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

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Abstract
Bad obstetric history (BOH) is associated with social and psychological impacts on society worldwide. The causes of BOH may be genetic, hormonal, abnormal maternal immune response, and maternal infection. In women with bad obstetric history (BOH), Toxoplasma (T) IgG high rate has been reported for Nepal (55.2%), while high (42.5%) and lowest (6.97%) active toxoplasma infections has been reported for India. In Arab countries, IgG and IgM higher and lowest seroprevalence rates were for Iraq. The higher susceptibility rates for Rubella in Arab countries excluding Iraq were reported in Morocco (83.4%), Sudan (34.7%), Qatar (25.1%), and Tunisia (20.3%). The lowest susceptibility was reported for Saudi Arabia (6.7%). In Iraq, studies indicate a high susceptibility rates in Thi Qar (98.05%), Kirkuk (91%), Baghdad (79%), and Waset (45.7%). The lowest susceptibility rates were reported for Diyala (0%) in women with previous abortion, and 3.9% in pregnant women without history of BOH.

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

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Introduction

Bad obstetric history (BOH) implies previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortions, history of intrauterine fetal death, intrauterine growth retardation, stillbirth, early neonatal death, and/or congenital anomalies [1]. The causes of BOH may be genetic, hormonal, abnormal maternal immune response, and maternal infection [2,3].

TORCH Complex:

The TORCH infections can lead to severe fetal anomalies or even fetal loss. They are a group of viral, bacterial, and protozoan infections that gain access to the fetal bloodstream transplacentally via the chorionic villi. Hematogenous transmission may occur at any time during gestation or occasionally at the time of delivery via maternal-to-fetal transfusion [4]. Primary infections caused by TORCH-*Toxoplasma gondi*i, *Rubella virus*, *cytomegalovirus* (CMV), and *herpes simplex virus* (HSV)-are the major causes of BOH [5]. These infections usually occur before the woman realizes that she is pregnant or seeks medical attention. The primary infection is likely to have a more important effect on fetus than recurrent infection and may cause congenital anomalies, spontaneous abortion, intrauterine fetal death, intrauterine growth retardation, prematurity, stillbirth, and live born infants with the evidence of disease [6].

Most of the TORCH infections cause mild maternal morbidity but have serious fetal consequences [7]. The ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues [8].

TORCH infections in the mother are transmissible to fetus in the womb or during the birth process and cause a cluster of symptomatic birth defects. Many sensitive and specific tests are available for serological diagnosis of TORCH complex [9]; however, ELISA test is more routinely used for its sensitivity. An attempt is being made to find out the correlation of TORCH infection during pregnancy in the Iraqi population. *Toxoplasma gondii* is an obligate intracellular protozoan parasite, which is linked to one of the most prevalent chronic infections affecting one third of the world's human population [10].

The infection is characterized by non-specific symptoms with the consequent formation of cysts that may remain in latent form in many organs [11]. Primary infection is usually subclinical but the infection hazard is its occurrence during pregnancy. There are four groups of individuals in whom the diagnosis of toxoplasmosis is most critical: a) pregnant women who acquire their infection during gestation, b) fetuses, c) newborns who are congenitally infected, immunocompromised patients, and d) those with chorioretinitis [12-14].

Although congenital toxoplasmosis is not a nationally reportable disease in Iraq, it represents a health care problem. Reported studies indicated an estimated 400 to 4,000 cases occur in the U.S. each year [11,15,16]. The overall prevalence and incidence varies in different communities and contributes significantly to heavy morbidity [10]. Congenital toxoplasmosis mainly results from a primary infection acquired during pregnancy [17], but not from the reactivation of a latent infection in immunocompetent pregnant women [18]. However, it is believed that latent toxoplasmosis could reactivate and cause a congenital transmission of the parasite to infants who then become infected in utero [19].

Countries with high disease prevalence have instituted successful secondary prevention programs via widespread maternal serologic screening [20], but universal maternal serologic screening for toxoplasmosis is not currently recommended in most of countries [21-24]. Instead, current practice suggests maternal serological screening when abnormal fetal findings or presence of infertility problem indicate possible infection [22]. ELISA methods is commonly performed in many countries to detect anti-toxoplasma antibodies [25]. ELISA results are generally well accepted by clinicians because of their excellent sensitivities and specificities, the rapid availability of results, and the relatively low costs of the tests. It is important to understand that a single serologic test is not enough for the diagnosis of toxoplasmosis [26]. In worldwide, commercial test kits for Toxoplasma-specific IgG and IgM antibodies are readily available. The presence of IgM antibodies is not always an indication of a recent infection since IgM maybe present for many months [27,28]. Misdiagnosis of recent infections may be as a result of the presence of specific *T. gondii* IgM antibodies in the chronic stage of an infection, or false-positive IgM positivity [17,29]. IgM test results are difficult to interpret and the reliability of test kits is largely dependent upon other factors. A negative IgM with a positive IgG result can indicate infection at least 1 year before. A positive IgM result may indicate more recent infection or may also be a false positive reaction [25].

Currently worldwide, there is no systematic screening of pregnant women to detect seroconversion during gestation and most clinicians make decisions depending on result of single serum sample. This approach is not effective to detect toxoplasma infections during pregnancy, thus monthly serological screening for pregnant women is the recommended approach [30]. The presence of elevated levels of Toxoplasma specific IgG antibodies indicates infection has occurred at some point, but does not distinguish between an infection acquired recently and one acquired in the distant past. In acute infection, IgG and IgM antibodies generally rise within 1 to 2 weeks of infection [31]. Given the potential for false-positive results, the true value of IgM testing is in ruling out the presence of acute infection. In other words, negative IgM results are reassuring, whereas positive results should be interpreted carefully, confirmed in a toxoplasmosis reference laboratory, and followed by serial titers at least 3 weeks apart [12,28,32].

There are different Toxoplasma seropositivity reports from all over the world. The population of Turkish childbearing age women has the seropositivity of *T. gondii* as 1.34% for IgM and 24.6% for IgG [33]. In Maracaibo, Venezuela the overall prevalence of toxoplasmosis was 33%, while 18.2% were positive IgM [34]. In Qatar among 823 women of childbearing age, the *T. gondii* IgG and IgM was 35.1% and 5.2% respectively [35].

Sixty-five studies [3,33,36-97] characterizing the prevalence of maternal infections with *T. gondii* in developing and developed countries and fifty-nine [35,98-155] studies in Arab countries (30 studies reported for Iraq) were identified. The features and results of these studies are summarized in Tables I and II.The majority of studies had small sample sizes, between 0– 4112 subjects. Most of these studies were conducted in antenatal clinics, hospitals, health care facilities or prenatal clinics. The remaining studies (3.3%) were community-based and the study setting was not specified in 7.4% of the studies. The most commonly used test was ELISA, which is the gold standard for T. gondii analysis. The median of IgG Toxoplasma prevalence was 38.5% [64] for Bangladesh. IgG high rate of detection was reported for Brazil [50] (75%, 832 pregnant women), while the lowest rate was for Thailand [38] (5.3%, 831 pregnant women). IgM lowest rate reported for China [49] (0%, 235 pregnant women) and Vietnam [59] (0%, 300 pregnant women), while the highest rate reported for Ghana [87] (76.1%, 159 pregnant women).

In women with bad obstetric history (BOH), IgG high rate was reported for Nepal [62] (55.2%, 345 BOH) and the lowest one was that reported by Natu et al [74] (19.44%, 499 BOH). IgM in BOH high rate was reported for India [36] (42.5%, 200 BOH), while the highest one for India also [91] (6.97%, 86 BOH).

In Arab countries, the median of IgG prevalence was 41.9% which was reported for Sudan [144]. IgG highest rate of detection reported for Iraq [132] (94%, 54 pregnant women) Bahrain [137] (15.8%, 146 Pregnant women), while the corresponding values for IgM were 55.5% (Iraq, 180 pregnant women) [129] and 2.8% (Egypt, 323 pregnant women) [153] respectively. Concerning BOH, IgG ranges between 77.1% (Iraq,122 BOH) [114] and 6.84% (Iraq, 190 BOH) [130], while the range of IgM was between 58% (Iraq, 50 BOH) [127] and 0.97% (Iraq, 310 BOH) [104].

Rubella virus

Rubella is a contagious viral disease caused by a togavirus and usually goes unnoticed. However, maternal infection during pregnancy may result in fetal loss or in congenital rubella syndrome (CRS) [156,157]. Infection in the first eight to ten weeks of pregnancy results in damage in up to 90% of surviving infantswhere multiple defects are common.

The risk of damage declines to about 10 to 20% with infection occurring between 11 and 16 weeks gestation [158]. Fetal damage is rare with infection after 16 weeks of pregnancy, with only deafness being reported following infections up to 20 weeks of pregnancy. Some infected infants may appear normal at birth but perceptive deafness may be detected later [157,158]. Before the introduction of Rubella immunisation, Rubella was commonly prevalent in children, and more than 80% of adults had evidence of previous rubella infection [159].

Article	Location, setting of study	Type, Duration	Population	Results
Wanachiwanawin et al [38]	Thailand, antenatal clinic	Cross sectional , 2 years	831 Pregnant women	5.3% IgG, IgM positive in 4.5% of IgG positive
Lopes et al [39]	Brazil, antenatal clinic	Cross sectional, 7 months	492 Pregnant women	49.2% IgG, IgM 1.2% of IgG positive
Varella et al [40]	Brazil, Hospital	Cross-sectional, 7 years	41112 Pregnant women	0.48% seroprevalence
Khurana et al [41]	India, antenatal clinic	Cross sectional, No information	300 Pregnant women	15.3% IgG, 3% IgM
Vaz et al [42]	Brazil, No information	Cross-sectional, 15 months	20389 Pregnant women	53.3% IgG, 3.26% IgM
Alvarado-Esquivel et al [43]	Mexico, Rural	Community based,	439 Pregnant women	8.2% IgG, 2.3% IgM
Sakikawa M et al [44]	Japan, antenatal clinic	All cases screening, 7.5 years	4466 Pregnant women	10.3% seroprevalence ,0.25% primary infection
Maggi et al [45]	Albania, General outpatient centre	Screening, 6 months	498 Pregnant women	48.6% IgG, IgM 1.3% of IgG positive
Sen MR et al [46]	India, Hospital	Descriptive case control, 2 years	380 pregnant women	19.4% IgM
Sarkar et al [47]	India, antenatal clinic	Descriptive case control, 10 months	105 Pregnant women	49.52% IgG, 21.9% IgM
Barbosa et al [48]	Brazil, Maternity hospital	Cross-sectional, 10 months	190 Pregnant women	66.3% IgG, 0.53% IgM
Liu et al [49]	China, antenatal clinic	Cross-sectional	235 Pregnant women	10.6% IgG, 0% IgM
Ribeiro et al [50]	Brazil, PHC	Cross sectional, 3.5 years	832 Pregnant women	75.1% IgG, 2% IgM
Rosso et al [37]	Colombia, Healthcare facility	Cross-sectional, 5 months	955 Pregnant women	45.8% IgG, 2.8% IgM
Abdi et al [51]	Iran,	Cross-sectional,	553 Pregnant women	44.8% IgG
Mostavi N [52]	Iran, Survey	Cross-sectional, 1 year	217 Child bearing age	47.5% seroprevalence (IgG)
Hajsoleimani [53]	Iran, PHC	Cross-sectional,	500 Pregnant women	37.2% IgG, 1.4% IgM
Ndiaye et al [54]	Senegal, Hospital	Cross-sectional, 1 year	109 Pregnant Women	22% IgG, 3% IgM
Spalding et al [55]	Brazil, PHC	Cross-sectional, 18 months	2128 Pregnant women	71.5% IgG, 3.6% IgM
Castilho-Pelloso et al [56]	Brazil, Public health care	Observational Retrospective, 3 years	290 Pregnant women	1.07% IgM
Sharifi-Mood et al [57]	Iran, Hospital	Cross sectional,	200 Pregnant women	27% serpositive
Ndir et al [58]	Senegal, Health centre	Case control, 6 months	70 Pregnant & 70 Abortion cases	37.1% in pregnant, 40% in abortion
Buchy et al [59]	Vietnam,	Cross-sectional,	300 Pregnant women	11.2% IgG, 0% IgM
Akoijam et al [60]	India, Antenatal clinic	Cross-sectional, 1 year	503 Pregnant women	41.75% seroprevalence
Mahdi et al [61]	Iran, Antenatal clinic	Cross-sectional,	245 Pregnant women	49.2% seroprevalence
Rai et al [62]	Nepal, Antenatal clinic	Cross-sectional, 2 years	345 BOH	55.2% seroprevalence
Chintana et al [63]	Thailand, Antenatal Clinic	Cross-sectional, 6 months	1200 Pregnant women	13.2% IgG
Ashrafunnessa et al [64]	Bangladesh, Antenatal clinic	Cross-sectional	286 Pregnant women	38.5% IgG
Zhang et al [65]	China	Cross-sectional	1250 Pregnant women	7.28% seroprevalence
Sroka et al [66]	Brazil, Hospital	Cohort, 10 weeks	963 Pregnant women	68.6% IgG, 0.5% IgM
Zhang et al [67]	China, antenatal clinic	Cross-sectional	4126 Pregnant women	3.38% IgM
Gonzalez-Morales et al [68]	Cuba, Health centres	Cross-sectional, 2 years	3913 Pregnant women	70.9% seroprevalence
Galvan Ramirez et al [69]	Mexico, Hospital	Case control	350 High risk pregnancy	34.9% IgG, 20.7% IgM
Lelong et al [70]	Madagascar,		599 Pregnant women	83.5% seroprevalence
Sun et al [71]	China, hospital	Cross sectional	1211 Pregnant women	39.14% IgG, 4.21% IgM
Martinez Sanchez et al [72]	Cuba, Community survey	Cross sectional, 6 months	362 Pregnant women	71% seroprevalence
Bari et al [73]	India, antenatal clinic	Cross sectional	302 Pregnant women	46% IgG, 27.7% IgM
Natu et al [74]		Case control	499 BOH	19.44% seroprevalence
Bittencourt [75]	Brazil, Public health services	Cross sectional, 16 months	4022 Pregnant women	59.8% IgG, 1.1% IgM
Shanmugam et al [76]	India, antenatal	Cross sectional	225 Pregnant women	23.6% Seropositive
Reis et al [77]	Brazil, Hospital	Cross sectional, 6 years	10468	61.1% Seroprevalence
Harma et al [78]	Turkey, Prenatal clinic	Cross-sectional,	1149 Pregnant women	60.4% IgG, 3% IgM
Hou et al [79]	China, Hospital	Cross-sectional	347 Pregnant and post partum women	5.5% seroprevalence.
Doehring et al [80]	Tanzania, Hospital	Cross-sectional	849 Pregnant women	35% Seropositive
Soto et al [81]	Venezuela, Hospital	Cross sectional	7969 Pregnant women	53.91% Seroprevalence

Table I. Characteristics and results of studies reporting prevalence of maternal Toxoplasma infection .

Article	Location, setting of study	Type, Duration	Population	Results
Khurana et al [82]	India, Antenatal clinic	Cross-sectional	300 Pregnant women	15.33% IgG, 3% IgM
Ouermi et al [83]	Burkina Faso, Healthcare facility	Cross-sectional 6 months	276 Pregnant women	27.2% IgG, 4.7% IgM
Zemene et al [84]	Ethiopia, Community based	Cross-sectional, 2 months	201 Pregnant women	81.1% IgG, 2.5% IgM
Flatt A & Shetty N [85]	UK, Antenatal clinic	Cohort, 2 years	5000 Pregnant women	17.32 % IgG
Surpam et al [86]	India, Antenatal clinic	Case control,	150 BOH	14.66% IgM
Ayi et al [87]	Ghana, Antenatal clinic	Cross-sectional, 4 months	159 Pregnant women	73.6% IgG, 76.1 IgM
Cvetkovic D et al [88]	Macedonia,	Retrospective, 2 years	235 Pregnant women	20.4% overall seroprevalence
Karabulut A et al [89]	Turkey, Antenatal clinic	Case control, 1 year	1102 Pregnant women	37% IgG, 1.4% IgM
Kumari N et al [1]	Nepal, Hospital	Case control, 4 months	12 BOH	50% seropositive
Nabi SN et al [90]	Bangladesh, Hospital	Case control, 10 months	111 Pregnant women	23.42% IgG, 0.9% IgM
Sadik MS et al [91]	India, Hospital	Case control, 2 years	86 BOH	20.93% IgG, 6.97% IgM
Akyar I [33]	Turkey, Hospital	Cross sectional, 7.5 years	17751 Child bearing age	24.6% IgG, 1.34% IgM
Frischknecht F et al [92]	Switzerland, Hospital	Cross sectional, 1 yr	723 Pregnant women	44.11% serpositive
Inagaki ADM, et al [93]	Brazil, Antenatal clinic	Cross sectional, 1 year	9559 Pregnant women	69.3% IgG, 0.4% IgM
Turbadkar D, et al [3]	India, Antenatal clinic	Case control, 1 year	380 BOH	42.1% IgG, 10.52% IgM
Linguissi LS et al [94]	Burkia Faso,	Cross sectional, 3 years	Pregnant women	20.37% IgG
Chopra S et al [36]	India, Antenatal clinic	Case control, 1 year	200 BOH	42.5% IgM
Koksaldi-Motor et al [95]	Turkey, Hospital	Cross sectional, 1 year	1103 Childbearing age	59.9% IgG
Vilibik-Cavlek T, et al [96]	Croatia, Hospital	Cross sectional, 5 years	Pregnant & non pregnant women	29.1% IgG, 0.25% IgM
Goncalves MA, et al, [97]	Brazil, Hospital	Retrospective, 2 years	574 Pregnant women	62% IgG, 3.4% IgM

Table I. Characteristics and results of studies reporting prevalence of maternal Toxoplasma infection (continued).

Article	Location, setting of study	Type, duration of study	Population	Results
Al-Ani RT [103]	Iraq, Al- Anbar, Hospital	Cross sectional, 6 months	50 Pregnant women	50% IgM
Razzak et al [104]	Iraq, Duhok, Hospital	Case control, 18 months	310 Women with BOH	0.97% IgM
El Mansouri et al [105]	Morocco, Institute National Hygiene	Cross-sectional	2456 Pregnant women	50.6% seroprevalence
Elnahas et al [106]	Sudan, Antenatal clinic	7 months	487 Pregnant women	34.1% IgG, 14.3% IgM
Abdel-Hafez et al [107]	Jordan,	Case control, 1 year	55 Aborted women 46 Pregnant women	58.2% Aborted women, 26.1% Pregnant women
Hammouda et al [108]	Egypt, Hospital	Case control,	100 BOH	65% seroprevalence
Abdulmohaymen N [99]	Iraq (Baghdad), Hospital	Case control, 9 months	119 Aborted women	24.2% IgM recurrent spontaneous abortion 14.7% IgM non recurrent spontaneous abortion. 8.1% IgG recurrent spontaneous abortion 5.9% IgG non recurrent spontaneous abortion
Salih HA [109]	Iraq, Najaf, Hospital	Case control	260 Aborted women	30.76% IgG, 11.92% IgM
Al-Mohammad et al [110]	Saudi Arabia, Maternity Hospital	Cross-sectional, 1 year	554 Pregnant women	51.4% IgG, 8.8 IgM
Jasim et al [100]	Iraq, Waset, Hospital	Case control, 1 year	162 Aborted women	53.9% IgG, 54.8% IgM
Al- Taie et al [101]	Iraq, Mosul, Private laboratory	Case control, 1 year	100 BOH	43% IgM
Al Seadawy MAH [111]	Iraq, Al Muthana, Hospital	Case control, 3 months	81 Aborted women	44.5% IgM
Mousa DA [112]	Libya, Hospital	Case control, 6 months	143 BOH	44.8% IgG, 8.4% IgM
Mahmood SH et al [113]	Iraq, Baghdad, Public Health Central Laboratory	Case control, 8 months	120 Aborted women	39.16% IgG, 17.79% IgM
Aziz & Drueish[114]	Iraq, Baghdad, Hospital	Case control	122 Aborted women	77.1% IgG, 58.1% IgM
Al-Hamdani & Mahdi [115]	Iraq, Basrah, PHC	Case control, 8 months	81 Habitual abortion	18.5% seropositive
Al-Sodany & Saleh [116]	Iraq, Basrah, Hospital	Case control, 8 months	81 Habitual abortion	81.5% seropositive

Table II. Characteristics and results of studies in Arab countries reporting prevalence of maternal Toxoplasmosis infection.

Article	Location, setting of study	Type, duration of study	Population	Results
Majeed AK [117]	Iraq, Baghdad,	Case control, 3 years	260 Aborted women for IgG 259 Aborted women for IgM	21.2% IgG35.1% IgM
Alsaeed et al [118]	Iraq, Al-Hila, Hospital	Case control, 6 months	120 Aborted women	41.66% seropositive
Almishhadani & Aljanabi [119]	Iraq, Al- Anbar, Medical Laboratory	Case control study, 3 years	230 Aborted women	58.3% IgG, 8.3% IgM
Khudair M K [120]	Iraq, Diala, Hospital	Case control, 5 months	50 Aborted women	54% seropositive
Hasan SF [121]	Iraq, Karbala, Immunology Centre	Cross sectional, 3 months	82 Childbearing age women	18.3% IgG
Ali AA [122]	Iraq, Al- Tameem, Hospital	Cross sectional, 1 year	100 Pregnant women 97 BOH	61% Seroprevalence 74.22% BOH non pregnant
Kadir MA et al [123]	Iraq, Kirkuk, Hospital & PHC	Cross sectional, 7 months	319 Pregnant women 121 Aborted women	36.6% seroprevalence LAT, 16.92 IgM ELISA52% LAT, 25.61% IgM ELISA
Alkulabi R [124]	Iraq, Najaf, Hospital	Cross sectional study	137 Pregnant women	60.5% IgG, 43.7% IgM
Yousif JJ et al [125]	Iraq, Najaf, PHC	Cross sectional, 3 months	120 Pregnant women 120 Non pregnant	40% IgG29.2% IgG
Al-khafaji & Mohsen [126]	Iraq, Thi Qar, Hospital	Case control, 10 months	74 Habitual abortion	23% IgG, 31.1% IgM
Alkhashab FMBA, et al [127]	Iraq, Mosul, Hospital	Case control, 16 months	50 Aborted women, 100 Pregnant women	34% IgG, 58% IgM20% IgG, 41% IgM
Alaa Z [128]	Iraq, Tikrit, Hospital	Case control, 15 months	226 BOH	26.1% IgG, 3.1% IgM
Rashid KN [102]	Iraq, Tikrit, Private laboratory	?????	100 Women 15 -45 years age	46% IgG, 32% IgM of IgG positive cases,
Al-Marzoqi AHM, et al [129]	Iraq, Babylon, Hospital	Cross sectional, 6 months	180 Pregnant women	62.2% IgG, 55.5% IgM
Hadi NJ [130]	Iraq, Thi Qar, Hospital	Case control	190 Aborted women	6.84% IgG, 12.63% IgM
Salman YG [131]	Iraq, Kirkuk, Hospital	Case control, 11 months	184 BOH	4.84% Seropositive, 17% IgM
Mossa HAL [132]	Iraq, Baghdad, Hospital	Retrospective, 2 years	54 Pregnant women	94% IgG, 33% IgM
Al- Shimmery MN [133]	Iraq, Diwanya, Hospital	Case control, 5 months	125 Aborted women	45.6% IgG, 29.6% IgM
Bouratbine A, et al [134]	Tunisia, Hospital	Cross sectional	1421 community sample	70% seroprevalence at age of 30 years
Barkat A et al [135]	Morocco, Hospital	Cross sectional, 1 year	368 Pregnant women	44.3% IgG
Bouhamdan SF et al [136]	Lebanon, Hospital & Private laboratories	Retrospective, 1year	3516 Female for IgG 3426 Female for IgM	62.2% IgG6.8% IgM
Tabbara & Saleh [137]	Bahrain, Hospital	Cross-sectional, 46 months	146 Delivering women	15.8% IgG
Ibrahim HM et al [138]	Egypt, Private Clinical Laboratory	Cross sectional,	101 Pregnant women	51.49% seroprevalence
Al-Hindi & Lubbad [139]	Palestine, Hospital	Case control, 6 months	312 Aborted women	17.9% IgG, 12.8% IgM
Abu- Madi MA, et al [35]	Qatar, Hospital	Cross sectional, 3 years	847 Women > 20 yr age	38.2% IgG, 5.1% IgM
Gashout A, et al [140]	Libya, Hospital	Case control, 5 years	692 Aborted women	45% IgG, 17.6% IgM
Al-Qahtani & Hassan [141]	Saudi Arabia, Hospital	Cross sectional, 5 months	75 Adult female	44% seroprevalence
Al-Harithi SA et al [142]	Saudi Arabia, Hospital	Cross sectional, 6 months	197 Pregnant women	29.4% IgG, 5.6% IgM
Elamin MH, et al [143]	Sudan, Hospital	Case control,	94 Pregnant Aborted during study 94 Pregnant with normal outcome	35.1% IgG, 15.2% IgM, 39.4% IgG, 16.2% IgM, Overall 37.2% IgG, 5.9% IgM
Khalil KM, et al [144]	Sudan, Hospital	Case control,	245 Pregnant women 209 Aborted women	35.9% seroprevalence58.3% Seroprevalence
Mohamad K, et al [145]	Sudan, Hospital	Cross sectional,	253 Childbearing age women	73.1% IgG
Al- Nahari AM, et al [146]	Yemen, Central Laboratory	Cross sectional, 2 years	463 Pregnant women	41.9% IgG, 11.88% IgM
Ghazi HO, et al [147]	Saudi Arabia, Hospital	Cross sectional	926 Pregnant women	35.6% IgG
Sellami H, et al [148]	Tunisia, Hospital	Cross sectional, 13 years	40 566 Pregnant women	39.3% seroprevalence, 1.3% acute infection during pregnancy.
Almogren A [149]	Saudi Arabia, Hospital	Retrospective, 1 year	2176 Pregnant women	38% IgG, 0% IgM
Al- Hindi A, et al [150]	Palestine, IVF centre	Retrospective, 6 years	1954 Women with infertility or abortion	7.9% IgM

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

Article	Location, setting of study	Type, duration of study	Population	Results
El-Gozamy BR, et al (151)	Egypt, Hospital	Cross sectional, 17 months		Rural 57.6% seroprevalence, 46.5% Urban
Hussein AH, et al (152)	Egypt, Hospital	Case control,	152 randomly selected individuals, 31 full term pregnant, 38 BOH	IgG- 57.9%, 58.1%, 44.7%IgM – 10.5%, 6.5%, 23.7%
El- Deeb HK, et al (153)	Egypt, Hospital	Cross sectional	323 Pregnant women	67.5% IgG, 2.8% IgM
El- Ridi AM, et al, (154)	Egypt, Hospital	Case control	72 BOH	27.8 % Seropositive
Jumaian NF (98)	Jordan, Antenatal	Cross sectional,17 months	280 Pregnant women	47.1 seropositive,
Mohammed TK (155)	Iraq, Baghdad, Hospital	Cross sectional, 6 months	212 Pregnant women	28.77% IgG, 23.8% IgM

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

Rubella infection of a pregnant woman may have devastating effects on the developing fetus and once congenital infection occurred there is no availability of treatment for the foetus. Thus the mainstay of prevention is the universal immunization of all infants and identification and immunization of women at risk [156].

Fetal infection is acquired hematogenously, and the rate of transmission varies with the gestational age at which maternal infection occurs, with higher frequency in first trimester [160]. Periconceptual maternal infection does not seem to increase the risk of CRS [160]. Maternal immunity, either after vaccination or naturally derived, is generally protective against intrauterine rubella infection [162,163]. However, there have been cases of CRS after maternal reinfection [163]. Therefore, CRS should always be considered in a fetus or neonate with a clinical picture suggestive of congenital infection [162]. It should be noted that no case of CRS has been reported when maternal reinfection occurred after 12 weeks of pregnancy [164].

Fifty- nine studies (Tabl. III) characterizing the epidemiology of maternal rubella were identified mostly for low and middle income countries [1,3,36,89-97,165-211] and 19 studies (Tabl. IV) for Arab countries [35,100,101,129-131,140,150,212-221]. Seven studies were with a retrospective (12.1%) study design and of the total 13 (22.4%) studies deals with women with bad obstetric history (BOH). These studies detected the presence of maternal anti-rubella IgG as a marker of past infection or immunization and mothers who did not possess these antibodies were susceptible to Rubella infection. Maternal IgM was detected in some studies as a marker of recent or current infection, which is associated with an increased risk of vertical transmission. The range of maternal susceptibility to Rubella was 2.1% to 43% in pregnant women [186,189] and 21.1% - 71.04% in women with BOH [91,190]. Higher susceptibility rates were reported [1,91,93,178,209,210] in Nigeria (84.8%), India (71%), Nepal (50%), Brazil (28.4%), Iran (25%), and Sri Lanka (24%).

The higher susceptibility rates for Arab countries excluding Iraq were reported [35,216,220,221] in Morocco (83.4%), Sudan (34.7%), Qatar (25.1%), and Tunisia (20.3%). The lowest susceptibility was reported [217] for Saudi Arabia (6.7%).

In Iraq, reports indicate a high susceptibility rates in Thi Qar (98.05%), Kirkuk (91%), Baghdad (79%), and Waset (45.7%). While the lowest susceptibility rates were reported for Diyala (0%) in women with previous abortion, and 3.9% in pregnant women without history of BOH [215]. The same figures was reported later by another research group in Babylon [213].

Article	Location, setting of study	Type, duration of study	Population	Results
Lin et al, [166]	Taiwan, Hospital	Cross-sectional, 7 yrs	10,089 pregnant women	Seronegativity was 14%
Tamer et al, [167]	Turkey, Antenatal clinic	Cross-sectional,	1972 pregnant women	Anti-rubella IgG 96.1% Anti-rubella IgM 0.2%
Ai & Ee, [168]	Malaysia, Antenatal & hospital	Cross-sectional	500 pregnant women	Seronegativity 11.4%
Majlessi et al, [169]	Iran, PHC	Cross-sectional, 2 yrs	965 Pregnant women	Seronegativity 8.9%
Das et al, [170]	India, hospital	Case control	1115 pregnant BOH	Seropositivity 3.6%
Ocak et al, [171]	Turkey, Antenatal	Retrospective, 23 months	1652 Pregnant women	Anti-rubella IgG 95% Anti-rubella IgM 0.54%
Pehlivan et al, [172]	Turkey, Community based	Cross-sectional, 7 months	824 Women	Anti-rubella IgG 93.8% Anti-rubella IgM 0.6% Negative 5.6%
Tseng et al, [173]	Taiwan, Hospital	Retrospective observational, 4 yrs	5007 pregnant women	13.4% susceptible

Table III. Characteristics and results of studies reporting prevalence of maternal rubella infection.

Article	Location, setting of study	Type, duration of study	Population	Results
Bareto et al, [174]	Mozambique, antenatal	Cross-sectional, 3 months	974 pregnant women	Anti-rubella IgG 95.3%
Corcoran & Hardie, [175]	South Africa, Antenatal clinic	Cross-sectional	1200 serum sample	96.5% immune
Desinor et al, [176]	Haiti, hospital	Cross-sectional, 4 months	495 pregnant women	95.2% seropositive
Weerasekera et al,[177]	Sri Lanka, antenatal	Cross-sectional, 2 yrs	500 pregnant women	82% positive for rubella IgG
Palihawadana et al, [178]	Sri Lanka, antenatal	Cross-sectional,	620 pregnant women	76% seropositive
Ashrafunnessa Khatun, et al [179]	Bangladesh, hospital	Cross-sectional, 11 months	609 pregnant women	14.1% seronegative
Dos Santos et al, [180]	Brazil, antenatal	Cross-sectional, 8 months	1024 pregnant women	77.4% seropositive
Surpam et al [181]	India, Antenatal clinic	Case control,	150 BOH	4.66% IgM
Uyar Y et al [182]	Turkey, Hospital	Cross sectional, 1 year	600 Pregnant women	94.3% IgG, 1.7% IgM
Karabulut A et al [89]	Turkey, Antenatal clinic	Cross sectional, 1 year	1268 Pregnant women	95.1% IgG, 0% IgM
Kumari N et al [1]	Nepal, Hospital	Case control, 4 months	12 BOH	50% Seropositive
Nabi SN et al [90]	Bangladesh, Hospital	Cross sectional, 10 months	111 Pregnant women	81.08% IgG, 6.3% IgM
Sadik MS et al [91]	India, Hospital	Case control, 2 years	86 BOH	29.06% IgG, 4.65% IgM
Fomda BA [183]	Kashmire, Hospital	Case control,	892 Pregnant with BOH1028 Pregnant with previous normal pregnancy	26.12% IgM8.96% IgM
Bamgboye AE et al [184]	Nigeria, Antenatal clinic	Cross sectional,	159 Pregnant women	68.5% IgG
Linguissi LS et al [94]	Burkina Faso,	Cross sectional, 3 years	Pregnant women	77% IgG
Jubaida N, et al [185]	Bangladesh, Outpatient clinic	Cross sections, 6 months	134 Pregnant women	84.33% IgG, 0.75% IgM
Amina MD et al [186]	Nigeria, Antenatal clinic	Cross sectional, 10 months	430 Pregnant women	97.9% IgG
Chopra S et al [36]	India, Antenatal clinic	Case control, 1 year	200 BOH	17.5% IgM
Ogbounnaya EC [187]	Nigeria, Hospital	Cross sectional, 1 year	190 Pregnant women	6.84% IgM
Koksaldi-Motor et al [95]	Turkey, Hospital	Cross sectional, 1 year	1103 women childbearing age	93.6% IgG
Langiano E et al [188]	Italy, Hospital	Cross sectional, 23 months	1242 Child bearing age	77.9% IgG
Onakewhor & Chiwuzie [189]	Nigeria, Hospital	Cross sectional,	270 Pregnant women	57% IgG, 91.3% IgM
Raveendran V et al [190]	India, Hospital	Case control, 1 year	182 BOH	78.9% IgG, 31.58% IgM
Fokunang et al [191]	Cameroon, Hospital	Cross sectional, 4 months	211 Pregnant women	88.6% IgG
Calimeri S et al [192]	Italy, Hospital	Cross sectional, 18 months	500 Pregnant women	85.8% IgG
Corcoran & Hardie [193]	South Africa, Hospital	Cross sectional, 1 year	1200 Pregnant women	95.3% - 98 % IgG
Mora- Garcia GJ et al [194]	Colombia, Hospital	Cross sectional, 1 year	1528 female 10-49 yrs	93% IgG
Uysal A et al [195]	Turkey, Hospital	Cross sectional, 8 years	5959 Pregnant women	97.8% IgG, 0.37% IgM
Combich JJ et al [196]	Kenya, Hospital	Cross sectional, 7 months	470 Pregnant women	92.9% IgG
Kearns MJ et al [197]	Canada, Provincial Public Health Laboratory	Retrospective Observational study, 3.5 years	140 473 Pregnant women	91.2% IgG
Jahromi AS et al [198]	Iran, Hospital	Case control, 8 months	220 Aborted women	91.2% IgG, 10.8% IgM
Ramana BV et al [199]	India, Hospital	Case control,	150 BOH	12.67% IgM
Cheong & Khoo [200]	Malaysia, Hospital	Cross sectional,	500 Pregnant women	11.4% susceptibility
Honarvar B, et al [201]	Iran, Hospital	Cross sectional, 3 months	138 Pregnant women	96% IgG
Nwanegbo et al [202]	USA, Prenatal care clinic	Retrospective Cross sectional, 1 year	642 Pregnant women	6.9% Non rubella immune
Eslamian L [203]	Iran, Hospital	Cross sectional, 10 months	500 Pregnant women	76% IgG
Ozdemir M et al [204]	Turkey, Hospital	Cross sectional, 6 months	249 Pregnant women	95.9% IgG, 0.4% IgM
Adesina OA [205]	Nigeria, Hospital	Cross sectional,	230 Childbearing age women	93.5% IgG
Frischknecht F et al [92]	Switzerland, Hospital	Cross sectional, 1 yr	723 Pregnant women in labor	93.08% seropositive
Ang LW et al [206]	Singapore,	Retrospective	Epidemiological data 1991-2007	84.2% Immune to rubella
Upreti SR et al [207]	Nepal,	Retrospective 2004-2009	2224 Childbearing age	90.8% IgG

Table III. Characteristics and results of studies reporting prevalence of maternal rubella infection (continued).

Article	Location, setting of study	Type, duration of study	Population	Results
Odland JO, et al [208]	Russia, Hospital	Case control, 4 months	182 Pregnant & 127 Aborted women	77.5% versus 59.8% seroprevalence
Goncalves MA, et al, [97]	Brazil, Hospital	Retrospective, 2 years	574 Pregnant women	93.1% IgG, 0.6% IgM
Turbadkar D, et al [3]	India, Antenatal clinic	Case control, 1 year	380 BOH	61.3% IgG, 26.8% IgM
Inagaki ADM, et al [93]	Brazil, Antenatal clinic	Cross sectional, 1 year	9559 Pregnant women	71.6% IgG, 0.1% IgM
Agbede OO, et al [209]	Nigeria, Antenatal clinic	Cross sectional, 3 months	92 Pregnant women	15.2% IgG, 3.3% IgM
Ebadi p, et al [210]	Iran, Hospital	Case control, 3 years	120 Aborted women	75% seropositive
Malarvizhi et al [211]	India, Private hospital	Cross sectional, 2 years	232 Pregnant women	50.9% IgG, 3.4% IgM
Vilibik-Cavlek T, et al [96]	Croatia, Hospital	Cross sectional, 5 years	Pregnant & non pregnant women	94.6% IgG, 0% IgM
Ballal M et al [165]	India, Hospital	Case control,	334 BOH	4.49% IgM

Table III. Characteristics and results of studies reporting prevalence of maternal rubella infection (continued).

Article	Location, setting of study	Type, duration of study	Population	Results
Abdulmohaymen N [99]	Iraq (Baghdad), Hospital	Case control, 9 months	119 Aborted women	4.8% IgM recurrent spontaneous abortion 2.9% IgM non recurrent spontaneous abortion. 6.5% IgG recurrent spontaneous abortion 20.6% IgG non recurrent spontaneous abortion
Jasim et al [100]	Iraq, Waset, Hospital	Case control, 1 year	162 Women with spontaneous abortion	54.3% IgG, 62.3% IgM
Al- Taie et al [101]	Iraq, Mosul, Private laboratory	Case control, 1 year	100 BOH	16% IgM
Hadi NJ [130]	Iraq, Thi Qar, Hospital	Case control	190 Aborted women	1.05% IgG, 4.21% IgM
Salman YG [131]	Iraq, Kirkuk, Hospital	Case control, 11 months	75 BOH	8.88% Seropositive, 6.75% IgM
Abdul-kareem ET, et al [212]	Iraq, Baghdad, Hospital	Case control, 8 months	79 Aborted women	34.2% seropositive
Al-rubaii B, et al [214]	Iraq, Babylon, Hospital	Cross sectional , 14 months	250 Childbearing age women	78.33% Pregnant, 75.71% non- pregnant
Hasan ARS, et al [215]	Iraq, Diyala, PHC	Case control	46 Pregnant - BOH, 52 Pregnant - Non BOH 47 Non pregnant Without Abortion 39 Non pregnant with Abortion	IgG- 76% IgG- 96.1 IgG – 85.1% IgG- 100%
Hammod AM, et al [213]	Iraq, Babylon, Hospital	Case control, 20.5 m0nths	46 Pregnant - BOH, 52 Pregnant - Non BOH 47 Non pregnant Without Abortion 39 Non pregnant with Abortion	IgG- 76% IgG- 96.1 IgG – 85.1% IgG- 100%
Hamdan HZ, et al [216]	Sudan, Hospital	Cross sectional, 2 months	231 Pregnant women	65.3% IgG, 3.4% IgM
Ghazi HO, et al [217]	Saudi Arabia, Hospital	Cross sectional	926 Pregnant women	93.3% IgG
Al-Marzoqi AHM, et al [129]	Iraq, Babylon, Hospital	Cross sectional, 6 months	180 Pregnant women	73.9% IgG, 53.9% IgM
Gashout A, et al [140]	Libya, Hospital	Case control, 5 years	692 Aborted women	89% IgG, 4.3% IgM
Abu- Madi MA, et al [35]	Qatar, Hospital	Cross sectional, 3 years	847 Women > 20 yr age	74.9% IgG
Barah & Chehada [219]	Syria, University Laboratory	Cross sectional, 3 months	90 university female students	85.6% IgG
Caidi H, et al [220]	Morocco, Hospital	Cross sectional, 1 year	967 childbearing age women 15-39 yrs	16.6% IgG
Hannachi N, et al [221]	Tunisia, Hospital	Cross sectional,	404 Pregnant women	79.7% seroprevalence
Al- Hindi A, et al [150]	Palestine, IVF centre	Retrospective, 6 years	1954 Women with infertility or abortion	7% IgM
Nama J et al [218]	Iraq, Najaf, Hospital	Case control, 10 months	300 Aborted women	77% IgG, 4.66% IgM

Table IV. Characteristics and results of studies in Arab countries reporting prevalence of maternal rubella infection.

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