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SEROEPIDEMIOLOGY OF *TOXOPLASMA*, *RUBELLA*, *CYTOMEGALOVIRUS* AND *HERPES SIMPLEX VIRUS -2* IN WOMEN WITH BAD OBSTETRIC HISTORY. PART II. *CYTOMEGALOVIRUS* AND *HERPES SIMPLEX VIRUS* INFECTIONS

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Abstract
Bad obstetric history (BOH) is reported worldwide and is associated with social and psychological impacts. Cytomegalovirus and herpes simplex virus play an important role in the induction of adverse outcomes of pregnancy. Highest CMV IgG prevalence rate was reported for India (91.05%), while the lowest rate was reported for Iran (14.28%). Unfortunately, six studies in Iraq reported a high prevalence of CMV IgM in non-married, pregnant and women with BOH. The range of recent CMV infection in pregnant women with BOH was from 1.4% in Jordan to 60.2% in Iraq. In women with BOH, the highest HSV 2 prevalence (16.8%) was noted in India, while the lowest rate (1.69%) was reported in India also. In Arab countries, among women with BOH, HSV 2 IgG and IgM seroprevalence higher rates were reported for Iraq. This literature review highlights the high bacterial and viral maternal infection rate in the developing world. Urgent, concerted action is required to reduce the burden of these infections. In addition to raising awareness about the severity of the problem of maternal infections in the developing world, data from this review will be beneficial in guiding public health policy, research interests and donor funding towards achieving improvement in health care delivery.

Key words: TORCH; Toxoplasma; Rubella; CMV; Cytomegalovirus; HSV

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Cytomegalovirus:

Primary *Cytomegalovirus* (CMV) infection during pregnancy is a frequent and serious threat to the fetuses of pregnant women [222]. The rate of susceptibility to CMV during pregnancy is also well established in many global countries [223,224]. Eight European countries (France, Belgium, Spain, Italy, Germany, Austria, Portugal, and the Netherlands) routinely screen the majority of pregnant women serologically for CMV [225,226]. This routine serologic screening occurs without the recommendations or guidelines of any governmental agency, authority, or a professional medical society. In Iraq, such screening program is not followed routinely and pregnant women screening order depends on personal interest of the clinicians. Routine serologic screening for CMV of pregnant women in Europe has yielded very important advances in our understanding of CMV infections among pregnant women [227-230].

The major risk factor for maternal acquisition of CMV during pregnancy is frequent and prolonged contact with a child less than three years of age [231-235]. This occurs among women with a child in the home or among women employed in child care centers or schools [236-241]. Another group of high-risk women are those who are seronegative, young, and poor. Even for this group, contact with a young child is an independent predictor of delivering a CMV congenitally infected infant, as is a history of frequent sexual activity [235]. A recent study suggested that C MV is likely transmitted not only via the oral mucosal route, but also via the vaginal mucosal route [231].

Characteristics and results of studies reporting prevalence of maternal

CMV infection

Forty studies [1,3,36,86,89-93,95,96,167,170,171,182,204, 208,210,242-263] on maternal cytomegalovirus infection prevalence were identified (Tabl. V). The median prevalence of maternal IgG to CMV (calculated from 28 studies that reported this) was 92%, indicating a high proportion of mothers with previous exposure to CMV. Two hospital-based study in India (29.5%) [36] and Iran (28.58%) [262] identified a statistically significant higher prevalence of CMV IgM (indicating active or recent infection) in mothers with Bad Obstetric History (BOH), highlighting a role for maternal CMV infection in adverse pregnancy outcome in this setting. The highest prevalence of IgG in pregnant women was in Turkey [95] (98.9%, 1103 childbearing age women), while the lowest prevalence reported for Ireland [253] (30.4%, 1047 pregnant women). However, in women with BOH, the highest IgG prevalence rate was reported for India [3] (91.05%, 380 BOH), while the lowest rate was reported for Iran [262] (14.28%, 42 Aborted women).

Active or recent infection high prevalence rate in pregnant women was reported for Poland [252] (13%, 1332 Pregnant women), while the lowest rate was reported for Turkey [204] (0%, 249 Pregnant women). In women with BOH the highest prevalence rate of IgM was reported for India [36] and the lowest one was reported for India [91].

In Arab countries, twenty- two studies [35,99-101,108,117-119,129-131,139,147,216,221,264-269] on maternal CMV infection prevalence were identified (Tabl. VI). The median prevalence of maternal IgG to CMV was 77.8% indicating lower proportion of mothers with previous exposure to CMV as compared to global studies. Unfortunately, six studies in Iraq [100,101,117,129,264,266] reported a high prevalence of CMV IgM in non-married, pregnant and women with BOH. The range of active or recent CMV infection in pregnant women was from 2.3% in Jordan [269] to 57.2% in Iraq [129], while the range in women with BOH was from 1.4% in Jordan [269] to 60.2% in Iraq [100]. In pregnant women, maternal IgG to CMV prevalence higher rate was reported in Jordan [269] (88%, 260 pregnant women), while the lowest one was reported for Iraq [129] (77.8%, 180 pregnant women). In addition, in women with BOH, maternal IgG to CMV prevalence higher rate was reported for Jordan [269] (95%, 898 Aborted women), and the lowest one was reported in Iraq [99] (4.8%, 119 Aborted women).

Article	Location, setting of study	Type, duration of study	Population	Results
Tabatabaee et al, [242]	Iran, hospital	Cross-sectional, 7 months	1472 pregnant women	97.68% seropositive, prevalence of active infection 4.35%.
Das et al, 2007 [170]	India, hospital	Cross sectional study	1115 BOH	11% prevalence in BOH, 4% prevalence in normal pregnant women
Ocak et al, [171]	Turkey, hospital	Retrospective observational study, 2 years	1652 pregnant women	94.9%seropositivity for anti-CMV IgG, 0.4%positive for anti-CMV IgM
Picone et al, [243]	France, Hospital	Cross sectional study prospective, 2 years	4287 pregnant women	46.8% IgG
Tamer et al, [167]	Turkey, antenatal Clinics	Cross sectional study,	1972 Pregnant women	97.1% IgG, 2.6% IgM
Surpam et al [86]	India, Antenatal clinic	Case control,	150 BOH	5.33% IgM
Uyar Y et al [182]	Turkey, Hospital	Case control, 1 year	600 Pregnant women	97.3% IgG, 1% IgM
Karabulut A et al [89]	Turkey, Antenatal clinic	Case control, 1 year	1000 Pregnant women	98.7% IgG, 1.2% IgM
Kumari N et al [1]	Nepal, Hospital	Case control, 4 months	12 BOH	8.3% seropositive
Nabi SN et al [90]	Bangladesh, Hospital	Case control, 10 months	111 Pregnant women	95.49% IgG, 0.9% IgM
Baschale MD [244]	Italy, Hospital	Cross sectional, 2 years	2385 Pregnant women	92% IgG, 0.4% IgM
Sadik MS et al [91]	India, Hospital	Case control, 2 years	86 BOH	23.25% IgG, 0% IgM
Chopra S et al [36]	India, Antenatal clinic	Case control, 1 year	200 BOH	29.5% IgM
Koksaldi-Motor et al [95]	Turkey, Hospital	Cross sectional, 1 year	1103 women childbearing age	98.9% IgG
Ozdemir M et al [204]	Turkey, Hospital	Cross sectional, 6 months	249 Pregnant women	98.7% IgG, 0% IgM
Frischknecht F et al [92]	Switzerland, Hospital	Cross sectional, 1 yr	723 Pregnant women in labor	4.7% seropositive
Vilibik-Cavlek T, et al [96]	Croatia, Hospital	Cross sectional, 5 years	Pregnant & non pregnant women	75.3% IgG, 0.09% IgM
Sarawathy TS, et al [245]	Malaysia, Antenatal clinic	Cross sectional, 2 years	125 Pregnant women	84% IgG, 7.2% IgM
Akinbami AA, et al [246]	Nigeria, Hospital	Cross sectional, 2 months	179 Pregnant women	97.2% IgG,
Bagheri L, et al [247]	Iran, Hospital	Cross sectional, 3 months	240 Pregnant women	69.6% IgG, 2.5% IgM
Arabpour M, et al [248]	Iran, Hospital	Cross sectional, 5 years	844 childbearing age women	93% IgG, 5.4% IgM

Table V. Characteristics and results of studies reporting prevalence of maternal CMV infection.

Article	Location, setting of study	Type, duration of study	Population	Results
Canon MJ, et al [249]	Global, Review	Review		45 – 100% seroprevalence
Ahmad RM, et al [250]	Nigeria, Hospital	Cross sectional,	90 Pregnant women	97.8% IgG
Seo S, et al [251]	Korea, Hospital	Cross sectional, 2 months	744 Pregnant women	98.1% IgG, 1.7% IgM
Gaj Z, et al , [252]	Poland, Hospital	Cross sectional, 11 years	1332 Pregnant women	76.7% IgG, 13% IgM
Knowles SJ, et al [253]	Ireland, Hospital	Cross sectional, 1 year	1047 Pregnant women	IgG 30.4% in Irish & 89.7% in non- Irish women [Africa, Asia, E. Europe]
Yamamoto AY, et al [254]	Brazil, Hospital	Cross sectional	985 Pregnant women	97% seroprevalence
Odland JO, et al [208]	Russia, Hospital	Case control, 4 months	182 Pregnant & 127 Aborted women	78% versus 81.1% seroprevalence
Chen MH, et al [255]	Taiwan, Hospital	Cross sectional, 10 months	483 Pregnant mother	91.1% IgG, 3.5% IgM
Gumber S et al [256]	India, Hospital	Cross sectional, 17 months	150 BOH	4.67% IgM
Dollard SC, et al [257]	USA, Hospital	Cross sectional,	6067 Women 12-49 yrs	58% IgG, 3% IgM
Enders G, et al [258]	Germany, Hospital	Retrospective, 15 years	40 324 Pregnant women	42.3% IgG
Correa CB, et al [259]	Cuba, Hospital	Cross sectional, 1 year	1131 Pregnant women	92.6% seropositive, 2.4% active infection
Rajaii & Pourhasan [260]	Azerbaijan, University Lab.	Cross sectional, 4 years	2049 Women 20-35 yrs [of them 75 Pregnant]	88.53% IgG, 8.29% IgM, In Pregnant 66.7%seropositive
Turbadkar D, et al [3]	India, Antenatal clinic	Case control, 1 year	380 BOH	91.05% IgG, 8.42% IgM
Ashrafunnessa et al [261]	Bangladesh, Hospital	Case control, 11 months	420 Pregnant women	68.6% IgG, 5% IgM
Inagaki ADM, et al [93]	Brazil, Antenatal clinic	Cross sectional, 1 year	9559 Pregnant women	76.6% IgG, 0.2% IgM
Falahi S, et al [262]	Iran, Hospital	Case control	42 BOH	14.28% IgG, 28.58% IgM
Ebadi p, et al [210]	Iran, Hospital	Case control, 3 years	120 BOH	78.33% seropositive
Oruc AS, et al [263]	Turkey, Hospital	Cross sectional,5 years	11 360 Pregnant women	98.5% IgG, 0.3% IgM

Table V. Characteristics and results of studies reporting prevalence of maternal CMV infection (continued).

Article	Location, setting of study	Type, duration of study	Population	Results
Hammouda et al [108]	Egypt, Hospital	Case control	100 BOH	51% Seroprevalence
Abdulmohaymen N [99]	Iraq, Baghdad, Hospital	Case control, 9 months	119 Aborted women	17.7% IgM recurrent spontaneous abortion 14.7% IgM non recurrent spontaneous abortion. 4.8% IgG recurrent spontaneous abortion 0% IgG non recurrent spontaneous abortion
Jasim et al [100]	Iraq, Waset, Hospital	Case control, 1 year	162 Aborted women	55.5% IgG, 60.2% IgM
Al- Taie et al [101]	Iraq, Mosul, Private laboratory	Case control, 1 year	100 BOH	24% IgM
Almishhadani & Aljanabi [119]	Iraq, Al- Anbar, Medical Laboratory	Case control study, 3 years	230 Aborted women	90.4% IgG, 6.1% IgM
Majeed AK [117]	Iraq, Baghdad,	Case control, 3 years	135 Aborted women	20.7% IgG45.9% IgM
Alsaeed et al [118]	Iraq, Al-Hila, Hospital	Case control, 6 months	120 Aborted women	79.5% IgG, 18.8% IgM
Hadi NJ [130]	Iraq, Thi Qar, Hospital	Case control	190 Aborted women	16.84% IgG, 9.47% IgM
Salman YG [131]	Iraq, Kirkuk, Hospital	Case control, 11 months	84 BOH	8.02% Seropositive, 7.89% IgM
Al- Azzawi RHM, [264]	Iraq, Baghdad, Hospital	Cross sectional, 8 months	161 Non married women 15-35 yrs	67.1% IgG, 41% IgM
Khalf MS, et al [265]	Iraq, Baghdad, Hospital	Case control, 17 months	108 BOH	15.7% IgM
Hannachi N, et al [221]	Tunisia, Hospital	Cross sectional,	404 Pregnant women	96.3% seroprevalence
Al- Hindi A, et al [139]	Palestine, IVF centre	Retrospective, 6 years	1954 Women with infertility or abortion	6% IgM
Al- Shimmery MN [266]	Iraq, Diwanya, Hospital	Case control, 5 months	125 Aborted women	49.6% IgG, 22.4% IgM

Table VI. Characteristics and results of studies in Arab countries reporting prevalence of maternal CMV infection.

Article	Location, setting of study	Type, duration of study	Population	Results
Al-Khafaji & Al-Zabaidi [38]	Iraq, Thi Qar, Hospital	Case control, 10 months	60 aborted women	85% IgG, 65% IgM
Kafi SK, et al [267]	Sudan, Hospital	Cross sectional, 2 months	100 Pregnant women	95% IgG
Hamdan HZ, et al [216]	Sudan, Hospital	Cross sectional, 2 months	231 Pregnant women	72.2% IgG, 2.5% IgM
Ghazi HO, et al [147]	Saudi Arabia, Hospital	Cross sectional	926 Pregnant women	92.1% IgG
Al-Marzoqi AHM, et al [129]	Iraq, Babylon, Hospital	Cross sectional, 6 months	180 Pregnant women	77.8% IgG, 57.2% IgM
Abu- Madi MA, et al [35]	Qatar, Hospital	Cross sectional, 3 years	847 Women > 20 yr age	96.8% IgG, 2.7% IgM
Barah F [268]	Syria, University Laboratory	Cross sectional, 15 months	316 Female university students	74.5% seropositive
Daboui & Al-Zaben [269]	Jordan, Medical centre	Case control, 2 months	260 Pregnant, 100 Unmarried women, 898 Aborted women	IgM- 2.3% pregnant, 1% unmarried, 1.4% Abortion. IgG- 88% pregnant, 79% unmarried, 95% abortion

Table VI. Characteristics and results of studies in Arab countries reporting prevalence of maternal CMV infection (continued).

Herpes simplex virus

Herpes simplex virus (HSV) is an ubiquitous, enveloped, and double stranded DNA virus, belonging to the family of Herpesviridae transmitted across mucosal membranes and non-intact skin, that migrate to nerve tissues, where they persist in a latent state [270]. HSV-1 predominates in oro-facial lesions, and it is typically found in the trigeminal ganglia, whereas HSV-2 is most commonly found in the lumbo-sacral ganglia [271]. Nevertheless these viruses can infect both oro-facial areas and the genital tract. In some developed countries type 1 has recently emerged as the prominent causative agent in genital lesions [272]. Changes in sexual behaviours of young adults may partly explain its higher incidence [273,274].

Herpes simplex virus (HSV) infections are caused by two strains, HSV-1 and HSV-2. Oro-labial infection is mainly caused by HSV-1, however, this strain is responsible for up to 53% of primary genital herpetic infection [270]. HSV-2 genital infection is much more likely to recur than genital HSV-1 infection, thus the presence of antibody to HSV-2 and a compatible clinical history would be strong presumptive evidence that the disease is recurrent genital herpes [275-277]. In addition to agent factor, genetic may play a role in susceptibility to HSV infection [278]. Primary genital HSV-1 or HSV-2 infection in pregnant women can result in abortion, premature labor and congenital and neonatal herpes [279-281]. HSV-2 infections in the newborn are particularly severe and frequently involve the CNS [282]. Recent changes in HSV-1 and HSV-2 infection epidemiology have been reported, with type incidence changes and sequential genital infections with HSV-1 and HSV-2 [272,283].

Little is known about the risk factors associated with HSV seropositivity in pregnant Iraqi women. Identification of the risk factors may help to improve the control measures of HSV infection. Although there is improve in the diagnosis and treatment of TORCH infections, it still represents a problem in developing countries. Clinical diagnosis of TORCH is difficult, since most of the maternal infections with adverse outcomes are initially asymptomatic. Routine TORCH complex screening during pregnancy is not recommended in Iraq and the extent to which it is performed is unknown.

A first primary infection develops when a susceptible person (lacking of preexisting HSV-1 and HSV-2 antibodies) is exposed to HSV. Indeed, a first non-primary episode occurs when a person with preexisting HSV antibodies (against type 1 or 2) experiences a first episode with the opposite HSV type. Recurrent infection occurs in a person with preexisting antibodies against the same HSV type [271]. Infections during pregnancy may be transmitted to newborns: HSV-1 and HSV-2 may cause eye or skin lesions, meningo-encephalitis, disseminated infections, or foetal malformations.

In recent years, genital herpes has become an increasing common sexually transmitted infection. From the late 1970s, HSV-2 seroprevalence has increased by 30%, resulting that one out of five adults is infected [284,285]. HSV seroprevalence in patients with STD varies from 17% to 40% (6% in the general population and 14% in pregnant women) [286,287]. Age and sex are important risk factors associated with the acquisition of genital HSV-2 infection. In fact, the prevalence of HSV infection rises with age, reaching the maximum around 40 years [284]. This infection appears related to the number of sexual partners, and regarding sex it is more frequent in women than in men [288,289]. In addition, ethnicity, poverty, cocaine abuse, earlier onset of sexual activity, sexual behavior, and bacterial vaginosis can facilitate a woman's risk of infection before pregnancy [290,291].

Regarding pregnant population, there is a high prevalence of genital herpes, however, it is varies from country to others, depending on social and sexual behaviors and activity [289,292-294].

The risk of neonatal infection varies from 30% to 50% for HSV infections that onset in late pregnancy (last trimester), whereas early pregnancy infection carries a risk of about 1% [295-297].

Thirty-one studies [1,3,90,91,96,204,256,298-320] outlining the prevalence of maternal Herpes simplex virus 2 (HSV-2) were identified (Tabl. VII). These studies detected the presence of antibodies to HSV as a marker of maternal infection. Median prevalence of IgG HSV-2 was 18.2% which was reported for Belgium [315,357]. In pregnant women, higher seroprevalences were noted in Germany (82%), Turkey (63.1%), Zimbabwe (51.1%), and Iran (43.75%) [298,299,309,313]. However, the lowest seroprevalences were reported in two studies in Turkey [204,314], which reported a rates of 4.4% and 5%. In women with BOH, the highest prevalence (33.58%) was reported in India [3], while the lowest one (18.6%) was reported in India also [91].

Concerning IgM, the highest prevalence in pregnant women was reported in Turkey (13.8%, 130 pregnant women) [298], while the lowest rate was reported in Turkey (0%, 249 pregnant women) also [204].

In women with BOH, the highest prevalence (16.8%, 450 BOH) was noted in India [320], while the lowest rate (1.69%, 86 BOH) was reported in India also [91].

In Arab countries, nine studies [35,99-101,129,147,268,319,320] outlining the prevalence of maternal HSV-2 were identified (Table VIII). The median IgG seroprevalence was 27.1%, which was noted in Saudi Arabia [147]. A higher (27.1%, 926 pregnant women) IgG maternal seroprevalence in pregnant women was reported in Saudi Arabia [147], while the lower rate (6.5%, 459 pregnant women) was noted in Saudi Arabia also [319]. In women with BOH IgG seroprevalence was 60.6%, which was reported in Iraq [100]. Concerning IgM, the highest prevalence's were reported in Iraq [100,129] for both pregnant women (28.9%, 180 pregnant women) and those with BOH (73.9%, 62 BOH).

Article	Location, setting of study	Type, duration of study	Population	Results
Kurewa et al, [299]	Zimbabwe, peri-urban clinics	Cross sectional, 19 months	691 Pregnant women	51.10% IgG
Yahya-Malima et al, [300]	Tanzania,antenatal clinics (6)	Cross sectional,	1296 Pregnant women	20.7% prevalence of genital herpes
Chen et al, [301]	China, antenatal clinic	Cross sectional, 3 months	502 pregnant women	10.8% seroprevalence
Haddow et al, [302]	Australia, antenatal clinic	Cross sectional, 2 years	535 pregnant women	30% seroprevalence
Joesoef et al, [303]	Indonesia, prenatal clinic	Cross sectional, 15 months	599 pregnant women	9.9% seroprevalence
Surpam et al [86]	India, Antenatal clinic	Case control,	150 BOH	8.66% IgM
Kumari N et al [1]	Nepal, Hospital	Case control, 4 months	12 BOH	33.3% Seropositive
Nabi SN et al [90]	Bangladesh, Hospital	Case control, 10 months	111 Pregnant women	9.91% IgG, 1.8% IgM
Sadik MS et al [91]	India, Hospital	Case control, 2 years	86 BOH	18.6% IgG, 1.69% IgM
Ozdemir M et al [204]	Turkey, Hospital	Cross sectional, 6 months	249 Pregnant women	4.4% IgG, 0% IgM
Xu F et al [304]	USA, Hospital	Cross sectional, 4 years	626 Pregnant women	22% seroprevalence
Kucera P et al [305]	Switzerland, Hospital	Cross sectional,	1030 Pregnant women	21.2% seroprevalence
Patrick MD et al [306]	Canada, antenatal clinic	Cross sectional, 1 year	1215 Pregnant women	17.3 % seroprevalence
Munjoma MW et al [307]	Zimbabwe, Antenatal clinic	Cross sectional, 6 months	354 Pregnant women	49.1% seroprevalence
Diawara S et al [308]	Senegal, Antenatal clinic	Cross sectional, 6 months	260 Pregnant women	22% seropositivity
Sauerbri A et al [309]	Germany, Hospital	Cross sectional, 8 years	200 Pregnant women	82% IgG
Ades AE et al [310]	UK, Hospital	Cross sectional, 2 years	3533 Pregnant women	10.4% IgG
Rathore S et al [311]	Kashmir, Antenatal clinic	Cross sectional, 2 year	200 Pregnant women	7.5% IgG
Duran N [298]	Turkey, Hospital	Cross sectional, 21 months	130 Pregnant women	63.1 % IgG, 13.8% IgM
Biswas D et al [312]	India, Hospital	Cross sectional, 2 years	1640 Pregnant women	8.7% HSV-2 IgG
Shahraki AD et al [313]	Iran, Hospital	Cross sectional,	96 Pregnant women	43.75% HSV-2 IgG
Dolar N et al [314]	Turkey, Hospital	Cross sectional,	300 Pregnant women	5% HSV-2 IgG
Bodeus M, et al [315]	Belgium, Hospital	Cross sectional,	1000 Pregnant women	18.2% HSV-2 IgG
Chen XS et al [301]	China, Hospital	Cross sectional, 3 months	504 Pregnant women	10.8% seroprevalence
Sasadeusz JJ et al [316]	Australia, Antenatal clinic	Cross sectional,	1371 Pregnant women	13.6% seroprevalence
Vilibik-Cavlek T, et al [96]	Croatia, Hospital	Cross sectional, 5 years	Pregnant & non pregnant women	6.8% IgG, 1.2% IgM
Straface G et al [317]	Italy, Review	Retrospective		7.6 – 8.4% seroprevalence Italy22% seroprevalence USA
Kim D et al [318]	Korea, Hospital	Retrospective, 19 months	500 Pregnant women	17% HSV-2 seroprevalence
Gumber S et al [256]	India, Hospital	Cross sectional, 17 months	150 BOH	3.33% IgM
Turbadkar D, et al [3]	India, Antenatal clinic	Case control, 1 year	380 BOH	33.58% IgG, 3.6% IgM
Li et al [319]	China, Hospital	Cross sectional	1740 Pregnant women	23.56% seroprevalence
Haider M, et al [320]	India, Hospital	Case control	450 BOH	16.8% IgM

Table VII. Characteristics and results of studies reporting prevalence of maternal HSV-2 infection.

Article	Location, setting of study	Type, duration of study	Population	Results
Abdulmohaymen N [99]	Iraq, Baghdad, Hospital	Case control, 9 months	119 Women with history of abortion	8.1% IgM recurrent spontaneous abortion 17.4% IgM non recurrent spontaneous abortion.
Jasim et al [100]	Iraq, Waset, Hospital	Case control, 1 year	162 Women with spontaneous abortion	60..6% IgG, 73.9% IgM
Al- Taie et al [101]	Iraq, Mosul, Private laboratory	Case control, 1 year	100 BOH	11% IgM
Alzahrani et al [319]	Saudi Arabia, Hospital	Cross sectional,	459 Pregnant women	6.5% IgG, 0.5% IgM
Obeid EO [320]	Saudi Arabia, Hospital	Cross sectional, 2 years	459 Pregnant women	6.8% IgG
Barah F [317]	Syria, University Laboratory	Cross sectional, 15 months	316 Female university students	52% seropositive
Ghazi HO, et al [192]	Saudi Arabia, Hospital	Cross sectional	926 Pregnant women	27.1% IgG
Al-Marzoqi AHM, et al [174]	Iraq, Babylon, Hospital	Cross sectional, 6 months	180 Pregnant women	22.2% IgG, 28.9% IgM
Abu- Madi MA, et al [87]	Qatar, Hospital	Cross sectional, 3 years	847 Women > 20 yr age	26.3% IgG, 7.6% IgM

Table VIII. Characteristics and results of studies in Arab countries reporting prevalence of maternal HSV-2 infection

Gaps in existing knowledge

In the process of reviewing the subject, we identified several facility-based retrospective studies reporting causes of maternal mortality. Many of these studies attributed a proportion of deaths to infection or sepsis, but were unable to provide microbiological or serological evidence of the specific underlying mortality causes. Our review confirms the suspected high prevalence of parasitic and viral maternal infections in the developing world, as demonstrated by the median prevalence rates calculated for each pathogen studied. Of particular concern are the aetiology of infection. The literature review highlights a gap in existing knowledge on the epidemiology and impact of maternal infection, especially on the aetiology of infectious agents that lead to puerperal sepsis and subsequent mortality. Increased surveillance and diagnostic capabilities in healthcare facilities and in the community is needed to identify the aetiological agents responsible for puerperal sepsis and maternal mortality.
The prevalence of maternal infection reported by the studies identified in this literature review may be an underestimate of actual rates of infection as not all pregnant women in developing countries may have access to or choose to access formalized antenatal care. This could be due to financial constraints, difficulties in accessing these facilities and personal or cultural beliefs. In addition, antenatal care services may not have the capacity to routinely screen for maternal infections, especially those that are asymptomatic and those that require serological tests such as PCR and ELISA to diagnose, due to limited resources or expertise. These infrastructural problems are essential contributors to the persistence of high maternal morbidity and mortality in developing countries and need to be overcome in order to accurately characterize the burden of maternal infections in these countries.

Conclusion

This literature review highlights the high bacterial and viral maternal infection rates in the developing world. Urgent, concerted action is required to reduce the burden of these infections. In addition to raising awareness about the severity of the problem of maternal infections in the developing world, data from this review will be beneficial in guiding public health policy, research interests and donor funding towards achieving improvement in health care delivery.

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