ACTA SCIENTIFIC MEDICAL SCIENCES

Volume 2 Issue 9 December 2018

Mini Review

A Mini Review on Rubella Virus

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Received: October 10, 2018; **Published:** November 02, 2018

Abstract

Rubella is predominantly a mild self - limiting disease when acquired postnatal and only limited to fever and rash the virus is transmitted 7 days after appearance of rash by aerosols generated while coughing or sneezing. Congenital Rubella Syndrome is of the serious complications in pregnant women as it is the leading cause of birth defects and miscarriages in pregnant women. The condition is the most severe when acquired in the first 12 weeks of gestation period. Although the complications are severe, and defects are irreversible, the condition can be easily prevented by proper vaccination. This review aims to address the importance of rubella vaccination in eradication of the highly contagious disease.

Keywords: Rubella Virus; Rubella Syndrome

Introduction

The name rubella is derived from Latin word where rubella stands for "LITTLE RED". Rubella was initially considered as scarlet fever, measles or third disease, later in the year 1814, the disease described as "GERMAN MEASLES" under German medical institute [1,6]. Rubella is a very common childhood illness. The symptoms are generally mild and self - limited to mild fever and rash but develops severe complications in pregnant women. During the first trimester of gestation the disease is responsible for causing complications like defects in the developing foetus [3,6]. It can lead to miscarriages, still birth or birth of the infants with serious congenital defects known as Congenital Rubella Syndrome (CRS). CRS is one of the most important cause of deafness, blindness, congenital heart disease and mental retardation [1].

Rubella virus

Rubella caused by the virus named Rubella virus the only member of Rubi virus of Togaviridae family [1]. The rubella virus is roughly spherical in shape of diameter 40 - 60 nm. The virus carries a positive sense single stranded RNA genome enclosed within icosahedral lipid capsid [4]. The virus consists of three structural proteins, two envelope proteins glycoproteins E1 and E2 and one core protein C protein surrounding the genome within its 3′ terminus. E1 proteins in the form of surface spike of 6 nm long. E1 is considered as immune dominate in humoral response induced against structural proteins and is associated with neutralizing and hemagglutinating determinates. E2 glycoprotein is embedded into the envelope [5].

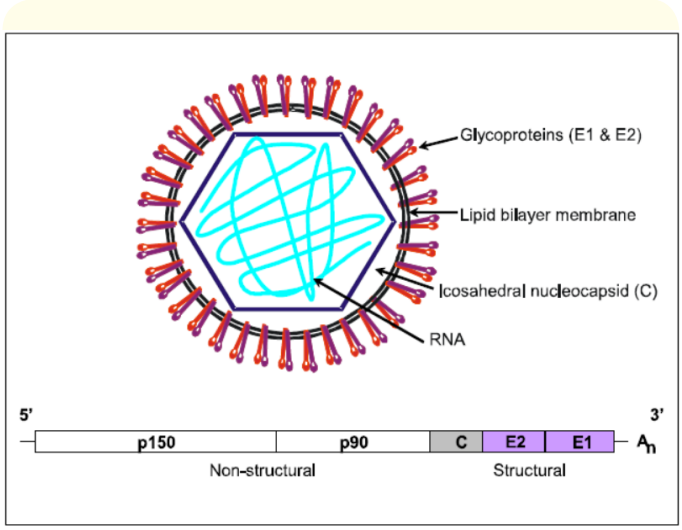

Figure 1: Diagram of rubella virus particle [1].

The genome consists of 9762 nucleotides and encodes for two non - structural polypeptide P90 and P150 within its 5´ terminus [4]. The genome encodes for several non - coding RNA structure, among which rubella virus 3´ cis is acting element that plays an important role in virus replication. The virus is highly temperature liable where the virus gets inactivated within 4 minutes at 70^0C or 2 minutes at 100^0C. The virus readily degrades at low temperatures (-20^0C) and is inactivated by lipids, trypsin, formalin, ultra violet rays and solvents.

Transmission

The disease is contagious from 7 days after appearance of rash. Postnatal rubella spreads by airborne respiratory droplets that result from coughing and sneezing, by direct contact with nasopharyngeal fluid of an infected person or from urine of infants with CRS [11]. Infected individuals may be contagious as early as a week before the appearance of the rubella rash, and for up to a week after it first appears. (It is most contagious at the time the rash first appears.) Children born with CRS may transmit the virus to others for more than a year [1,3,7,8]. Rubella cases typically peak in late winter or early spring.

Clinical manifestation

In non - pregnant conditions, rubella remains mild and self - limited. The incubation period for rubella ranges from 12 to 23 days [9]. The infectious period is from 7 days before to 5 - 7 days after the rash onset [3]. The infection starts from initial appearance of rash on face and then gradually spreads down the neck [8]. Infection occurs due to inhalation of aerosols and infects the upper respiratory tract wherein the virus enters the cell through cell - mediated endocytosis [2]. On day 0, the virus from respiratory tract of the infected person comes into contact with epithelial surface of nasopharynx of the host. On day 3 - 8 the virus localized in the epithelium tissue where it replicates and start shielding into the lymph nodes by day 20. This results into Viremia where the infection spread into different organs through blood stream from the lymph nodes. This is the state where maximum shedding of virus occurs.

Symptoms

In case of children:

- Rash beginning on the face, which spreads to the rest of the body.
- Low fever of less than 38.3°C (101°F).
- Posterior cervical lymphadenopathy.

In older children and adults' additional symptoms may be present including.

- Swollen glands
- Coryza (cold like symptoms): Coryza in rubella may convert to pneumonia, either direct viral pneumonia or secondary bacterial pneumonia, and bronchitis.
- Aching joints (especially in young women).

Serious problems can occur including the following:

- Brain infections
- Bleeding problems.
- Birth Defects (Congenital)
- Inflammation of lymph nodes
- Cataracts
- Maculopapular rashes.
- Heart Defects
- Hearing Loss [1,2,3].

Mostly rubella occurs in children and young adults. Mostly rubella infection remains subclinical therefore detections are confirmed through laboratory confirmation only [4,5].

Immune response

Both humoral and cell mediated immune response counter rubella virus infection. IgM and IgG antibodies are detected during the infection where IgM antibodies are detectable for 2 months. After 2 months IgM antibodies disappears whereas IgG antibodies persist. Cell mediate immune response beings after 1 week of humoral immune response and persists lifelong [1,4].

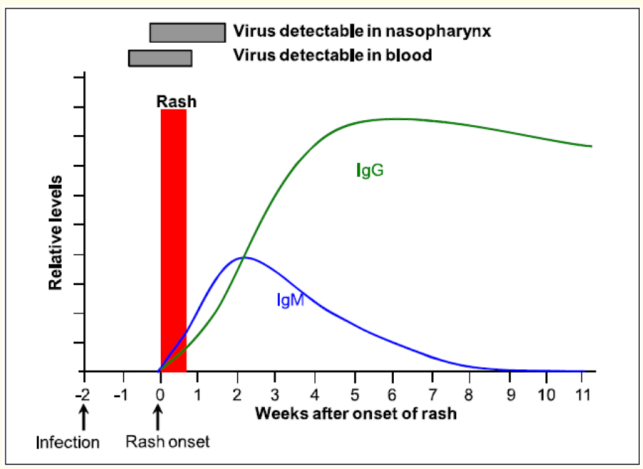

Figure 2

Complications

Postnatally acquired rubella infection is associated with complication rather than joint symptoms [2]. Complications like CRS, Arthralgia, encephalopathy, Guillian barre syndrome, Transient inflammation, Thrombocytopenia and Haemolytic anaemia are associated with Rubella as listed in table 1.

Sr. no.	Complications	Cases	References
1	Congenital Rubella Syndrome	90% of infants born to mothers infected in the first trimester	[15]
2	Arthralgia (Fingers, wrists, join and knees)	70 percent of adult females	[5]
3	Post infection encephalopathy	1 in 5,000 cases of rubella infection	[17]
4	Guillian barre disease	Rare	[16]
6	Thrombocytopenia	1 in 3500 cases	[18]
7	Haemolytic anaemia	Rare	[2,5,8,9,11]

Table 1: Complications of rubella.

Congenital rubella syndrome

The most severe condition caused by rubella is congenital rubella syndrome (CRS). Up to 90% of infants born to mothers infected in the first trimester will develop the physical anomalies referred to as congenital rubella syndrome. The symptoms of CRS include vision loss due to cataract, congenital heart disease, hearing loss, bleeding underneath the skin, enlargement of spleen, behavioural disorder, mental retardation, miscarriage, growth retardation, bone disease purple skin lesions and lymph nodes and developmental delay [1,5,9,11]. Some effects may not be apparent at birth. Reinfection has been demonstrated on rare occasions, but only very rarely has resulted in CRS. The severity of the CRS defects depends upon the gestational age, the most dangerous period is the first 12 weeks of gestation. For CRS reduction alone, adolescent and adult females should be vaccinated through either routi services or supplementary immunization activities (SIAs).

Currently, epidemiological studies assessing the prevalence of Congenital Rubella syndrome are lacking. Serosurveys in India have reported 6 - 47% of school girls aging 11 - 18 are susceptible to Rubella Infection [19-21]. Effective immunization programmes can control rubella infection leading to reduction in serious complications like CRS.

Diagnosis

Presence of rubella virus or infection are detected by the following laboratory tests:

Rubella IgM test

Presences of IgM antibodies are in the test. Commercially IgM test specimen are available. The specimen should be drawn at least three days after onset of rash and within six weeks of rash onset (sample required is 2 ml of serum) [11].

Rubella total antibody paired - titter test

Paired total antibody testing can be helpful when rubella IgM results are not interpretable. Acute serum should be collected as soon as possible after rash onset; convalescent serum should be collected 14 days later [11].

Polymer chain reactions

The test involves the detection of positively sense RNA genome in the test sample.

Vaccines

MMR II (Measles, Mumps and Rubella virus vaccine live) is the vaccine which is recommended to boost immune system and prevent serious, life threatening diseases. MMR II consist of live, attenuate strains Measles, Mumps and Rubella virus. It is a sterile lyophilized preparation of ATTENUVAX (Measles virus), MUMPSVAX (Mumps virus), MERUVAX (Rubella virus) [10].

MMRV (Measles, Mumps, Rubella and Varicella (2005) is another vaccine given for rubella [9]. Centre for disease control and prevention, American academy of paediatrics, American academy of family physicians all have recommended MMR vaccine for the treatment of Rubella infection [6].

Doses

Children should get two doses of MMR vaccines

- **First dose:** The recommended range is 12 - 15 months of age.
- **Second dose:** the recommended range is 4 - 5 years of age.

However, the second dose can be given earlier after the first dose with recommended interval of 28 days [6,7]. The vaccine is injected subcutaneously into the skin [10].

The first dose is to reduce the complication of CRS and second dose is to prevent the transmission of rubella virus [12-15].

Side effects

The most common side effects of MMR vaccine are fever in 15% of the cases, in 5% cases mild rashes are observed, swelling of glands in cheeks and neck, low platelets count, Pain in fingers, knees and wrists. The rare problems that are observed are allergic reaction, deafness, and brain damage This symptom occurs usually after 12 days of vaccination [1,6,7].

Conclusion

After eradication of smallpox and polio in many countries, Rubella is a perfect candidature for eradication. Rubella vaccine being safe and highly effective, when administered properly has shown no transmission of rubella in US since 2009. Even in the presence of such highly potent vaccine there are cases of Rubella in India. Proper administration of the vaccine will reduce CRS and eventually prevent transmission of rubella virus. Proper awareness and vaccination programmes are needed to eradicate Rubella. Although rubella vaccine has been available since 1970s, it is still underused. New strategy, needs to focus on increasing and strengthening routine immunisation which encourages better planned, more data - driven campaigns.

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