DOI: https://doi.org/10.30841/2708-8731.3.2025.331563

Molecular detection of Rubella virus (1E genotype) in clinical sample of pregnant women, and it's related to abortion

T. S. Jassim[1], A. M. M. Al-Fendi[2], S. T. Hashim[3], T. H. Saleh[3], B. A. L. Al-Rubaii[4]

[1]Department of Plant Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq
[2]Department of Biotechnology, Institute of Genetic Engineering and Biotechnology for Postgraduate Studies, Baghdad University, Iraq
[3]Department of Biology, College of Science, Mustansiriyah University, Baghdad, Iraq
[4]Department of Biology, College of Science, University of Baghdad, Iraq

Pregnant women who have rubella may potentially pass the infection on to their unborn offspring. A congenital rubella infection can result in a miscarriage, stillbirth, and congenital rubella syndrome. The only member of the *Togaviridae* family's *Rubivirus* genus, the Rubella virus (RV) is a positive-polarity, single-stranded RNA virus genome surrounded by a lipoprotein envelope with spike-like, hemagglutinin-containing surface projections.
The objective: **to determine the *Rubella virus* (1E genotype) in pregnant woman and its relation to spontaneous miscarriage.**
Materials and methods**. A total of 174 women which visited Al-Elweya Teaching Hospital, Baghdad, Iraq, were screened according to the following criteria: women with a history of spontaneous abortion, women with recurrent pregnancy loss (recurrent miscarriages), and women without pregnancy loss, who were included in the serological control group. The age of the women infected with RV ranged from 17 to 45 years. Two methods were used to detect RV: serological tests (IgM and IgG to RV antigens) and molecular diagnostics (detection of RV strains by reverse transcription polymerase chain reaction).**
Results**. It was found that 55 women had spontaneous abortions. In the age group 25–29 years, a significant increase ($p \leq 0.05$) in cases of suspected RV infection was determined (33.33%) compared to other groups. In the same age group, a significant increased number of women who had a miscarriage (23.64%) was observed compared to other age groups. IgM and IgG levels to RV antigens were significantly increased ($p \leq 0.01$) in 32.95% of patients in the same age group. In this study, 23 women had recurrent miscarriages. Among women 25–29 years old, recurrent miscarriages occurred in 26.09%. Among all examined patients in 10 women fetal malformations were diagnosed.**
Conclusions**. The sensitivity, specificity, and accuracy of the enzyme immunoassay test for RV identification were lower than those using the reverse transcription polymerase chain reaction method for RV detection, and total IgM antibody levels were more prevalent in patients who had experienced miscarriage. In addition, this study demonstrated the high incidence of rubella caused by genotype 1E and its association with miscarriage.**
Keywords: *Rubella virus, genotype 1E, miscarriage, reverse transcription polymerase chain reaction.*

Молекулярна діагностика виявлення вірусу краснухи (генотип 1Е) у клінічних зразках вагітних жінок і його зв'язок із самовільними викиднями

T. S. Jassim, A. M. M. Al-Fendi, S. T. Hashim, T. H. Saleh, B. A. L. Al-Rubaii

Вагітні, хворі на краснуху, потенційно можуть передавати інфекцію своїй майбутній дитині. Інфікування вірусом краснухи може призвести до викидня, мертвонародження та синдрому вродженої краснухи. Єдиний представник роду *Rubivirus* родини *Togaviridae*, вірус краснухи є одноланцюговим РНК-вірусом із позитивною полярністю, оточений ліпопротеїновою оболонкою з шипоподібними поверхневими виступами, що містять гемаглютинін.
Мета дослідження: визначення вірусу краснухи (генотип 1Е) у вагітних і встановлення його значення у виникненні самовільних викиднів.
Матеріали та методи. Обстежено 174 жінки, які спостерігались в Al-Elweya Teaching Hospital (Багдад, Ірак) за трьома критеріями: жінки, які в анамнезі мали самовільний викидень, жінки зі звичним невиношуванням вагітності (звичні викидні) та жінки без втрат вагітності, які входили до групи серологічного контролю. Вік жінок, інфікованих вірусом краснухи, коливався від 17 до 45 років. Для виявлення вірусу краснухи використовували два методи: серологічні тести (IgM та IgG до антигенів вірусу краснухи) та молекулярну діагностику (виявлення штамів вірусу краснухи за допомогою полімеразної ланцюгової реакції зі зворотною транскрипцією).
Результати. Встановлено, що у 55 жінок відбувся самовільний викидень. У віковій групі 25–29 років зафіксовано (33,33%) суттєве збільшення ($p \leq 0,05$) випадків підозр на інфікування вірусом краснухи порівняно з іншими групами. У цій же віковій групі спостерігалося вірогідне збільшення кількості жінок, які перенесли викидень (23,64%), порівняно з іншими віковими групами. Рівні IgM та IgG до антигенів вірусу краснухи були значуще підвищеними ($p \leq 0,01$) у 32,95% пацієнток у тій же віковій групі. У цьому дослідженні 23 жінки мали звичне невиношування вагітності (викидні). Серед жінок 25–29 років звичні викидні відбулись у 26,09%. Серед усіх обстежених у 10 пацієнток виявлено вади плода.

Висновки. Чутливість, специфічність і точність тесту імуноферментного аналізу для ідентифікації вірусу краснухи були нижчими, ніж при використанні методу полімеразної ланцюгової реакції зі зворотною транскрипцією для виявлення вірусу краснухи, а загальний рівень антитіл IgM був більш поширеним у пацієнток, які перенесли викидень. Крім того, це дослідження продемонструвало високу захворюваність на краснуху, спричинену генотипом 1E, та її зв'язок із викиднями.
Ключові слова: *вірус краснухи, генотип 1E, викидень, полімеразна ланцюгова реакція зі зворотною транскрипцією.*

The first clinical diagnosis of German measles was authored by a German chemist in 1740 and scientists have later confirmed it [1]. Rubella is a major global disease that causes severe diarrhea. It is known as rubella (rubella, little red measles, or measles) but is highly contagious [2]. Humans are the only reservoir of the virus [3]. The incubation period of the virus is 2–3 weeks. In the postpartum and placental pathway during pregnancy, transmission occurs by air [4]. Up to 50% of rubella cases are early onset [5]. If not in pregnant women, the infection Rubella is relatively harmless and in most scenarios the infection is mild and bodily [6]. Rubella virus (RV) has a slow replication rate, which is reflected in the long latent duration of the virus from 8 to 12 hours [7]. In terms of viral distribution, RV is unable to infect any cell at any given minute, regardless of virus titer [8, 9]. Furthermore, the proportion of cells infected with RV at any given time depends on the cell type [10]. Rubella is an acute infectious disease caused by the German measles virus. It is usually mild. Rubella is transmitted to children and young adults mostly through the respiratory tract. The infection could be asymptomatic or result in a self-limiting disease with symptoms including lymphadenopathy and low-grade fever [11]. Rubella may also be transmitted to unborn children by infected pregnant mothers. Miscarriage, stillbirth, miscarriage, congenital rubella syndrome (CRS), or asymptomatic infection in a baby are all possible outcomes of a congenital rubella infection. Symptoms of CRS include heart, brain, ocular, and auditory defect [12]. Depending on the gestational age of the fetus at the time of infection, the risk of developing a birth defect ranges from 10 to 90%. Rubella infection occurs early in pregnancy, especially during the first 12 weeks, which increases the risk of more serious outcomes. RV is a positive-polarity, single-stranded RNA virus and the sole member of the *Rubivirus* genus of the *Togaviridae* family. The virus causes a mild childhood disease, but is also a potent teratogenic agent when contracted by a pregnant woman [13]. The genetic characterization has identified 2 clades which differ by 8–10% at the level. Clade 1 is divided into 10 genotypes (1a, 1B, 1C, 1D, 1E, 1F, 1G, 1h, 1i, and 1j), of which 6 are recognized and 4 are provisional (designated by lower case letters). Clade 2 contains 3 genotypes (2A, 2B, and 2C). RV was declared eliminated from the United States in 2005 [14]. This study aimed to determine the *Rubella virus* (1E genotype) and it is related with abortion.

The objective: The present study aimed to determine the *Rubella virus* (1E genotype) and it is related with abortion.

MATERIALS AND METHODS

Collection of specimens: A group of pregnant women who underwent abortion and samples were examined, Total number of samples collected from 174 samples from Al-Elweya Teaching Hospital-Baghdad-Iraq, depending on the following criteria: abortion, recurrent abortion and serological test. A blood sample was collected from pregnant women who underwent abortion by drawing (3–5 ml) the samples were divided into two parts: EDTA tube for gene expression and plain tube for serological test. The serum obtained by centrifuge plain tube at 5,000 rpm for 5 minutes. The serum kept in the freezer until use. The technique detects the total IgM -RUV EIA to measure quantitatively the level of IgM and depend on a Sandwich ELISA in microplates. Virus RNA Extraction kit used for extraction from the blood. As per the guidelines provided by the manufacturer. Total RNA was conversely translated to cDNA utilizing WizScript™ RT FDmix Kit. The procedure was carried out in a reaction volume of 20 µl according to the manufacturer's instructions. Three main steps were applied to conversion by thermo cycler (step 1: 42 °C for 60 min, step 2: 94 °C for 5 min, and 4 °C for 5 min: one step). The Measurement of RNA concentration and purity carried out by Nino drop device (Eppendorf/Bio photometer plus). In most of the samples, RNA preparation gave an A260/A280 ratio between 1.7 and 2.0, which was considered suitable for viral gene identification.

Gene expression:

RV strains were detected by (RT-PCR)/analytic Jena, and GoTaq *qPCR Master Mix (EVA green) was used. Primers design according to the Primer 3 web version (online at website https://primer3.ut.ee). The reaction program of the gene 1E: 95 °C for 5 min/1 cycle, Intervention: 95 °C for 40 sec, Annealing: 57 °C for 40 sec, Extension: 72 °C for 40 sec F: 5-, done. Carry out the scale using 35 cycles and then press 4 °C for 1 cycle. 1E sequence sets F: 5′-TCGTGCAATGTCACCACTGA3′, R: 5′-CTGGTAACCCCGTGACAC-3′.

Statistical analysis:

The Statistical Analysis System – SAS [13] program was used to detect the effect of difference factors in study parameters. For statistical analysis, the Chi-square test was employed. 1. The system for statistical analysis was (38) Used to determine the effect of different factors in Study parameters. Test T. Pressure between means. Value p for all tests it was considered statistically important if $p (< 0.05)$.

RESULTS AND DISCUSSION

The current study showed there were (174) suspected women infected with RV and (55) of them was aborted. The age group (25–29) years recorded (33.33%) in significant increases ($p \leq 0.05$) to other groups. In same group there are a significant increase in aborted women (23.64%) compared to the other age groups. IgM and IgG showed the high significance ($p \leq 0.01$) levels (32.95%) in the same age group. This study obtained (23) recurrent abortion. The age group (25–29) recorded (26.09%) with non-significant differences. From the all suspected women there were (10) women had deformity of fetus, Table 1.

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

Table 1

Relationship between Age groups and distribution of the study's sample in accordance with the ELISA technique's dedication results

	Dedication by ELISA technique					
Age (year)	Suspected women No (%)	Abortion No (%)	Rubella IgG No (%)	Rubella IgM No (%)	Recurrent abortion No (%)	Deformity of fetus No (%)
17–19	14 (8.05)	6 (10.91)	8 (9.90)	8 (9.90)	2 (8.70)	0 (0.00)
20–24	46 (26.44)	12 (21.82)	23 (26.15)	23 (26.15)	5 (21.74)	2 (20.00)
25–29	58 (33.33)	13 (23.64)	29 (32.95)	29 (32.95)	6 (26.09)	3 (30.00)
30–34	26 (14.94)	11 (20.00)	13 (14.77)	13 (14.77)	4 (17.39)	1 (10.00)
35–39	18 (10.34)	7 (12.73)	9 (16.36)	9 (16.36)	3 (13.04)	2 (20.00)
40–45	12 (6.90)	6 (10.91)	6 (6.82)	6 (6.82)	3 (13.04)	2 (20.00)
Total	174	55	88	88	23	10
Chi-Square- χ^2 (p-value)	18.902** (0.0001)	5.681* (0.0419)	15.256** (0.0003)	15.256** (0.0003)	1.988 NS (0.0836)	1.074 NS (0.277)

Notes: * – Non-significant (NS), $p \leq 0.05$; ** – $p \leq 0.01$.

Table 2

Relationship between Age groups and distribution of the study's sample based on the findings of dedication by RT-PC of RUV (1E strain)

	Dedication by RT-PC strain of RUV				
Age (year)	Suspected women No (%)	Abortion No (%)	1E strains No (%)	Recurrent abortion No (%)	Deformity of fetus No (%)
17–19	14 (8.05)	6 (10.91)	9 (9.18)	2 (8.70)	0 (0.00)
20–24	46 (26.44)	12 (21.82)	24 (24.49)	5 (21.74)	2 (20.00)
25–29	58 (33.33)	13 (23.64)	31 (31.63)	6 (26.09)	3 (30.00)
30–34	26 (14.94)	11 (20.00)	13 (13.27)	4 (17.39)	1 (10.00)
35–39	18 (10.34)	7 (12.73)	13 (13.27)	3 (13.04)	2 (20.00)
40–45	12 (6.90)	6 (10.91)	8 (8.16)	3 (13.04)	2 (20.00)
Total	174	55	98	23	10
Chi-Square-χ^2 (p-value)	18.902** (0.0001)	5.681* (0.0419)	16.027** (0.0001)	1.988 NS (0.0836)	1.074 NS (0.277)

Notes: * – $p \leq 0.05$; ** – $p \leq 0.01$.

The qualitative RT-PCR used to compare and confirm the results of serological tests. Specific primers were used to detection the *Rubella virus* (1E genotype). The results showed more accurate (16.027) in qualitative RT-PCR than Elisa technique (15.256), Table 2.

The amplification plots of qRT-PCR showed the ct values of 1E strain ranged between (15–30). The threshold baseline fixed in (4.5), Fig. 1. The EVA green is a fluorescent dye that intercalated with double strand DNA, so this study conducted the melting carve to confirm there is no primer dimer interaction, Fig. 2.

In this study, 11.26% of women were positive for Antibodies against rubella IgG and IgM with poor postpartum history and the results were similar to those performed previously. By comparing ELISA and RT-PCR. Serological tests used to determine the type of virus take a long time (1 to 2 weeks) and this in turn affects immunocompromised patients [15]. Moreover, up to 50% of infections during pregnancy are subclinical, and many of them go unnoticed. As a consequence, the true incidence of deafness associated with rubella (along with other CRS defects) is probably lower than the estimated incidence, but also in the second and third trimesters of pregnancy [16]. Using the ELISA test, the seroprevalence of rubella was found in 580 women, 80 of whom were part of the Amritsar district medical community. Rubella IgG seropositivity was 68.8% overall, but it was 80% in women in the medical field. Among women aged 26 to 35, the highest percentage (77.2%) were seropositive the results agree with the women aged more than 30 years are in risk to have cervical abnormalities more than those less in age [17]. Women from lower socioeconomic classes and those living in metropolitan locations showed noticeably higher rates. While women with a history of unfavorable pregnancy outcomes had a higher rate of seropositivity than women with normal obstetric performance, the difference was not statistically significant ($p > 0.05$). Immunological state and history of prior RV-like infection did not correlate well, according to serological data. Epidemiologists link appearances, novel infections and their spread for a high density of people and animals. The proximity between people and interaction is one of the main factors of urbanization, Urbanisation is increasing lyproblematised as the increasing densities and interconnections are argued to facilitate the rise and proliferation of infectious diseases [18]. But, these

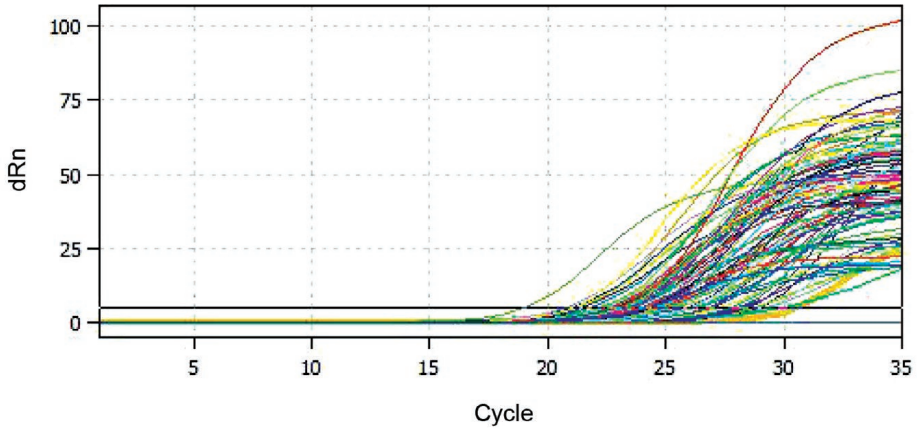

Fig. 1. 1E gene amplification plots by qRT-PCR. Ct values ranged from 17–30 for samples. The picture was shot directly from qTOWER 2.0/2.2, 176, Threshold (4.5) gain Green: 10.0

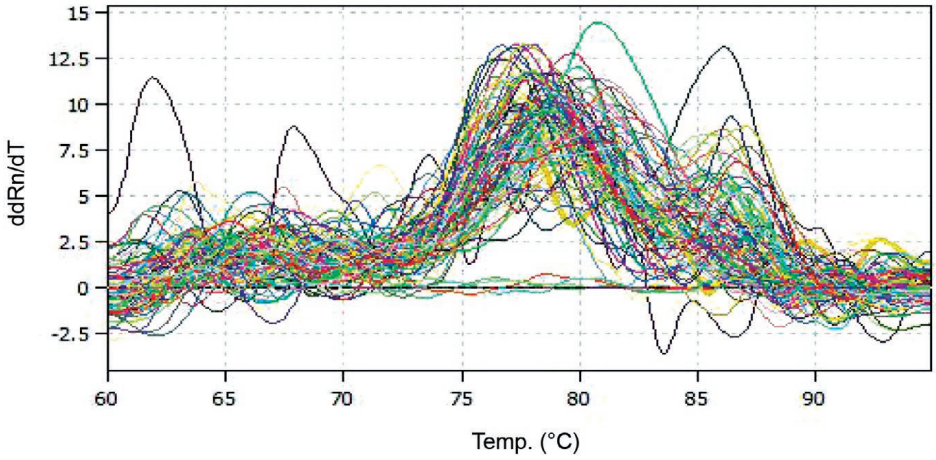

Fig. 2. 1E gene melting curves by RT-PCR Samples included all study groups. Melting temperature ranged from 75 °C to 80 °C, there is no primer dimer in reaction. The photograph was taken directly from qTOWER 2.0/2.2, 176

public health crises, which mainly affected cities, also raised awareness that poor hygiene. The conditions of the poor were also of the rich hence a collective problem [19]. We have noticed during the research that miscarriage may not be the main cause of RV infection. Abortion may be due to a functional or mechanical defect inside the uterus, such as the widening of the vagina, exposure to a specific virus, for example, herpes simplex virus or cytomegalovirus, or infection with a parasite such as *Toxoplasma gondii*, which is transmitted to the uterus in some stages of pregnancy and this is what confirmed [20]. The risk of reproductive failure lies in the first trimester of pregnancy when exposed to infection [21]. During pregnancy due to a weakened immune system, the mother's immunity can reduce the transmission of the virus to the fetus and this was confirmed by [22]. Fetuses of a woman infected during the initial trimester of pregnancy with the virus are 30 to 50%. During pregnancy, it is possible for the virus to be transmitted to the baby through the placenta [23]. As for RV infection during the first trimester of pregnancy, the possibility of miscarriage is low compared to confirmed congenital malformations such as deafness and/or vision loss [24]. In this table, we review the results obtained by searching for the extent of the impact of injury on different age groups and who are the most vulnerable to it. Through the table below, we find that the ages most affected by miscarriage are between 25–29 years, compared to the rest of the ages. There may be reasons that are far from the main reason we are looking for. However, it becomes clear to us that age has nothing to do with infection and abortion, as all ages are exposed to infection with the virus and abortion if the appropriate conditions are available for that to happen. Although the rates of infection vary. Perhaps among those reasons is the lack of vaccination due to social ignorance, the presence of genetically transmitted diseases, or due to a disease of the era such as diabetes, for example, which is associated with pregnancy. The percentages of women with rubella aged 15–30 years in serum increased with age. This confirms the existence of an elevated risk of infection throughout the childbearing years [25]. In other words, the prevalence of rubella antibodies in tropical Africa among women of reproductive age varies with different countries [26]. The rubella affects children in many developing countries of all ages and the different percentages of women did not acquire antibodies when they reached reproductive age [27]. Measles vaccination may be limited. Restricting vaccination to a specific age group increases the age of infection and thus the incidence of CRS [28]. To avoid this, girls are vaccinated before puberty, as well as women

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

before or after pregnancy, and the vaccination of infants should precede or accompany it; Vaccine so that the goal is to register age groups [29]. The results that appeared to us according to the age groups most exposed to infection (35–39 years) were more prevalent by (60%) of patients, and this is consistent with a study that showed results that the age group 21–30 years was the most prevalent among (67.9%) of patients, and showed other studies found that (44.5%) of injuries in Iraq were in the age of 21–30 years, (22.7%) of injuries in Kosovo were between 20–25 years of age, and (81.7%) of injuries in China were aged 29.20 years [30]. The age groups ranged from 31 to 40 years and from 11 to 20 years (16.9%) and (13.07%), respectively, (7.8%) of injuries in Greece were older than 35 years, and in Iraq the study showed that the percentage ranged between 17 and 45 years old, younger women are at risk of contracting primary toxoplasmosis, CMV and rubella during pregnancy [31]. Other researchers in the study revealed severe RV infections in Turkey with an average age of (30.7) years [32]. In Iraq the spread of the disease for age groups between (24–29 years) lies for reasons related to weak immune system or exposure to chronic diseases that make women more. It is generally recommended to apply the PCR approach to assess the detection of infected viruses, as this molecular technique is utilized in various fields of microbiology and medicine, as referenced in sources [33–45].

CONCLUSIONS

The current study's results led to the following conclusions: The sensitivity, specificity, and accuracy of the ELISA test for identifying the RV were lower than those of the RT-PCR method, and total IgM antibodies were more common in patients who experienced an aggravation of abortion. Additionally, this study demonstrated the high incidence of rubella infection caused by the 1E genotype and its association with abortion.

Ethical clearance. This research was ethically approved by the Research Ethical Committees of the Ministry of Environmental and Health and the Ministry of Higher Education and Scientific Research, Iraq, and the approval is numbered (N 4,790 dated 27\12\2023).

Acknowledgement. We are grateful to Dr. and labs. assistants in the surgical pathology department of the teaching laboratories Al-Elweya Teaching Hospital-Baghdad-Iraq.

Funding. Self-funding.

Competing interest. The authors declare that there is no conflict of interest.

Authors' contributions. All authors contributed to the study's conception and design. Material preparation, data collection, laboratory investigations, and analysis. All authors reviewed and commented on previous versions of the manuscript and approved the final version.

Information about the authors

Jassim Tabarak Sabah – College of Biotechnology, Al-Nahrain University, Baghdad, Iraq; tel.: +964 772 652 9385. *E-mail: tabarak.sabah@nahrainuniv.edu.iq*
ORCID: 0000-0003-1263-605X

Al-Fendi Ali MR Murad – Institute of Genetic Engineering and Biotechnology for Postgraduate Studies, Baghdad University, Iraq; tel.: +964 783 421 7105. *E-mail: ali.m@ige.uobaghdad.edu.iq*
ORCID: 0000-0002-9264-3964

Hashim Saba Talab – College of Science, Mustansiriyah University, Baghdad, Iraq; tel.: +964 771 204 6033. *E-mail: dr.sabatalib@uomustansiriyah.edu.iq*
ORCID: 0000-0002-3888-7212

Saleh Tahreer Hadi – College of Science, Mustansiriyah University, Baghdad, Iraq; tel.: +964 771 118 7008. *E-mail: dr.tahreer80@uomustansiriyah.edu.iq*
ORCID: 0000-0001-7945-7609

Al-Rubaii Bahaa Abdullah Laftaah – College of Science, University of Baghdad, Iraq; tel.: +964 770 978 0888. *E-mail: bahaa974@gmail.com*
ORCID: 0000-0003-4546-1815

REFERENCES

1. Xu J, Kong J, Lyu B, Wang X, Qian Q, Zhou X, et al. The Capsid Protein of Rubella Virus Antagonizes RNA Interference in Mammalian Cells. Viruses. 2021;13(2):154. doi: 10.3390/v13020154.
2. Nedeljkovic J, Jovanovic T, Oker-Blom C. Maturation of IgG avidity to individual rubella virus structural proteins. J Clin Virol. 2001;22(1):47-54. doi: 10.1016/s1386-6532(01)00161-5.
3. Al-Mughales J, Al-Rabia MW. Antenatal Screening for Toxoplasmosis and Rubella in Saudi Arabia: Assessing the Need for Screening. J Multidiscip Healthc. 2023;16:3897-905. doi: 10.2147/JMDH.S438895.
4. Mangga HK, Aminu M, Inabo H. Seroprevalence of Rubella Specific IgG Antibody among Pregnant Women Attending Ante-Natal Clinics in Kaduna Metropolis, Nigeria. Nigerian J Basic Appl Sci. 2014;4:63-6.
5. Fappani C, Gori M, Bianchi S, Terraneo M, Bilardi E, Colzani D, et al. Differential diagnosis of fever and rash cases negative for measles and rubella to complement surveillance activities. J Med Virol. 2023;95(10):e29141. doi: 10.1002/jmv.29141.
6. Hyle EP, Rao SR, Bangs AC, Gastañaduy P, Fiebelkorn AP, Hagmann SHF, et al. Clinical Practices for Measles-Mumps-Rubella Vaccination Among US Pediatric International Travelers. JAMA Pediatr. 2020;174(2):e194515. doi: 10.1001/jamapediatrics.2019.4515.
7. Toptygina A, Grebennikov D, Bocharov G. Prediction of Specific Antibody- and Cell-Mediated Responses Using Baseline Immune Status Parameters of Individuals Received Measles-Mumps-Rubella Vaccine. Viruses. 2023;15(2):524. doi: 10.3390/v15020524.
8. Sakuragi S, Liao H, Yajima K, Fujiwara S, Nakamura H. Rubella Virus Triggers Type I Interferon Antiviral Response in Cultured Human Neural Cells: Involvement in the Control of Viral Gene Expression and Infectious Progeny Production. Int J Mol Sci. 2022;23(17):9799. doi: 10.3390/ijms23179799.
9. Akib M, Muhiddin HS, Ichsan AM, Maharani RN. mRNA Expression of PITX3 gene in Congenital Cataract Caused by Rubella Virus Infection. Indian J Foren Med Toxicol. 2020;14(4):690.
10. Bonner KE, Sukerman E, Liko J, Lanzieri TM, Sutton M, DeBess E, et al. Case report: Persistent shedding of a live vaccine-derived rubella virus in a young man with severe combined immunodeficiency and cutaneous granuloma. Front Immunol. 2022;13:1075351. doi: 10.3389/fimmu.2022.1075351.
11. Andriatahina TN, Ravaoarisoa L, Ranivoson A, Rahajamanana V, Randriananahirana Z, Andrianirinarison J, et al. Epidemio-clinical aspects of congenital rubella syndrome in Madagascar. Inter J Res Med Sci. 2020;2:424.
12. Wang S, Liang B, Wang W, Li L, Feng N, Zhao Y, et al. Viral vectored vaccines: design, development, preventive and therapeutic applications in human diseases. Signal Transduction Targeted Ther. 2023;149.
13. Huang Y, Wu R, He J, Xiang Y. Evaluating ChatGPT-4.0's data analytic proficiency in epidemiological studies: A comparative analysis with SAS, SPSS,

and R. J Glob Health. 2024;14:04070. doi: 10.7189/jogh.14.04070.
14. Tushabe P, Bakamutumaho B, Eliku JP, Birungi M, Aine F, Namuwulya P, et al. Rubella virus genotype 2B endemicity and related utility of serum-based molecular characterization in Uganda. BMC Res Notes. 2023;16(1):218. doi: 10.1186/s13104-023-06499-5.
15. Armah NB, Sagoe KW, Nuamah M, Yawson AE, Nartey ET, Essuman VA, et al. Rubella virus IgM and IgG antibodies with avidity in pregnant women and outcomes at a tertiary facility in Ghana. PLoS One. 2022;17(12):e0279733. doi: 10.1371/journal.pone.0279733.
16. Hiebert J, Saboui M, Frost JR, Zubach V, Laverty M, Severini A. Mumps resurgence in a highly vaccinated population: Insights gained from surveillance in Canada, 2002–2020. Vaccine. 2023;41(25):3728-39. doi: 10.1016/j.vaccine.2023.04.078.
17. Masresha B, Shibeshi M, Kaiser R, Luce R, Katsande R, Mihigo R. Congenital Rubella Syndrome in The African Region – Data from Sentinel Surveillance. J Immunol Sci. 2018 Aug 2;Suppl:146-150.
18. Blader IJ, Coleman BI, Chen CT, Gubbels MJ. Lytic Cycle of Toxoplasma gondii: 15 Years Later. Annu Rev Microbiol. 2015;69:463-85. doi: 10.1146/annurev-micro-091014-104100.
19. Alirol E, Getaz L, Stoll B, Chappuis F, Loutan L. Urbanisation and infectious diseases in a globalised world. Lancet Infect Dis. 2011;11(2):131-41. doi: 10.1016/S1473-3099(10)70223-1.
20. Smith NC, Goulart C, Hayward JA, Kupz A, Miller CM, van Dooren GG. Control of human toxoplasmosis. Int J Parasitol. 2021;51(2-3):95-121. doi: 10.1016/j.ijpara.2020.11.001.
21. Sen MR, Shukla BN, Tuhina B. Prevalence of Serum Antibodies to TORCH Infection in and Around Varanasi, Northern India. J Clin Diagn Res. 2012;6(9):1483-5. doi: 10.7860/JCDR/2012/4550.2538.
22. Zhylka NY, Pedachenko NY, Shcherbinska OS, Gruzieva TS, Pakharenko LV. Improvement of the health services for the prevention of hiv transmission from mother to child at the level of primary health care. Wiad Lek. 2022;75(10):2507-13. doi: 10.36740/WLek202210136.
23. Kijlstra A, Jongert E. Control of the risk of human toxoplasmosis transmitted by meat. Int J Parasitol. 2008;38(12):1359-70. doi: 10.1016/j.ijpara.2008.06.002.
24. Voordouw B, Rockx B, Jaenisch T, Fraaij P, Mayaud P, Vossen A, et al. Performance of Zika Assays in the Context of Toxoplasma gondii, Parvovirus B19, Rubella Virus, and Cytomegalovirus (TORCH) Diagnostic Assays. Clin Microbiol Rev. 2019;33(1):e00130-18. doi: 10.1128/CMR.00130-18.
25. Shields BE, Perelygina L, Samimi S, Haun P, Leung T, Abernathy E, et al. Granulomatous Dermatitis Associated With Rubella Virus Infection in an Adult With Immunodeficiency. JAMA Dermatol. 2021;157(7):842-7. doi: 10.1001/jamadermatol.2021.1577.
26. Korchynska O, Baloga O. The experience of pregnancy management by suspicion of fetal intrauterine infection in Ukraine and other countries. Reprod Health Woman. 2021;7-8:28-33. doi: 10.30841/2708-8731.7-8.2021.250828.
27. Sirin MC, Agus N, Yilmaz N, Bayram A, Derici YK, Samlioglu P, et al. Seroprevalence of Toxoplasma gondii, Rubella virus and Cytomegalovirus among pregnant women and the importance of avidity assays. Saudi Med J. 2017;38(7):727-32. doi: 10.15537/smj.2017.7.18182.
28. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. Clin Microbiol Infect. 2002;8(10):634-40. doi: 10.1046/j.1469-0691.2002.00485.x.
29. Cutts FT, Vynnycky E. Modelling the incidence of congenital rubella syndrome in developing countries. Int J Epidemiol. 1999;28(6):1176-84. doi: 10.1093/ije/28.6.1176.
30. Mirambo M, Nyawale H, Michael F, Mamba P, Hassan K, Ali H, et al. The Susceptibility to Rubella Virus Infection among Pregnant Women Attending Antenatal Clinics in Unguja, Zanzibar: The Need to Employ Multiple Strategies to Control Congenital Rubella Syndrome in Tanzania. Inter J Tropical Dis Health. 2023;24:41-8.
31. Perelygina L, Icenogle J, Sullivan KE. Rubella virus-associated chronic inflammation in primary immunodeficiency diseases. Curr Opin Allergy Clin Immunol. 2020;20(6):574-81. doi: 10.1097/ACI.0000000000000694.
32. Bouthry E, Perillaud-Dubois C, Lebraud P, Soutière MP, Grangeot-Keros L, Vauloup-Fellous C. Positive predictive value of seroconversion or positive rubella IgM in diagnosis of maternal rubella infection: Seven-years review of French National Reference Laboratory for Rubella. J Clin Virol. 2021;134:104708. doi: 10.1016/j.jcv.2020.104708.
33. Al-Jumaily RM, AL-Sheakli II, Muhammed HJ, Al-Rubaii BA. Gene expression of Interleukin-10 and Foxp3 as critical biomarkers in rheumatoid arthritis patients. Biomedicine. 2023;43(4):1183-7. doi: 10.51248/.v43i4.3107.
34. Sabah FS, Noori HZ, Abdul-elah BW, Abdullah Laftaah AL, Rubaii B. Identification of methicillin-resistant strains of Staphylococcus aureus isolated from humans and food sources by Use of mecA 1 and mecA 2 genes in Pulsed-field gel electrophoresis (PFGE technique). Revis Bionatura. 2022;7(2):44. doi: 10.21931/RB/2022.07.02.44.
35. Sultan RS, Al Khayali BD, Abdulmajeed GM, Al-Rubaii BA. Exploring small nucleolar RNA host gene 3 as a therapeutic target in breast cancer through metabolic reprogramming. Opera Medica Physiol. 2023;10(4):36-47. doi: 10.24412/2500-2295-2023-4-36-47.
36. Bassi AG, Al-Rubaii BA. Detection of pyocin S and the effects of lactobacillus acidophilus cell-free supernatants on multi-drug resistant Pseudomonas aeruginosa isolated from patients of Baghdad Hospitals. Journal of Communicable Diseases. 2024;56(1):135-44.
37. Husain AG, Alrubaii BA. Molecular detection and expression of virulence factor encoding genes of Pseudomonas aeruginosa isolated from clinical samples. Biomedicine. 2023 Nov 9;43(5):1514-9.
38. Muhsin HY, Al-Humairi RM, Alshareef DQ, Ad'hiah AH. Interleukin-22 is up-regulated in serum of male patients with ankylosing spondylitis. Egypt Rheumatol. 2022;44(4):351-5. doi: 10.1016/j.ejr.2022.07.002.
39. Bresam S, Alhumairi RM, Hade IM, Al-Rubaii BA. Genetic mutation rs972283 of the KLF14 gene and the incidence of gastric cancer. Biomedicine. 2023;43(4):1256-60. doi: 10.51248/.v43i4.3112.
40. Abdulkaliq AH, Hammed ZN, Hamzah SS, Saleh TH, Al-Rubaii BA. Molecular identification of intracellular survival related Brucella melitensis virulence factors. Biomedicine. 2022;42(4):761-5. doi: 10.51248/.v42i4.1642.
41. Saleh TH, Hashim ST, Abdulrazaq Al-Obaidi RA, AL-Rubaii BA. A biological study of chitinase produced by clinical isolates of pseudomonas aeruginosa and detection of chia responsible gene. Inter J Res Pharm Sci. 2020;11(2):1318-30.
42. Ibrahim GJ, Laftaah BA. The Efficiency of Certain Amino Acids in Regulating chABCI Gene Expression in Proteus mirabilis. Iraqi J Sci. 2024;65(9):4983-92. doi: 10.24996/ijs.2024.65.9.15.
43. Hamoode RH, Alkubaisy SA, Sattar DA, Hamzah SS, Saleh TH, Al-Rubaii BA. Detection of anti-testicular antibodies among infertile males using indirect immunofluorescent technique. Biomedicine. 2022;42(5):978-82. doi: 10.51248/.v42i5.1963.
44. Hassoon AH. Evaluating the role of mitochondrial DNA quantification inblastocyst transfers potential. AIP Conf Proc. 2022;2386(1):020046. doi: 10.1063/5.0067093.
45. Abdullah MM, AL-Rubaii BA. Effect of Lactobacillus supernatant on swarming-related gene expression in Proteus mirabilis isolated from urinary tract infections. Ukrainian Journal of Nephrology and Dialysis. 2024;84(4):39-48.

Стаття надійшла до редакції 04.11.2024. – Дата першого рішення 08.11.2024. – Стаття подана до друку 03.12.2024

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)