Diagnosis of Acute Rubella infection during early Pregnancy in Iraq

Basima A. Abdullah *   PhD
Hulia K. Mohammed **   BSc
Hayfaa D. Salman   ***   BSc, Msc

Summary:

Background: To study prevalence and method of diagnosis of acute rubella Infection during early pregnancy in Iraq.

Patients and Methods: Clinical signs and symptoms of acute rubella infection were looked for in (170) pregnant women looked before (12) weeks of gestation .Serial rubella specific IgG and IgM serological testing was done in these (170) women before (12) weeks of pregnancy, after (3) weeks, and again at (18-20) weeks of gestation.

Results: Three woman had clinical signs and symptoms of rubella infection from (26) woman were IgM positive at (9) weeks of pregnancy; (94) were IgG +ve but IgM –ve initially and also on repeat sampling after (3) weeks; while (50) women were nonimmune (IgG and IgM negative) in the first trimester, after (3) weeks and again at (18-20) weeks.

Conclusion(S): Acute rubella infection was diagnosed by serial serologic screening in (26) women in early pregnancy.

Key Words: Rubella, pregnancy**,** bad obstetric history, IgG, IgM.

Introduction:-

The name rubella is derived from Latin meaning "little   red" rubella was initially considered to be a variant of measles or scarlet fever and was called "third disease" it was first described as a separate disease in the German medical literature (1, 2, and 3).Rubella virus is classified as aTogavirus genus Rubivirus. It is most closely related to group A Arboviruses. It is an enveloped +ssRNA virus, with a single antigenic type that does not cross react with other members of the toga virus group, Rubella virus is relatively unstable and is inactivated by lipid solvents, trypsin, formalin, ultraviolet light, low pH, heat, and amantadine (3, 4).

Rubella is a common cause of maculopapular rash illness with fever. The disease has few complications unless it is contracted by a pregnant woman especially in the early weeks of gestation. Rubella infection in pregnancy can lead to miscarriage, stillbirth, or an infant born with congenital rubella infection. The international classification of disease classifies rubella as two diseases rubella (ICD-9 056; ICD-10 B06) and congenital rubella syndrome (ICD-9 771.0; ICD-10 P35.0) (5, 6). The clinical diagnosis of rubella is unreliable, as it is one of many diseases causing maculopapular rash with fever. The incubation period of rubella is 14 days, with a range of 12-23 days. Symptoms are often mild, and up to 50% of infections may be subclinical or in apparent and nearly one half of individuals infected with the virus are asymptomatic.

Dept.of Biology ,College of science, University of Mosul.

**Dept. of Biology, Diabetic Center, University of Almustansriea.*

***College of Medicine, University of Baghdad.*

Rubella-specific IgM is diagnostic of acute infection; IgM usually appears within four days after onset of the rash and can persist up to 4-12 weeks (7, 8). Rubella-specific IgG is a long-term marker of previous rubella infection; IgG begins generally lasts for life, because of the successful immunization program.Women at high risk for contracting rubella in pregnancy are those who are nonimmune to rubella and are exposed to the infection. More than half of the women infected with rubella do not show the classical signs and symptoms of fever and 3 day rash. Hence, serologic tests are used to diagnose acute infection in the pregnant woman. In general, IgM production is the acute reaction, followed by IgG in 1-3 weeks. Diagnosis of acute maternal infection is made by seroconversion (IgG-ve mother becoming IgG +ve), a four fold increase in IgG serial titer over 2-3 weeks, or the demonstration of pathogen specific IgM (8,9,10) .In Iraq, women serologic status is rarely known before pregnancy and there are no studies on serial screening for diagnosis and prevalence of acut rubella infection during pregnancy.This study was therefore, planned to diagnose acute rubella infection during early pregnancy, clinically and by serial immunological testing.

Methods:

This cohort study was carried out from jully 2006 to December 2007in Iraq (Baghdad and Mosul).One hundred siventy BOH pregnant women attending the private clinic in the first trimester of pregnancy were included in the study.

Protocol for diagnosis of acut rubella infection by serology was carried out:

At<12 weeks gestation, positive rubella specific IgG and IgM.

If IgM negative and IgG positive , repeat IgG levels after 3 weeks for evidence of significant (3-4 times) rise in tires , signifying acute infection. At 18-20 Weeks, repeat estimation of IgG and IgM levels in seronegative women.For evidence of seroconversion. Clinically fever, rash, and any other signs and symptoms of acute rubella infection were looked for by the physican and IgG and IgM levels determined for confirmation. Enzyme immunoassay for the detection of IgM and IgG antibodies to rubella virus by Biocheck, Inc .323 vintage park Dr.Foster city, CA 94404. Purified rubella antigen is coated on the surface of microwells dilute patient serum is added to the wells, and the rubella IgM specific antibody, if present, binds to the antigen during incubation .After washing the wells to remove unbound sample, antibody to human IgM conjugated with horseradish peroxides (HRP) is added and incubated at 37^0C for 30 minutes. Unbound conjugate is removed by a subsequent washing step. A solution of TMB reagent is then added to the microwells.The enzyme conjugate catalytic reaction is stopped at specific time.The intensity of the color generated is proportional to the amount of IgM-specific antibody in the sample. The results read by a microwell reader compared in a parallel manner with calibrator and controls. This study was therefore, planned to diagnose acute rubella infection during early pregnancy, clinically and by serial immunological testing (7, 9).

Results and Discussion:

Clinical feature: Three women had clinical evidence of rubella, fever or rash , in the first half of pregnancy were diagnosed by clinicians.In our study ,out of 170 pregnant women with BOH ,A total of 26(15.3%) were positive for IgM and IgG.The maximum number(9.4%)of BOH cases belonged to the age group of (21-30) years and (2.9%) belonged to the age group (10-20)year & (31-40)year (Table -1-) Repeated abortions was seen at age group (21-30) years.22 BOH woman had two abortion (Table -2-) Before 12 weeks-26 women were IgM +ve and IgG+ (Acute infection) at 9weeks (Group 1), 94 women were IgG +ve and IgM –ve (Group 2), and 50 women were with IgG and IgM negative (Group 3).

Table-1-The seroposativity of Rubella infection and age of the patients

Age ((Year))	Seropositive(+) IgG+,IgM+ NO. (%)	Seronegative (-) IgG+,IgM- NO. (%)	Control IgG-,IgM- NO. (%)
	Group 1	Group 2	Group 3
10-20	5 (2.9)	13 (7.7)	24(14.1)
21-30	16 (9.4)	54 (31.8)	7(4.1)
31-40	5 (2.9)	23 (13.5)	16(9.4)
> 41	Zero	4 (2.4)	3(1.8)
Total	26(15.3)	94(55.3)	50(29.4)

Table -2- Rubella infection with different presentation of BOH cases and age

Bad Obstetric History BOH					
Age (Year)	Abortion (1)	Abortion (2)	>(3)	Intraute-rine death	Con-genital Malfor-mation
10-20	7	2	3	4	2
21-30	12	22	10	3	2
31-40	6	6	5	1	\
> 40	(1)	(1)	2	1	\

After 3 weeks, repeat serology showed that none of 94 women who were +ve for IgG in(group 2) showed any rise in IgG titers and more of the 50 women who were IgG and IgM negative in(group 3) showed seroconversion at 18-20 weeks IgG and IgM levels were still negative in the50 sero-negative women of (group 3).These acute infection was documented in only 26 out of the 170 pregnant women with BOH.

Since 10-20 % of women in child bearing age are susceptible to rubella (10) increased incidence of rubella will lead to increase reporting of pregnant women with rubella infection. In present study (15.3%) pregnant women were positive for rubella.IgM as has been reported earlier (12).Prior to the 1970s the incidence of congenital rubella infection was approximately 3-6\10,000 births. Ten years following the introduction of the vaccine the rat dropped six – fold to approximately 1\10,000 birth.the rat of fetal infection varies depending on when in gestation the exposure occurred over 70% cases occur in women more than 15 years of age and in the reproductive age (7). Rubella is world wide distribution and tend to occur in epidemics in nonimmunizied population every 4-9 years in seasonal pattern during winter and spring (9,10). The infection of rubella virus can be disastrous in early gestation. the virus may affect all organs and cause avariety of congenited defects it may lead to fetal death , spontaneous abortion , or premature delivery.The severity of disease depends largely on the time of gestation at witch infection occurs. as many as 85% of infants infected in the first trimester of pregnancy will be found to be affected if followed pregnancy, defect are rare when infection occur after 20th week of gestation. The over all trimester is probably no greater than associated with uncomplicated pregnancies.The nonimmune pregnant women can get infected directly by droplets from the nose and throat on contact with clinical or more often a subclinical case of rubella .Infectivity probably ranges from a week before symptoms to about a week after the rash appears(1,9,10,13).Many rash illnesses can mimic rubella infection, and as many as 50% of rubella infection may be subclinical. The only reliable

evidence of acut rubella infection is a positive viral culture for rubella or detection of rubella virus by polymerase chain reaction, the presence of rubella specific IgM antibody, or demonstration of a significant rise in IgG antibody from paired acut and convalescent phase sera (13, 14, 15).Rubella virus can be isolated from nasal, blood, throat, urine and cerebrospinal fluid specimens from rubella and CRS patients. Virus may be isolated from the pharynx. One week before and until 2 weeks after rash onset. Although isolation of the virus is diagnostic of rubella infection, viral culture are labor intensive, and therefore not done in many laboratories; they are generally not used for routine diagnosis of rubella. Viral isolation is an extremely valuable epidemiologic tool and should be attempted for all suspected cases of rubella or CRS.A state laboratory or CDC should be consulted for details of viral isolation (2, 3, 4, 5).Serology is the most common method of confirming the diagnosis of rubella. Acut rubella infection can be serologically confirmed by a significant rise in rubella antibody titer in acute and convalescent-phase serum specimens or by the presence of serum rubella IgM. Serum should be collected as early as possible (within 7-10 days) after onset of illness, and again 14-21 days (minimum of 7) days later (10, 13, 14, 15).False-positive serum rubella IgM tests have occurred in persons with parvovirus infections, with a positive heterophile test for infections mononucleosis, or with a positive rheumatoid factor.

The serologic tests available for laboratory confirmation of rubella infections vary among laboratories. The state health department can provide guidance on available laboratory services and preferred tests. Enzyme-linked immunosorbent assay (ELISA).ELISA is sensitive, widely available, and relatively easy to perform. It can also be modified to measure IgM antibodies. Most of the diagnostic testing done for rubella antibodies uses some variation of ELISA (16, 17, 18).Hence, it is very important that if rubella screening is done at all, testing should be done serially as in our study protocol, starting in the early first trimester.Abaseline pregnancy screen is most useful for the immunological status which also enables prescription of vaccination (1-3) monthes before planning a pregnancy in seronegative women (9-10).Many cases are referred to us with rubella IgG +ve report and request for prented diagnosis. Thus, Knowledge of the pathogenesis of the infection and interpretation and correct timing of testing in relation to period of gestation is vital for diagnosis of rubella in pregnancy at present,in Iraq ,data is scant and not uniform and ideally screening protocols should be done to study the magnitude of the problem and their cost effectiveness .Attention may be focused by specific laboratory tests on the high risk group of women.PrePregnancy universal vaccination is more practical in developing countries like Iraq.

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