

## Rubella infections among Libyan aborted women in Ajdabiya City- Eastern Libya

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### عدوى الحصبة الألمانية بين النساء الليبيات المجهضات في مدينة أجدابيا- شرق ليبيا

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قسم تكنولوجيا المختبرات الطبية ، المعهد العالي للعلوم والتكنولوجيا ، أجدابيا ، ليبيا

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#### Abstract

The rubella virus is a potent teratogen that can lead to spontaneous abortion, stillbirths, and multiple birth defects known as congenital rubella syndrome (CRS) if infection occurs in the first trimester of pregnancy, especially in women without specific immune protection. The incidence of the viral infection is unknown among women who suffer from spontaneous abortion in most developing countries, and there are no specific treatments available to prevent complications. However, many developed countries have specific vaccination programs, and the disease has been eradicated, but it is still prevalent in some countries, especially developing countries. Rubella infection routine adult vaccinations have not yet been implemented in the EPI of Libya, and the prevalence of rubella antibodies among women continues to be reported in some Libyan cities, raising concerns about pregnancy outcomes and fetal health. So, the aim of the current study is to estimate the prevalence of rubella infections among aborted women in the city of Ajdabiya, to improve the introduced vaccination program and prevent abortion. Blood samples were collected from 42 aborted women, serum separated, and tested. The results showed that the total seropositivity of IgM (acute infection) and IgG levels of women were 19% and 71.4%, respectively. 26.2% of the study population were negative for IgM and IgG, suggesting a lack of immunization, either due to a lack of natural exposure or vaccination, which poses a risk to reproductive health. A third booster dose could be recommended to women who are planning to become pregnant at a sufficient time before pregnancy to avoid side effects. Also, a regular third booster dose could be recommended to women after puberty with continuous screening through a rubella survey program to prevent outbreaks of infection and abortion by combined efforts to develop an immunization program in this city and countrywide, and by contacting the relevant authorities to implement these programs.

**Keywords:** AJdabyia, Spontaneous abortion, infections, Rubella, Vaccination.

#### المخلص

فيروس الحصبة الألمانية فيروسٌ مُشوَّهٌ قويٌّ قد يؤدي إلى الإجهاض التلقائي، وولادة جنين ميت، وعبوب خلقية متعددة تُعرف بمتلازمة الحصبة الألمانية الخلقية (CRS) إذا حدثت العدوى في الأشهر الثلاثة الأولى من الحمل، خاصةً لدى النساء اللواتي يفتقرن إلى مناعةٍ مكتسبة. لا يُعرف معدل الإصابة بالفيروس بين

النساء اللواتي يُعانين من الإجهاض التلقائي في معظم الدول النامية، ولا توجد علاجات مُحددة للوقاية من المضاعفات، ولكن العديد من الدول المُتقدمة لديها برامج تطعيم مُحددة. وقد تم القضاء على المرض، ولكنه لا يزال منتشرًا في بعض الدول، وخاصةً الدول النامية. لم تُطبق بعد التطعيمات الروتينية للبالغين ضد عدوى الحصبة الألمانية في برنامج التحصين الوطني في ليبيا، ولا تزال حالات العدوى بالحصبة الألمانية بين النساء تُسجّل في بعض المدن الليبية، مما يثير المخاوف بشأن نتائج الحمل وصحة الجنين. لذا، تهدف هذه الدراسة إلى تقدير معدل انتشار عدوى الحصبة الألمانية بين النساء المُجهضات في مدينة أجدابيا، بهدف تحسين برنامج التطعيم المُطبّق ومنع الإجهاض. تم جمع عينات الدم من 42 امرأة مُجهضة، وتم فصل المصل واختباره. أظهرت النتائج أن مستويات المصل الإيجابية الكلية لـ IgM (العدوى الحادة) و IgG لدى النساء 19% و 71.4% على التوالي. كان 26% من مجتمع الدراسة سلبيين لـ IgM و IgG مما يشير إلى عدم التحصين، إما بسبب عدم التعرض الطبيعي أو عدم تلقى التطعيم، مما يشكل خطرًا على الصحة الإنجابية. يمكن التوصية بالجرعة المعززة الثالثة للنساء اللاتي يخططن للحمل في وقت كافٍ قبل الحمل لتجنب الآثار الجانبية. كما يمكن التوصية بالجرعة المعززة الثالثة المنتظمة للنساء بعد سن البلوغ مع الفحص المستمر لبرنامج مسح الحصبة الألمانية لمنع تفشي العدوى والإجهاض من خلال الجمع بين الجهود لتطوير برنامج التحصين في هذه المدينة وفي جميع أنحاء البلاد ومخاطبة الجهات المختصة لتنفيذ هذه البرامج.

**الكلمات الدالة:** اجدابيا، الإجهاض التلقائي، التطعيم، الحصبة الألمانية، عدوى.

## Introduction

Rubella infection is a viral disease with profound effects, particularly on the immune system and its effects during pregnancy. It is an acute infection influenced by various factors, such as climate, dietary habits, and hygiene practices, and is transmitted through the spread of droplets of nasopharyngeal secretions. It has no animal reservoir. [1] [2][3] Until 1814, it was thought to be a type of measles, then reclassified as a separate disease called German measles, which usually presents as a mild febrile rash with adenopathy in adults and children. [4] A growing body of research demonstrates rubella virus is a potent teratogen that can lead to spontaneous abortion, stillbirths, and multiple birth defects known as congenital rubella syndrome (CRS) if infection occurs in the first trimester of pregnancy, especially in women without specific immune protection. Ninety-one percent of clinically confirmed miscarriage cases had rubella virus isolated, indicating a strong link between maternal infection and adverse pregnancy outcomes. [5] The rubella vaccine does not adversely affect pregnancy outcomes, underscoring the importance of vaccination programs. Therefore, its role in preventing congenital rubella syndrome and miscarriage is crucial.[6] On the other hand, individuals with prior immunity to rubella, whether from vaccination or previous infection, have been shown to have strong resistance to clinical rubella upon exposure, enhancing the effectiveness of vaccination in preventing infection. Antibody levels also affect resistance to reinfection. However, the presence of antibodies provides protection against disease, prevents the virus from forming in the blood, and hinders the replication of the pharyngeal virus.[7] The study of rubella infection and its relationship to the immune response is of utmost importance, particularly with regard to vaccination and reinfection. Studies have demonstrated the effectiveness of immune responses resulting from natural infection compared to vaccination, in addition to identifying population groups at risk of immunodeficiency. This highlights the importance of developing integrated vaccination programs. Cellular immunity persists longer after natural rubella infection than that induced by vaccination, which may explain the higher rates of reinfection among vaccinated individuals [8] Understanding the relationship between rubella and abortion

can help inform effective health policies and vaccination strategies to minimize risks in pregnant populations [9][10][11]. The incidence of the viral infection is unknown among women who suffer from spontaneous abortion. In most centres in developing countries, there are no specific treatments available to prevent complications, but many developed countries have specific vaccination programs. In developing countries, surveillance campaigns for German measles are insufficient [12]. Live attenuated rubella vaccines are among the most successful ever developed, inducing antibodies in more than 95% of recipients and providing protection against infection for 15 years. Globally, only 57% of countries have rubella vaccination programs. [13] Rubella virus infection occurs worldwide and still causes periodic winter or spring epidemics throughout the world. After the launch of the effective rubella vaccine in 1969 and its widespread use by 2015, the Pan American Health Organization of the World Health Organization (WHO) announced that the Americas were the first region in the world to eliminate endemic rubella. As of mid-2016, 45 of the WHO's 194 member states did not offer the rubella vaccine.[14] The introduction of the rubella vaccine is effective but requires continued strengthening of routine immunization services and surveillance systems [15]. The CDC recommends two doses of the measles, mumps, and rubella (MMR) vaccine for children. Teens and adults should be aware of the vaccine, especially those who received the vaccine between 1963 and 1967, as it was an ineffective vaccine. Women of reproductive age and non-pregnant women with no presumptive evidence of immunity should receive at least one dose of the MMR vaccine. [16] The MMR vaccine is part of Libya's broader immunization program, which has faced challenges such as measles outbreaks despite vaccine availability. Understanding the reality of measles and rubella vaccination and routine immunizations is critical to public health strategies in Libya. The Expanded Program on Immunization (EPI) in Libya covers 17 infectious diseases, but routine adult vaccinations, including measles, mumps, and rubella (MMR), have not yet been implemented. [17] The prevalence of rubella antibodies among women in Libya highlights a worrying prevalence of antibodies that may affect pregnancy outcomes and fetal health. Rubella remains a major public health concern in Libya, particularly among women, as evidenced by various studies examining its prevalence and impact on reproductive health. Available data highlight the urgent need to improve vaccination coverage and awareness to reduce the impact of rubella infection in this population. Among women who had abortions in Al Bayda, one study reported a significant 18.9% positive rate for rubella antibodies, indicating a significant presence of rubella among this population [18] There are differences in susceptibility to rubella among women in different Arab countries, with notable rates in Libya indicating the need for targeted interventions to improve health outcomes in this population group [19] Vaccination is recommended for women who are planning to become pregnant [20], whereas preventing miscarriage resulting from rubella is closely linked to vaccination efforts against rubella and congenital rubella syndrome. Studies confirm the importance of rubella vaccination in protecting maternal and fetal health, especially in women of childbearing age, and highlight the benefits of vaccination programs, as well as the risks associated with vaccination during pregnancy. Since the 1990s, there have been intensive global vaccination efforts to improve vaccination programs. If implemented effectively, vaccination programs can significantly reduce the incidence of rubella [21] , the low risk of fetal malformations and adverse effects after vaccination should not prevent vaccinations in women of childbearing age, although vaccination is contraindicated during pregnancy. [22] Most women lack awareness of their rubella status when planning pregnancy, so prevention strategies should include preconception counseling regarding rubella immunity to reduce the risk of congenital rubella syndrome (CRS). [23] Rubella vaccination is a critical

public health intervention aimed at reducing the incidence of congenital rubella syndrome (CRS) and subsequent miscarriages. Ensuring that women, especially of reproductive age, receive effective vaccination significantly reduces the risk of rubella infection during pregnancy. A significant number of women remain vulnerable to rubella infection, highlighting the need for targeted immunization strategies for women of reproductive age to prevent infection that may lead to miscarriage and birth defects. [24][25] More comprehensive and broader rubella immunity screening programs for women should be implemented before and during pregnancy to identify susceptible women and thus reduce the risk of adverse outcomes associated with rubella.[25][26] It is very important to ensure that rubella vaccination is given well before pregnancy to avoid potential complications; careful timing of vaccinations prevents inadvertent exposure to the virus during pregnancy.[27] The studies shed light on various aspects of rubella vaccination and epidemiology, particularly in the context of Libya and the Eastern Mediterranean region, as well as the challenges and progress of rubella vaccination programs, including their prevalence and health impacts. As of 2002, 58% of countries reported using rubella vaccines, with lower rates in developing regions, highlighting the need to strengthen vaccination initiatives in Libya. Improving surveillance and routine immunization services is essential to address immunity gaps against rubella and congenital rubella syndrome in Libya and similar areas. Between 2019 and 2022, the Eastern Mediterranean region maintained an approximate 83% coverage of the first dose of measles and rubella vaccine, indicating stable immunization efforts but also highlighting areas for improvement.[28] Rubella is usually diagnosed serologically. Detection of rubella Immunoglobulin M antibody (IgM) in a serum taken 3–6 days after the onset of the rash is the method of choice for the diagnosis of acute rubella. Methods for the detection of rubella IgM were first developed for the rapid diagnosis of rubella in the late 1960s. These techniques were somewhat cumbersome and were replaced by radioimmunoassay and later by enzyme immunoassay (EIA), which are more rapid and have higher throughput. Detection of rubella-specific IgM remains the method of choice for the diagnosis of both postnatally and congenitally acquired rubella.[29]

### **The objective of study.**

The objective of this study was to evaluate the prevalence of rubella infections among women with spontaneous abortions in Ajdabiya, eastern Libya and related risk factors to inform decisions regarding vaccination program options, and prevention measures.

## **2. Materials and Methods**

### **2.1. Study area description**

This cross-sectional study was conducted in the city of Ajdabiya, which is located in the northeastern part of Libya. Its climate is Mediterranean; rain falls from November to March at most, and December is the month that witnesses the most rainfall in Ajdabiya.[30] The study was conducted in the period between November 2004 and January 2005, on aborted women referred to the only central hospital in the city and its suburbs that received cases requiring hospitalization. Forty-two cases were women who were identified with spontaneous miscarriage by a gynaecologist during the study period.

### **2.2. Sample and data collection and processing**

The study was conducted on 42 women who had aborted and were admitted to the central hospital of the city. The ages of the women ranged between 16 and 48 years. A questionnaire was designed to collect data on demographic characteristics such as age and nationality, as well as the woman's occupation and educational level, whether the patient received any third booster

dose of vaccination against Rubella before pregnancy or at any age. About five mL of venous blood was collected by needle and syringe technique aseptically from each of the aborted women., then it was put in a sterile dry tube. The serum was separated from the whole blood by using a centrifuge for five minutes at 5000 rotations per minute. The serum was kept in tubes free of any preservatives and frozen at -20 degrees Celsius until tested. All serum samples were transferred to room temperature to detect immunoglobulin G (IgG) and immunoglobulin M (IgM) against Rubella , and analysed by using Eco Test RV-IgG/IgM Cassette Test (serum)-based commercial kits and assayed according to the manufacturer's instructions. This test is a lateral flow chromatographic immunoassay for the qualitative detection and differentiation of antibodies (IgG and IgM) to the Rubella virus. For the accuracy of IgG and IgM detection using this kit compared to the ELISA test, the overall concordance rate of results is 99.0% for IgG and 99.9% for IgM. It is suitable for epidemiological investigation. In general, a negative test result indicates that a person is not at risk for a primary infection. A positive IgM-only test result indicates an acute infection, while a positive IgM and IgG test result indicates a late-stage acute infection. A positive IgG-only test result indicates a previous infection or rubella vaccination.

### 2.3. Statistical analysis

Data were processed using SPSS version 25 to assess the prevalence of rubella antibodies (frequencies and percentages), and correlation test was used to examine the relationship between variables and statistical differences within a 95% confidence interval. A p-value <0.05 was considered statistically significant.

## 3. Results

### 3.1. Sociodemographic characteristics of study population

The study population's age ranged from 16 to 48 years, with the highest percentage (23.8%) in the 26-30 age group, followed by the 21-25, 41-45, 36-40, 16-20, and 31-35 age groups with percentages of 21.4%, 16.7%, 14.3%, 14.3%, and 9.5%, respectively. Not all patients had received rubella booster doses before pregnancy or at any age other than the two doses they received in infancy. 13 cases (31%) of the participants were illiterate, 16 cases (38%) received an intermediate education, and 13 cases (31%) received higher education. The total percentage of educated women is 69%. About 73.8% of the participants were unemployed (housewives) and 26.2% were employed (11.9%) of them were female teachers, and 14.3% had medical jobs), as shown in Table 1.

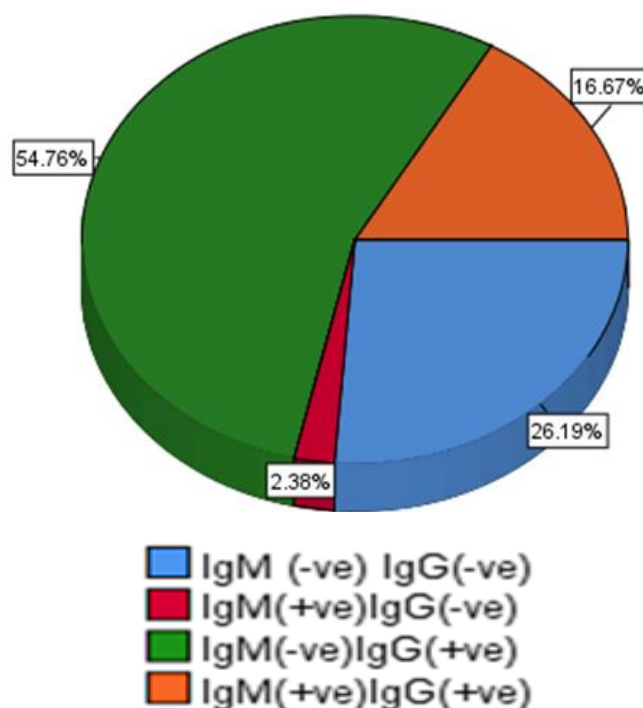
**Table 1. The details of sociodemographic characteristics of the study population.**

		Frequency	Percent
<b>Groups of Age</b>	(16-20)	6	14.3%
	(21-25)	9	21.4%
	(26-30)	10	23.8%
	(31-35)	4	9.5%
	(36-40)	6	14.3%
	(41-45)	7	16.7%
<b>Occupation</b>	Unemployed	31	73.8 %
	Employed	11	26,2%
<b>Education</b>	Uneducated	13	31%
	Educated	29	69%



### 3.2. Seroprevalence of Rubella Infection

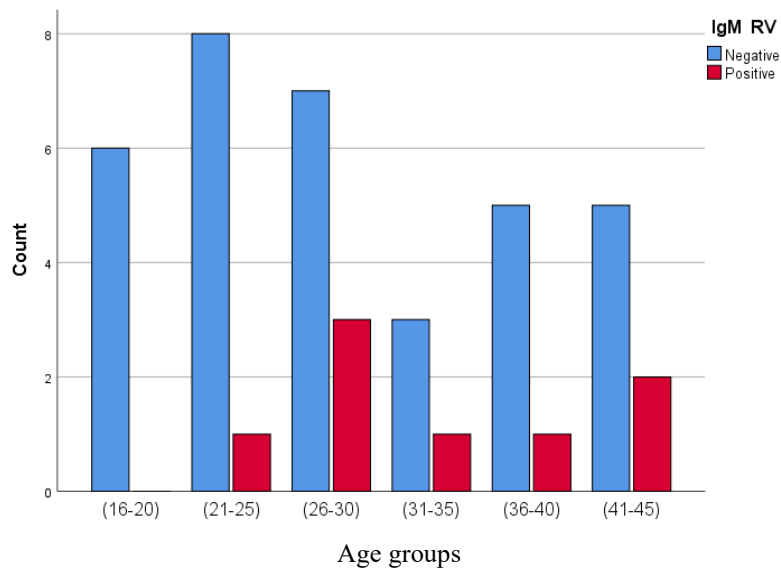
Eight women with spontaneous abortions developed an acute infection; one of whom (IgM positive and IgG negative) had a rate of 2.4%. The other seven cases (IgM positive and IgG positive) had a rate of 16.7%. A previous infection (IgM negative and IgG positive) accounted for 54.8% of the total cases, while 26.2% of the total cases had no infection., both IgM and IgG antibodies were negative. The total IgG level in women who had miscarried was 71.4 % .



**Fig .1.** Seroprevalence of Rubella antibodies among aborted women.

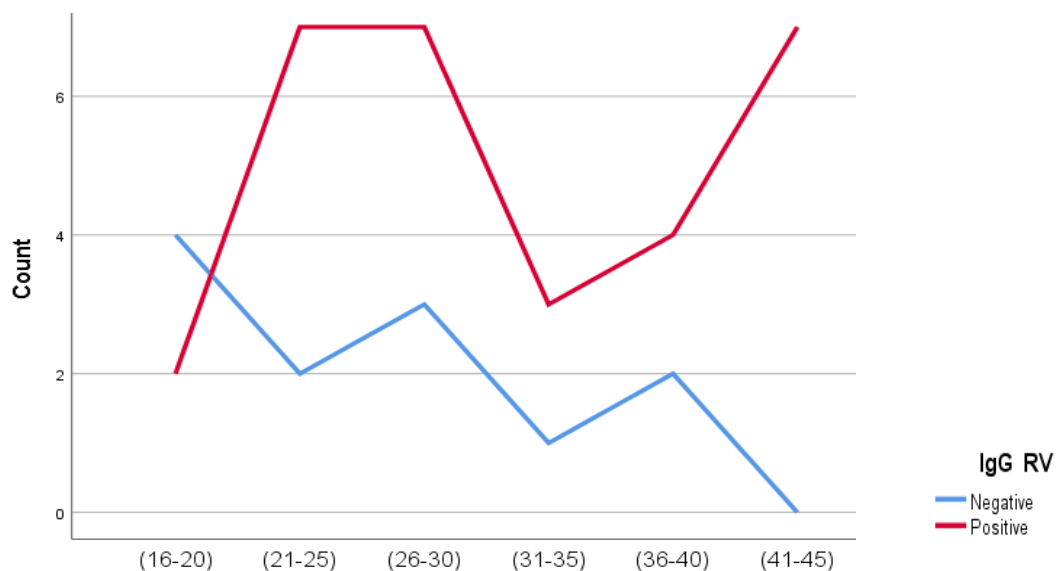
**Table .2.** Seroprevalence of Rubella antibodies among aborted women

		Frequency	Percent
Total IgM	Negative	34	81.0%
	Positive	8	19.0%
Total IgG	Negative	12	28.6%
	Positive	30	71.4%



**Fig .2.** Prevalence of Rubella infection among aborted cases according to age groups.

The relationship between age and acute infection was studied using the correlation test. The result was that there is no significant correlation between them ( $P = 0.971$ ), as for past infection and its relation to age, there is a statistically significant positive weak correlation between age and past infection according to the Pearson correlation test ( $P = 0.014$ ), and the Pearson coefficient was ( $R = 0.353$ ). In the same way, a correlation test to study the relationship between acute infection and education was conducted, and there was no significant relationship ( $P = 0.809$ ), and also between acute infection and employment, and there were no statistically significant relationships ( $P = 0.934$ ). Also, the relationship between past infection and education was studied. There was no statistically significant correlation ( $P = 0.245$ ). Likewise, between past infection and employment, there was no statistically significant correlation ( $P = 0.387$ ).



**Fig. 3 .** Seroprevalence of IgG antibodies among aborted women according to age groups.

#### 4. DISCUSSION

Rubella infection is still endemic disease in all nations that had no a successful immunization. The study was conducted in the city of Ajdabiya, eastern Libya, and it is the first study conducted in this region on rubella. Regional prevalence estimates are of great importance for countries without a national adult screening program, such as Libya. In this study, the rubella virus seroprevalence rate among women with spontaneous abortions in our region was determined to estimate patients' susceptibility to infection and guide vaccination decisions by responsible authorities. The prevalence of this infection among women varies from one geographic region to another. Periodic determination of regional seroprevalence rates is essential for developing vaccination strategies. In this study seropositivity of IgM antibodies to rubella (acute/recent infection) was 19%, and this percentage agrees with a study conducted in the city of Al-Bayda (18.9%). [18]. On the other hand, our findings regarding acute rubella infection were greater than those of another study conducted in western Libya, in the capital, Tripoli (4.3%) [31], and greater than the findings reported from other studies in Egypt (2.5%), [32], Sudan (6.7%) [33], China (0.63%) [34], Turkey 1.2% [35], and Tanzania (3.7%) [36]. suggesting the population study more susceptible to infection, low specific immunity either it does not exposure to past infection or take vaccine and may due to the weather factors that contributed to the transmission of the virus, as the study was conducted in the rainy months in the study area, especially the month of December, which led to an increase in airborne water droplets that contribute to the transmission of the virus through the respiratory route. While the rate of anti-rubella IgG was determined to be 71.4 %, these findings are greater than the rate reported from a study in Al-Bayda (44.2%) [18], and other studies in Egypt (27.3%) [32], and lower than the findings of the study conducted in Tripoli (89%) [31], as well as another study conducted in western Libya in the Al-Alasaba region on women of fertile age (87.6%) [37] and other studies in Sudan [33]. (91.1%) Turkey (93.1%) [35] China (90%) [34]. As for the negative cases who had never been exposed to infection or received vaccination against rubella, they were determined to be 26.2%, these findings are greater than those reported from other studies in Tripoli (6.5%) [31] and Al-Asaba (13.3%) [37] and lower than the findings from Al-Bayda (36.8%) [18]. This difference indicates a variation in immunization, either due to vaccination or previous exposure to infection. The current study indicates that unimmunized women are mostly of childbearing age, as the percentage of immunization increases with age. ( $P=0.007$ , Pearson coefficient = 0.412). This positive correlation indicates that the rate of immunization increases at an average rate with age because the chance of exposure to infection is greater, whereas the older group (41-48 years) was all immune, while the more susceptible group was aged 16 to 30.

On the other hand, there were no significant differences in acute infection between educated and uneducated women, as well as between employed and unemployed women. As for past infection, there were no significant differences in previous infection between educated and uneducated women, as well as between employed and unemployed women. That is, education and employment have no significant effect on rubella infection, suggesting that socio-economic factors do not play a significant role in the outbreak of the disease among women. Whether educated, employed, or otherwise, there are no significant differences between women in terms of lifestyle that affect their health. All of them are unaware of the risk of contracting rubella on their reproductive health and the health of their fetuses. The percentage of IgG antibodies in women who had miscarried was 71.4%, while the percentage of women who lacked antibodies was 26.2%. This indicates that the study sample is not sufficiently immune. There are still



seronegative or unvaccinated women of childbearing age. Seronegative women should be advised to receive the rubella vaccine before pregnancy to prevent miscarriage.

## 5. Conclusions and Recommendations

The study attempted to detect rubella antibodies in women who had miscarried in Ajdabiya city. The results showed that rubella infection remains widespread and poses a risk to pregnancy, reaching 19% of the study population. Furthermore, 26.2% of the study population were not immune to rubella, either due to a lack of natural exposure or vaccination, which poses a risk to reproductive health. It must be recommended to combine efforts to develop an immunization program in this city and nationwide by giving women who are planning to become pregnant a booster vaccine dose at a sufficient time before pregnancy to avoid side effects. Also, a regular third booster dose could be recommended to women after puberty, along with continuous screening through a rubella survey program to prevent outbreaks of infection, abortion, and contacting the relevant authorities to implement these programs. Additionally, raising awareness among women of childbearing age about the need to take the vaccine before pregnancy is essential.

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