in Sana'a tested positive for CMV IgG[11]. Furthermore, studies indicate that CMV infection is prevalent among cancer patients, with seropositivity rates as high as 99.5%[12].

The deteriorating healthcare system in Yemen, compounded by ongoing conflict and political instability, has exacerbated the spread of infectious diseases, including CMV. The destruction of the healthcare infrastructure, shortage of medical supplies, and lack of preventive healthcare services have

significantly hindered disease control efforts. Overcrowded living conditions, poor sanitation, and limited access to clean water facilitate the transmission of infectious pathogens[13], [14], [15]. As a result, CMV, like many other infectious diseases, has become endemic, particularly among vulnerable populations, such as pregnant women and immunocompromised patients[16], [17], [18], [19].

Despite these alarming figures, CMV diagnostics in Yemen primarily rely on serological methods, such as enzyme-linked immunosorbent assay (ELISA) and electrochemiluminescence immunoassay (ECLIA), which detect CMV-specific IgG and IgM antibodies. Although these methods are cost-effective and readily available, they lack the sensitivity and specificity required to distinguish between active and past infections[20]. Furthermore, the absence of molecular diagnostics such as polymerase chain reaction (PCR), significantly hampers the accurate detection and monitoring of CMV reactivation, particularly in immunocompromised patients.

Another critical issue is the limited awareness and knowledge of CMV among healthcare professionals and the general public. Studies have shown that despite high exposure rates among healthcare workers, many lack adequate knowledge regarding CMV transmission, risk factors, and preventive measures[11], [21]. This gap in awareness contributes to continued transmission and inadequate prevention strategies, particularly among high-risk populations such as pregnant women and healthcare providers.

Therefore, addressing CMV in Yemen requires a multifaceted approach, which includes improving diagnostic accuracy through the adoption of molecular techniques, enhancing healthcare workers' knowledge, and increasing public awareness of CMV risks and preventive measures. This review aimed to provide a comprehensive assessment of CMV seroprevalence across Yemen, evaluate diagnostic practices, and identify critical research gaps, particularly in molecular epidemiology and public awareness. By integrating advanced diagnostic methods and promoting targeted educational initiatives, CMV transmission can be mitigated, and its associated health burdens can be reduced.

2. Materials and methods

2.1. Study Design

This study adopted a comprehensive literature review approach to assess CMV seroprevalence and diagnostic practices in Yemen. The review encompasses published studies from 2003 to Feb. 2025, including peer-reviewed articles, academic theses, and official reports. Both cross-sectional and retrospective studies are included to obtain a comprehensive understanding of CMV epidemiology and diagnostic challenges.

2.2. Data Sources

Data were extracted from diverse academic databases, including PubMed, Google Scholar, and institutional repositories from Yemeni universities and medical research centers. Only studies conducted in Yemen and published in English or Arabic were considered. Additionally, unpublished theses and dissertations from medical universities were included to capture local and region-specific data.

2.3. Inclusion and Exclusion Criteria

- Inclusion Criteria: Studies reporting CMV seroprevalence data in Yemen, studies using diagnostic methods such as ELISA, ECLIA, or PCR, and studies focusing on specific population groups (e.g., pregnant women, healthcare workers, and cancer patients).
- Exclusion Criteria: Studies with incomplete or ambiguous data, studies that did not utilize standardized diagnostic methods, and non-Yemeni studies were excluded.

2.4. Data Extraction and Synthesis

Data were manually extracted from the selected articles, focusing on seroprevalence rates, diagnostic methods, population groups, and geographical regions. Data synthesis involved the quantitative aggregation of prevalence rates and critical analysis of diagnostic techniques.

3. Results and Discussion

3.1. CMV Seroprevalence Rates

CMV seroprevalence in Yemen remains remarkably high, with rates ranging from 68% to 100% across diverse population groups and geographical regions[8], [9], [22], [23], [24], [25]. This high prevalence underscores the pervasive exposure to CMV among the Yemeni population, posing significant public health challenges. Pregnant women, in particular, represent one of the most affected groups, with seroprevalence rates reaching 100% in Sana'a[8] and 98.7% in Hodeidah [9]. These alarming figures reflect the risk of vertical transmission, where maternal CMV infection during pregnancy can result in congenital CMV, leading to severe outcomes such as hearing loss, neurological impairment, and developmental delays. The high prevalence among pregnant women highlights the critical need for improved maternal healthcare practices and heightened awareness of CMV transmission risks.

Table 1: CMV Seroprevalence Rates and Diagnostic Methods across Yemen

City	Study Design	Study Period	Sample Size	Population Studied	Age Range (years)	Diagnostic Method	Prevalence		Referances
							IgG	IgM	
AdDhale'e	Cross-sectional	Sep. to Dec. 2021	130	Pregnant women	16 - 44	ECLIA	93.8 %	3.8%	[24]
Aden	Cross-sectional	-	88	Aborted women	16 - 45	ELISA	77.6%	83.3%	[26]
Aden	Case-Control	Nov. 2016 to Dec. 2017	200	100 children with T1DM and 100 healthy children	1- 19	ECLIA	34.5%	-	[27]
			100	Healthy children			13%	-	
			100	Children with T1DM			21.5%	-	
Aden	Cross-sectional	-	538	General population	-	ELISA	94%	-	[28]
			174	Young adults			80%	-	
			364	Children			99%	-	
			280	Males			95%	-	
			258	Females			94%	-	
Dhamar	Cross-sectional	Dec. 2017 to Jan. 2019	299	Women with a previous history of abortion	15 – 45	-	99.3 %	3.7 %	[25]
Hodeidah	Cross-sectional	Apr. 2014 to Apr. 2015	384	Healthy pregnant women	15 - 45	ECLIA	98.7%	1.8%	[9]
Ibb, Yarim	Cross-sectional	2022 to 2023	190	Pregnant women	20 -40	ELISA	75.79%	5.26%	[29]
Ibb	Cross-sectional	Sep. 2021 to Apr. 2022	150	Aborted women	16 - 50	ECLIA	98.67%	7.33%	[30]
Ibb	Cross-sectional	2008 to 2009	100	Pregnant women	-	ELISA	68%	28%	[22]
Sana'a	Cross-sectional	Sep. 2017 to Sep. 2018	268	Pregnant women with a bad obstetrical history.	16 - 45	ELISA	-	5.2%	[31]
Sana'a	Cross-sectional	2001 to 2002	112	Pregnant women	-	ELISA	100%	9.8%	[8]
Sana'a	Cross-sectional	-	235	Male healthy voluntary donors	20 - 48	ELISA	96.6 %	5.5 %	[10]
Sana'a	Cross-sectional	June 2017 to June 2018	178	Yemeni female doctors	-	ELISA	86.5%	-	[11]
Taiz	Cross-sectional	Apr. to Sep to 2014	100	Pregnant women	14 - 42	ELISA	99%	2%	[32]
Taiz	Cross-sectional	Mar. 2019 to Dec. 2020	194	Females of childbearing age	-	ECLIA	97.9%	2.1%	[33]
Taiz	Cross-sectional	Aug. 2021 to Feb. 2023	200	Cancer patients	1 - 90	ECLIA	99.5%	-	[12]
Taiz & Sana'a	Cross-sectional	2021 to 2024	920	General Population	Various	ECLIA ELISA	90.8%	15.3%	[23]

Blood donors in Sana'a also demonstrated substantial CMV exposure, with a seroprevalence rate of 96.6%[10]. This is particularly concerning given the potential risk of CMV transmission through blood products. Although CMV screening of blood donors is a standard practice in many developed countries, such preventive measures are not consistently implemented in Yemen. As a result, immunocompromised recipients, including those undergoing chemotherapy or organ transplantation, remain vulnerable to CMV transmission through transfusion.

The situation among cancer patients is even more critical, with seroprevalence rates reaching 99.5% in Taiz[12]. These patients, who are often subjected to immunosuppressive therapies, are at heightened risk of CMV reactivation, which can lead to severe complications such as CMV pneumonitis and gastrointestinal disease. The lack of active infection detection, particularly through molecular techniques, means that many cases of CMV reactivation remain unnoticed, resulting in inadequate management and increased morbidity.

Healthcare workers, who are expected to possess a higher level of knowledge and adherence to preventive practices, also show a high seroprevalence rate of 86.5% [11]. This rate not only reflects significant occupational exposure but also raises concerns about the adequacy of infection control measures within healthcare settings. The fact that many healthcare workers, including female doctors, lack essential knowledge about CMV transmission further compounds this issue, suggesting systemic shortcomings in professional training and infection control protocols.

General population studies conducted in Taiz and Sana'a have reported a combined seroprevalence rate of 90.8% [23], indicating that CMV is endemic across various demographic groups. This widespread prevalence, coupled with limited public awareness, highlights the need for comprehensive public health interventions aimed at reducing transmission and raising community awareness.

The comprehensive results are summarized in Table 1, which presents CMV seroprevalence rates across different populations, diagnostic methods used, and the period of study.

3.2. Diagnostic Techniques and Limitations

The diagnostic landscape for CMV in Yemen predominantly relies on serological methods such as ELISA and ECLIA. These methods are favored due to their affordability and practicality in low-resource settings. However, both ELISA and ECLIA are inherently limited in their ability to distinguish between active and latent infections. ELISA, although widely used, primarily detects CMV-specific IgG and IgM antibodies, indicating past exposure or recent infection, respectively. However, the presence of IgG alone does not signify active replication, which is a crucial distinction for guiding clinical management, especially among high-risk groups like pregnant women and cancer patients [34], [35], [36], [37].

ECLIA, while offering improved sensitivity and specificity over ELISA, also suffers from similar drawbacks. It can detect IgM antibodies more accurately, indicating possible recent or reactivated infection, but fails to confirm active viral replication. The reliance on antibody detection, rather than direct viral identification means that both methods are susceptible to false positives, particularly due to cross-reactivity with other herpesviruses. Consequently, these serological techniques are insufficient for the accurate diagnosis and monitoring of active CMV infections[20], [36], [38], [39].

A critical gap in CMV diagnostics in Yemen is the lack of molecular techniques, particularly Polymerase Chain Reaction (PCR), which is recognized as the gold standard for detecting active CMV infections. PCR provides unparalleled sensitivity and specificity by directly detecting the viral DNA from clinical specimens, enabling the identification of active infections and quantification of viral load. Its application is crucial for monitoring reactivation in immunocompromised patients, such as those undergoing chemotherapy or those with HIV. Despite its proven effectiveness, PCR remains underutilized in Yemen due to financial, infrastructural, and technical limitations. The absence of PCR-based studies not only hinders accurate epidemiological assessments but also impedes the identification of circulating CMV strains and their genetic variations.

This diagnostic gap is not just a technical oversight but reflects broader systemic challenges, including insufficient funding and inadequate training of laboratory personnel. Addressing this issue requires significant investment in diagnostic infrastructure and capacity building, particularly in tertiary care centers where high-risk populations are treated.

3.3. Awareness and Knowledge Gaps

The low level of awareness regarding CMV transmission and prevention among healthcare workers and the general public compounds this problem. Despite being at the frontline of patient care, healthcare professionals in Yemen often lack basic knowledge of CMV, its transmission routes, and preventive strategies. A study conducted in Sana'a revealed that although 86.5% of female doctors tested positive for CMV IgG, only 20% correctly identified crucial transmission routes such as kissing and diaper changes[11]. This deficit in knowledge not only compromises infection control practices, but also highlights gaps in medical education and training.

The situation among the general public, especially among pregnant women, is even more concerning. In Hodeidah, none of the seronegative pregnant women knew about CMV or its transmission route[9], [40]. This profound lack of awareness reflects failure in public health communication and education. Without adequate awareness, preventive behaviors such as hand hygiene and careful handling of infant excretions remain neglected, perpetuating high transmission rates[41].

The absence of public health campaigns specifically targeting CMV awareness leaves many high-risk groups uninformed and vulnerable. Community-based education programs are essential to disseminate accurate information and encourage preventive practices. Healthcare professionals themselves need targeted training to enhance their understanding of CMV transmission dynamics and the importance of proper infection control measures.

3.4. Research and Knowledge Gaps

The findings of this review highlight critical research gaps that hinder the effective management of CMV infection in Yemen. The foremost among these gaps is the lack of molecular epidemiological studies. Despite the established genetic diversity of CMV and its relevance to disease severity and transmission, there have been no comprehensive efforts to characterize circulating strains within the Yemeni context. Understanding strain-specific differences in virulence and transmission potential is essential for formulating targeted public health strategies.

Furthermore, the heavy reliance on serological methods without molecular confirmation undermines the accuracy of the prevalence data. The predominance of ELISA and ECLIA without validation through PCR may lead to either overestimation or underestimation of the CMV prevalence. This discrepancy is particularly concerning in immunocompromised patients, where active infections can have severe consequences if not accurately detected and managed.

In addition to diagnostic challenges, inconsistencies in study designs and methodologies between different research efforts create challenges for data comparability. Variations in sample sizes, diagnostic protocols, and population characteristics result in conflicting findings, limiting the robustness of epidemiological conclusions. Moreover, the absence of longitudinal and case-control studies further impedes efforts to track reactivation events and comprehend transmission dynamics.

The lack of structured educational programs for healthcare professionals exacerbates the existing knowledge gaps. Training curricula in medical and nursing schools seldom comprehensively cover CMV, leaving graduates ill-prepared to address CMV-related health challenges. Similarly, public health interventions aimed at raising awareness among communities remain inadequate, allowing misconceptions to persist and risky behaviors to continue unchecked.

3.5. Public Health Implications

Addressing these gaps requires a multifaceted approach that integrates molecular diagnostics, enhanced public awareness, and consistent surveillance practices. Improving diagnostic accuracy through the adoption of PCR and next-generation sequencing (NGS) is crucial for identifying active infections and monitoring the viral load. In parallel, awareness campaigns targeting both healthcare workers and the public should be prioritized to bridge knowledge gaps and foster preventive practices. Standardizing diagnostic protocols and incorporating educational initiatives into healthcare training are vital steps toward mitigating CMV transmission and associated health risks.

4. Conclusion

CMV seroprevalence in Yemen is alarmingly high; however, diagnostic practices remain outdated and insufficient. Reliance on serological methods such as ELISA and ECLIA fails to accurately detect active infections, where the absence of molecular techniques such as PCR hinders precise epidemiological assessment. Research gaps, particularly in molecular characterization, limit our understanding of transmission dynamics and strain diversity. Addressing these challenges requires investment in modern diagnostics and standardized protocols to enhance surveillance and intervention, ultimately reducing the public health burden of CMV.

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مقالة بحثية

الانتشار المصلي والفجوات البحثية في الدراسات حول الفيروس المضخم للخلايا في اليمن: مراجعة شاملة

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المُلخّص

يُعتبر فيروس المضخم للخلايا (Cytomegalovirus) فيروسًا شائعًا يشكل تحديات كبيرة للصحة العامة، لا سيما في البلدان النامية مثل اليمن. وعلى الرغم من انتشاره الواسع، إلا أن هناك فجوة كبيرة في فهم العبء الوبائي الحقيقي بسبب القيود التشخيصية وانخفاض الوعي بين العاملين في الرعاية الصحية وعامة الناس. هدفت هذه المراجعة الشاملة إلى تقييم الانتشار المصلي لفيروس المضخم للخلايا عبر مناطق وفئات سكانية مختلفة في اليمن، وتحليل الأساليب التشخيصية المستخدمة بشكل نقدي، وتقييم مستويات الوعي بين الجهات المعنية الرئيسية. تشير النتائج إلى ارتفاع معدلات الانتشار المصلي بشكل ملحوظ، حيث تصل إلى 100% بين النساء الحوامل و99.5% بين مرضى السرطان. ومع ذلك، فإن الاعتماد الكبير على الأساليب المصلية، مثل اختبار الممتز المناعي المرتبط بالإنزيم (ELISA) والتحليل المناعي الكيميائي الكهربائي (ECLIA)، مع عدم الاستخدام للتقنيات الجزيئية مثل تفاعل البلمرة المتسلسل(PCR) ، يعيق بشكل كبير الكشف الدقيق عن العدوى النشطة. علاوة على ذلك، لا يزال الوعي بين العاملين في الرعاية الصحية وعامة السكان منخفضًا بشكل حرج، مما يزيد من مخاطر انتقال العدوى. تُحدد هذه المراجعة فجوات بحثية حرجة، بما في ذلك نقص الدراسات الوبائية الجزيئية والحملات الشاملة لزيادة الوعي. يتطلب سد هذه الفجوات نهجًا متكاملًا يجمع بين الأساليب التشخيصية المتقدمة، وتعزيز تدريب العاملين في مجال الرعاية الصحية، ومبادرات توعية الجمهور للحد من انتقال فيروس المضخم للخلايا وتقليل تأثيره على الصحة.

الكلمات المفتاحية: الفيروس المضخم للخلايا، الانتشار المصلي، تقنيات التشخيص، التوعية، اليمن.

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