Original Research Article

Cost-effectiveness analysis of serological prenatal screening for pregnant women in King Abdulaziz University Hospital: a single-center retrospective study

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ABSTRACT

Background: Congenital primary infections with Toxoplasma gondii, cytomegalovirus (CMV), Epstein–Bar virus (EBV), rubella, and hepatitis B virus (HBV) are viral infections transmitted transplacentally through the blood to the fetus and can be life-threatening. Therefore, we aimed to determine the prevalence of these infections and assess the cost-effectiveness of blood tests among pregnant women with positive serologies.

Methods: This retrospective review was conducted among pregnant women with positive prenatal screening serology test results between January 2013 to July 2018. A p-value of <0.05 was used to calculate statistical significance.

Results: Overall, 9095 pregnant women delivered in the last 5 years. Of these, 97 had positive prenatal screening serology and were enrolled in our study. Of 97, 61 (62.9%) were Saudis and 36 (37.1%) non-Saudis. The prevalence rates of rubella, CMV, EBV, and HBV were 78.35%, 59.79%, 14.43%, and 5.15%, respectively. Additionally, 44 of 97 women developed undesired antepartum outcomes, whereas 47 had adverse neonatal outcomes. CMV, HBV, and rubella were significantly associated with adverse pregnancy outcomes (P<0.005). During the study period, USD 1460228.27 was spent to screen 9095 pregnant women and USD 15573.68 to diagnose 97 pregnant women with positive serology.

Conclusions: Because infections with toxoplasma, CMV, EBV, rubella, and HBV can cause serious risk to the mother and fetus during pregnancy. Thus, setting new hospital policies regarding early screening for high-risk pregnancies and early detection of these infections during prenatal visits are inevitable to avoid undesired outcomes.

Keywords: Prenatal screening, Congenital primary infections, Fetal health

INTRODUCTION

Congenital primary infections have serious effect on fetal health compared to recurrent infections due to its close association with prenatal morbidity and mortality, leading to critical conditions, such as prematurity, intrauterine growth retardation, abortion, and stillbirth.¹² Toxoplasma gondii (T. gondii), cytomegalovirus (CMV), rubella, and hepatitis B (HBV) are group of infections transmitted transplacentally through the blood to the fetus in the uterus or during delivery,¹ causing severe complications seen at birth, infancy, or remain asymptomatic for years.⁴
Mothers infected with *T. gondii* long before the pregnancy have low risk of transmitting the infection to the fetus compared to mothers infected at the time of conception or during the first trimester causing toxoplasmosis.\(^5\)\(^6\) Infection may be acquired from drinking contaminated water or ingestion of undercooked meat according to a study documented on northern communities with high seroprevalence of 59.8%.\(^7\) Another study conducted in a European multicenter showed that the prevalence of *T. gondii* infection in pregnant women was 30% to 63%, with a close result of 60% in the United States.\(^8\)

Prenatal CMV infection may be transmitted from the mother to the fetus via placenta or during delivery through blood or cervical secretion, with clinical manifestations ranging from asymptomatic (10%–15%) and chances of developing a clinical sequelae at infancy.\(^9\) This infection occurs in 0.15%–2.0% of pregnancies, and transmission is seen in up to 40% of the cases.\(^10\)\(^11\) On contrary, a study documented in Italy showed that the prevalence of anti-CMV IgG antibodies was 68.3% and in Pakistan, a prevalence of 97.55% for CMV IgG and 12.71% for IgM was observed.\(^12\)\(^13\) In Turkey, the prevalence was 97.3% for anti-CMV IgG antibody and 1.0% for IgM.\(^14\)

Rubella is a viral disease transmitted from infected individuals to the mother via inhalation of aerosolized particles.\(^15\) The risk of fetal malformations can increase to 50% if the infection occurs in the first month of gestation, decrease to 25% in the second month, and further decline to 10% in the third month.\(^16\)\(^17\) Higher susceptibility rates to rubella virus infection were observed in Nigeria (84.8%), India (71%), Nepal (50%), and Brazil (28.4%), whereas in the Middle East, higher rates were observed in Morocco (83.4%) and Sudan (34.7%).\(^18\)\(^19\)\(^20\)

The HBV is one of the major causes of liver diseases, such as cirrhosis, chronic hepatitis, and hepatocellular carcinoma.\(^21\) It can be transmitted via infected blood transfusion, contaminated needles, and syringes either sexually or vertically from the mother to the fetus during delivery. A higher prevalence of HBV infection among pregnant women was observed in Congo and Zambia (6.5%) and Hong Kong (10%), and a lower prevalence recorded in the United States (0.14%–0.97%).\(^22\)\(^23\)\(^24\)\(^25\) According to a study conducted in Makkah, Saudi Arabia, the prevalence of antibodies against these infections detected in Saudi pregnant women was 92.1% for CMV, 93.3% for rubella, 35.6% for *T. gondii*, and 1.6% for hepatitis B.\(^26\)\(^27\) The costs associated with the complications of these infections have a high influence on the economy of the hospital.\(^28\) Thus, immunization and early detection, including prenatal screening, is recommended to prevent fetal infections.\(^29\)\(^30\)

Here we aim to determine the benefits and economic impact of screening and immunization of pregnant women.

**METHODS**

Overall, 9095 pregnant women were screened for prenatal serology tests in the past 8 years at the King Abdulaziz University Hospital (KAUH). Of these, 97 had positive prenatal screening test results and delivered their babies in the KAUH. Of the 97 women, 61 (62.9%) were Saudis and 36 (37.1%) non-Saudis. We conducted this retrospective study by reviewing the medical records of these pregnant women who had a prenatal screening test at KAUH, Jeddah, Saudi Arabia, between 2010 and 2018. The hospital had applied prenatal screening for toxoplasmosis, CMV, EBV, hepatitis, and rubella as a standard care for all pregnant women.

First, we collected demographic data and other comorbidities (diabetes, hypertension, hypothyroidism, systemic lupus erythematosus, antiphospholipid syndrome, GERD, and bronchial asthma) of the pregnant women, followed by maternal morbidities like GDM, PROM, placenta previa (low-lying placenta), oligohydramnios, and polyhydramnios. Obstetric information, including number of previous pregnancies, miscarriages, intrauterine fetal demise, stillbirth, neonatal death, preterm birth, modes of delivery, and complications, for each pregnancy was assessed. In addition, the gestational age was determined at each prenatal screening test. Furthermore, we analyzed the fetal data, including birth weight, APGAR Score, neonatal intensive care unit (NICU) admission, and neonatal complications, and evaluated the documented serology screening test, including HBsAb and HBsAg, IgG (CMV), IgG (EBV), and IgG rubella. Other laboratory data such as hemoglobin level, platelet count, WBC count, and ESR were collected. Finally, data entry and statistical analysis were performed by using SPSS software (version 21). Ethical approval was obtained from the institutional review board (IRB) of KAUH.

**RESULTS**

Mean maternal age at the time of delivery was 29 years (15–44), gravidity 3 (1–8), parity 1 (0–5), and abortion 0.85 (0–7). Mean maternal BMI was 28.4 (±SD 5.8). The nurses collected 53 (54%) maternal blood samples in the third trimester, 30 (30.9%) in the second, and 14 (14.4%) in the first trimester. Of these, 45 (46.4%) were anemic, whereas the hemoglobin level was average in the remaining pregnant women. Eighteen (18.6%) of these women had maternal comorbidities, including 9 (9.3%) with hypothyroidism, 3 (3.1%) with GERD, 2 (2.1%) with HTN, 2 (2.1%) with DM type 1, 1 (1%) with DM type 2, 1 (1%) with SLE, 1 (1%) with bronchial asthma, and 1 (1%) with antiphospholipid syndrome. The mean and standard deviation for hemoglobin, platelets, and WBCs were 11.6 (±SD 6.6), 253.9 (±SD 78.8), 9.4 (±SD 4.5) respectively. The only statistically significant correlation was between CMV IgG and platelet count, with a p-value of 0.005. The most predominant maternal infection was rubella and CMV, commonly seen in 47
and 34 Saudi women, respectively, and 29 and 24 non-Saudi women, respectively. Multigravida women were more infected compared to primigravida women; however, the most prominent infected viruses in both multigravida and primigravida women were rubella, CMV, EBV, and hepatitis (Table 1). Likewise, multipara women were more infected compared to nullipara women. Unlike gravidity, CMV was more common compared to rubella in multipara and nullipara women, and the most prominent infected viruses in both multigravida and primigravida women were CMV, rubella, EBV, and hepatitis. The prevalence rate of these viral infections was 78.35% rubella, 59.79% CMV, 14.43% EBV, and 5.15% hepatitis. Twenty-three (23.7%) of those women had maternal morbidity, and the most common maternal morbidity was GDM 16 (16.5%), followed by 7 (7.2%) PROM, 3 (3.1%) low-lying placenta, and 2 (2.1%) mild preeclampsia. Sixteen of those women who have GDM, 11 had rubella infection, 9 with CMV, and 1 with EBV (Table 2). Seven (7.2%) women had fetomaternal complications 4 (4.1%) of them have, and 3 (3.1%) had polyhydramnios. No statistical significant correlation was observed between maternal infection and maternal morbidity. Rubella and CMV IgG were the only viral positive serology we observed in women with fetomaternal complications (Table 3). With respect to fetal outcome, 6 (6.1%) of the fetuses were admitted to NICU, 3 (3.1%) had neonatal hypoglycemia, 14 (14.4%) miscarriages, 3 (3.1%) intrauterine fetal demise, 4 (4.1%) neonatal deaths, and 8 (8.2%) preterm births. Rubella was the highest positive serology found among all fetal outcomes, as shown in Table 4.

Table 1: Demographic and viral serology.

<table>
<thead>
<tr>
<th>Viral serology</th>
<th>Saudis</th>
<th>Non-Saudis</th>
<th>Primigravida</th>
<th>Multigravida</th>
<th>Nullipara</th>
<th>Multipara</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>47</td>
<td>29</td>
<td>13</td>
<td>63</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>34</td>
<td>24</td>
<td>12</td>
<td>46</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>EBV IgG</td>
<td>6</td>
<td>8</td>
<td>2</td>
<td>12</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>HBsAg</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>HBs Ab</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

CMV IgG: cytomegalovirus; EBV IgG: Epstein–Bar virus; HBsAg: hepatitis B surface antigen; HBs Ab: hepatitis B surface antibody.

Table 2: Maternal morbidity and viral serology.

<table>
<thead>
<tr>
<th>Viral serology</th>
<th>GDM</th>
<th>MPE</th>
<th>PROM</th>
<th>Placenta previa</th>
<th>Low-lying placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>11</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>9</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>EBV IgG</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HBsAg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HBs Ab</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>


Table 3: Fetomaternal complications and viral serology.

<table>
<thead>
<tr>
<th>Viral serology</th>
<th>Fetomaternal complications</th>
<th>Oligohydramnios</th>
<th>Polyhydramnios</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>EBV IgG</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HBsAg</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HBs Ab</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

CMV IgG: cytomegalovirus; EBV IgG: Epstein–Bar virus; HBsAg: hepatitis B surface antigen; HBs Ab: hepatitis B surface antibody.

Pertaining to birth weight groups, 13 (13.4%) was classified as low birth weight, 56 (57.7%) normal birth weight, and 1 (1%) high birth weight. APGAR score at 1 min was good for 64 (66%) of the fetuses, while 6 (6.2%) had poor APGAR scores. APGAR score at 5 min was good for 67 (69.1%) of the fetuses, while 3 (3.1%) had poor APGAR scores. A statistical significant correlation was observed between maternal infection with rubella and preterm birth with a p-value of 0.001 and between HBsAg and birth weight with a p-value of 0.000. We found that the most predominant positive serology in women with low birth weight fetus was rubella, although women with high birth weight fetuses were found to either have rubella or HBsAg positive serology.
Furthermore, poor APGAR scores were often found in women with CMV IgG positive serology (Table 5). Finally, the estimated total price of the serological tests for the 9095 women screened between January 2010 and December 2018 was SAR 5,475,190 (USD 1460228.27), and for the 97 positive pregnancies, the cost was SAR 58,394 SAR (USD 15573.68). The cost of a single prenatal screening serological test was SAR 602 (USD 160.55).

<table>
<thead>
<tr>
<th>Viral serology</th>
<th>NICU admission</th>
<th>Neonatal hypoglycemia</th>
<th>Miscarriage</th>
<th>IUFD</th>
<th>Stillbirth</th>
<th>Neutal death</th>
<th>Preterm birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>4</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>EBV IgG</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>HBs Ag</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HBs Ab</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

NICU: neonatal intensive care unit; CMV IgG: cytomegalovirus; EBV IgG: Epstein–Bar virus; HBs Ag: hepatitis B surface antigen; HBs Ab: hepatitis B surface antibody.

Table 4: Fetal outcome and viral serology.

Table 5: Fetal outcome and viral serology.

<table>
<thead>
<tr>
<th>Viral serology</th>
<th>Birth weight</th>
<th>Poor APGAR score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Rubella</td>
<td>9</td>
<td>44</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>8</td>
<td>34</td>
</tr>
<tr>
<td>EBV IgG</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>HBs Ag</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>HBs Ab</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

APGAR: Appearance, pulse, grimace, activity, and respiration; CMV IgG: cytomegalovirus; EBV IgG: Epstein–Bar virus; HBs Ag: hepatitis B surface antigen; HBs Ab: hepatitis B surface antibody.

DISCUSSION

In this study, we determined the prevalence of viral infections among pregnant women admitted to KAUH. The prevalence of rubella infection obtained in this study was 78.35%, a high prevalence rate in comparison to that obtained in the study of Hamdan et al in Sudan, Uysal et al in Turkey and Muliyil et al in India at 97.8%, 65.3%, and 83.4% respectively. The findings of this study suggest the benefit of our routine national vaccination program. 21,31,32

The prevalence of CMV infection obtained in this study was 59.79%, which is lower than that in studies conducted by Mujtaba et al in Pakistan, Uysal et al in Turkey, El Sanousi et al in Yemen, Maingi et al. in Kenya and Shigemi et al in Japan at 97.55%, 98.3%, 91.3%, 77.3%, and 69.1%, respectively. 31-33 However, a study conducted at Makkah, Saudi Arabia, showed that the prevalence of antibodies against CMV infections among Saudi pregnant women was 92.1%, which was significantly higher than our findings. This could be due to a smaller sample size of our study. In this study, the prevalence rate of EBV was 14.43%, a significantly lower rate in comparison to that obtained in the study of Pembrey et al in Bradford where the EBV seroprevalence was 93.6%. 36

The prevalence rate of HBV infection in our study was 5.15%, comparatively higher than those obtained in Pakistan, United States, and Ethiopia at 1.16%, 0.14%–0.97%, and 3.7% respectively. 19,26,31 However, the rates were lower in Congo and Zambia and Hong Kong at 6.5% and 10%, respectively. 24,35 Special consideration should be given to pregnant women with a diagnosis and referral for a specific vaccination, and the essential integration of immunoprophylaxis in all newborns. 36 As reported in other studies, congenital primary infections have serious effect on fetal health compared to recurrent infections due to its close association with prenatal morbidity and mortality, causing severe complications seen at birth, infancy, or remains asymptomatic for years. 1,24 However, in our study we aimed to determine the benefit and economic impact of pregnant women screening and immunization. Furthermore, this study suggested that the most predominant positive serology found in women with low birth weight fetus was rubella at 78.35%, CMV at 59.79%, EBV at 14.43%, and hepatitis at 5.15%, although women with high birth weight fetus were found to have rubella and HBsAg positive serology. Poor APGAR scores were commonly noticed in women with CMV IgG and rubella positive serology. These results were obtained from our tertiary center for all new born babies, and we recommend that all data should be interpreted with caution to prevent further complications, resulting from failure to diagnose or misdiagnosis in women infected with serious viruses to protect the babies from congenital conditions and prevent miscarriages.
On the contrary, we studied the cost-effectiveness of clinical decision based on these prenatal tests and patient outcome. During our study, we found a research conducted on the cost-effectiveness of a computer-assisted Clinical Decision Support System (CDSS) in the identification of maternal complications in Ghana. The outcome of the research showed that computer-assisted CDSS has the potential to identify complications during pregnancy and marginal reduction in labor complications. Implementing computer-assisted CDSS is more costly, but more effective in the detection of pregnancy complications compared to routine maternal care at the intervention health centers. The average cost per pregnancy complication detected during ANC (cost-effectiveness ratio) decreased from USD 17,017.58 (before intervention) to USD 15,207.5 (after intervention). In addition, other research concluded that women receiving free ANC incurred a considerable amount of time and direct costs, which resulted in unsteady use of maternal care. Improving the availability of essential medicines and supplies at health care facilities as well as focusing on efficient utilization of community health workers may reduce these costs. Based on the findings of this study, and follow-up of 97 patients who were counted during the research, take into consideration the budget for conducting the necessary analysis for our patients which cost 160$ for each patient, we established the relationship between positive serologic tests with postnatal fetal complications.

**Limitations of our study**

The sample size was small and heterogeneous with respect to age, weight, and other comorbidities (diabetes, hypertension, hypothyroidism, systemic lupus erythematosus, anti-phospholipid syndrome, GERD, and bronchial asthma), followed by maternal morbidities like GDM, PROM, placenta previa (low-lying placenta), oligohydramnios, and polyhydramnios. Obstetrical information, including the number of previous pregnancies, miscarriages, intrauterine fetal demise, stillbirth, neonatal death, preterm birth, modes of delivery, and complications for each pregnancy was assessed. Furthermore, we assessed the gestational age and other lifestyle-related factors in each prenatal screening test. To improve the validity of the data, a cross-over study of each virus and their effects and outcome on pregnancy is required, and to minimize the cost of prenatal screening serology to determine the types of serology testing needed for investigation in pregnant women.

**CONCLUSION**

For future research, we recommend inclusion of more pregnant women in the study; early pregnancy monitoring to determine the requirement for lab serology and other investigative procedures; monitoring the progress of pregnancy till birth to restrict viruses and the degree of their effects on pregnancy; and minimize unnecessary labor work and costs. Nonetheless, conclusions pertaining to the analysis of prenatal screening serology were limited to rubella and CMV IgG; the only viral positive serology we found in women with fetomaternal complications. Highest positive serology was found in rubella among all fetal outcomes, including women with low birth weight fetus.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**


